目　次

I. 本プロジェクトの意義と研究経過

1．本プロジェクトの背景と目的

「動く」ことは，人間存在の根幹をなすものである．しかし，現代社会において，特に先進国と言われている国々では，日常的な身体活動の機会が減少し，それが人々の心身に重大な影響を与えていることが指摘されている．我が国においても，健康阻害が問題となっており，生活習慣病予防のための運動の推進が国の施策にも取り上げられているところである．このような危機的状態は成人のみならず，子ども達にも当てはまり，遊びや運動の減少が彼らの心身の健全な発達を阻害していると危惧されている．すなわち，すべての人々にとって，意図的な運動の実施が極めて重要になっているのが現状である．

このような背景を踏まえて，身体運動の推進が提唱され，国レベルの運動目標値が設定されているが，すべてを網羅した明確な指針が示されているわけではない．その理由は，「動く」ことに対する身体適応のメカニズムとそれを根拠とした至適運動について，必ずしも十分な科学的エビデンスが蓄積されているとは言えないからである．なかでも，生命の安全性に直結し，かつ多数の因子が複雑に作用する運動時の循環調節機序解明は，すべての人々の運動を推進する前提として必要不可欠なことである．運動は心身に特異的な影響を与えるものであり，対象者の特性に合わせた適切な運動でなければ効果がないだけでなく安全性も確保されないからである．

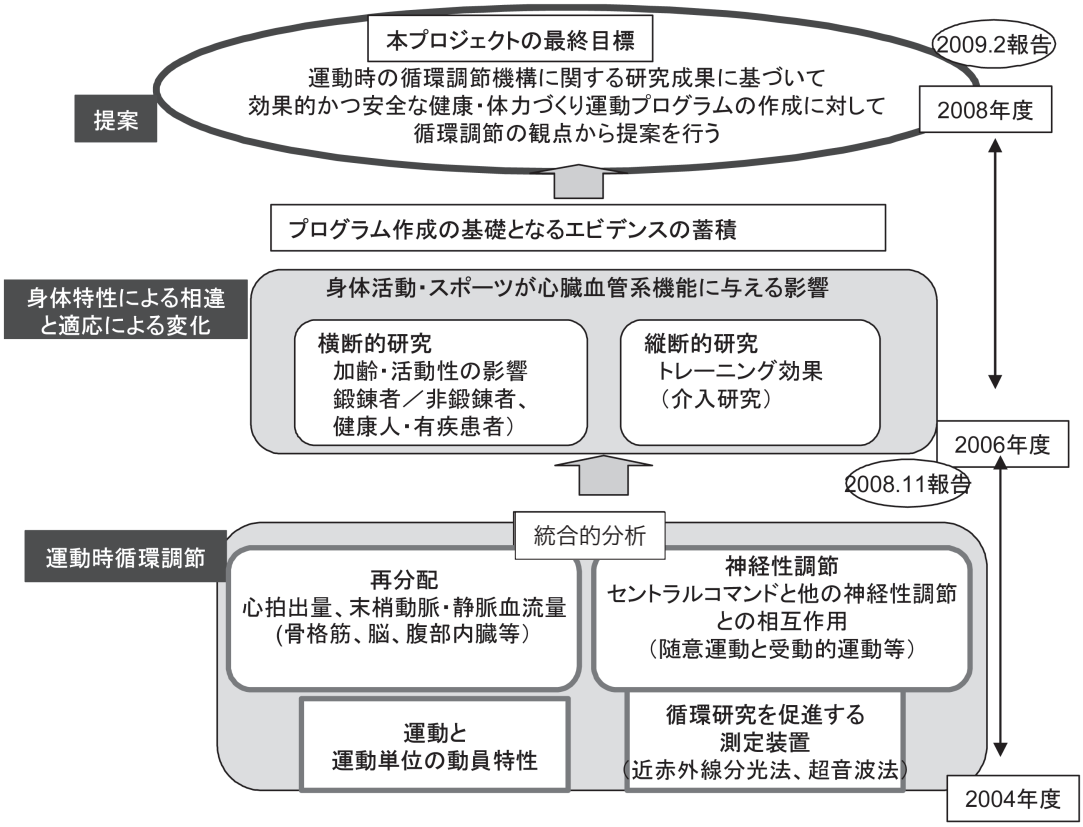
運動に対する循環系の適応は極めて巧妙にできている．複雑な仕組みになっていることは，1つの系が破綻しても他の系が補償し，生命維持に必要な循環システムを破綻させないような安全弁が用意されているということでもある．安静時につくられた循環システムの安定性は，運動という外乱によって一旦はその整合性が破られる．そこで，運動開始と同時に，運動を遂行するに必要な循環調節が行われ，同時に生命を維持するための循環調節という2つの方向の再調整がなされる．効果的な運動と同時に運動の安全性を考えなければならない所以である．しかし，運動に対する循環系調整の機序はまだ全貌が明らかにされていない．

ヒトの運動時における循環調節機構に関する最近の研究は，微小電極交感神経図法による神経性調節，超音波法による心拍出量と身体各部位への動脈血流分配，近赤外線分光法を用いた活動筋代謝と筋循環，生化学的手法による血管内皮細胞由来の物質（NO，エンドセリン）の分泌とその調節機構などの課題に焦点があてられてきた．しかし，神経性調節のうち，セントラルコマンドの作用機序に関しては長い研究史があるにもかかわらず，運動時の機序については着手されたばかりである．また，血流分配に関しても，骨格筋や皮膚への循環に関しては多くの知見があるものの，脳や腹部内臓への血流分配とその調節については，十分な解明がなされていない．さらに，血液の“循環”を可能にする静脈還流に関する研究成果は極めて少ない．また，それらの成果も個別的であり，相互に補完し合って整合性を維持しようとする循環調節機序の統合的解明にはなっていなかった．運動推進を考えるにあたってさらに重要な問題点は，これらの循環調節機序が，運動様式，使用筋群（局所的・全身的，使用部位），運動強度・運動頻度・運動持続時間の様な運動特性別に明らかにされてこなかったことである．

このような研究の現状を踏まえて，本プロジェクトでは，活動性だけでなく，生命の安全性に直結する運動時の循環調節に関する科学的エビデンスを，運動特性と関連させて蓄積し，それらを統合して得られたエビデンスを基盤とし，健康・体力づくりのための運動プログラムの構築に向けた提案を行うことを目指している．本プロジェクトで得た新知見は，学術的な貢献をすると同時に，国の重要かつ喫緊の課題になっている国民の運動推進に対しても多大な貢献ができると考えている．

2．本プロジェクトの課題への取り組み方

課題解明に向けた本プロジェクトでの取り組み方は図I.1-1に示した通りである．5年間のプロジェクト研究期間の最初の3年間（2004～2006年度）は，運動時の循環調節に関する基礎的知見を集積し，それを統合して循環調節の解明に貢献することを目指した．そのために，運動時の生体応答研究の基盤となる運動単位の動員特性を明らかにするとともに，人を対象とした循環研究に必要な非侵襲的計測法（近赤外線分光法，超音波法など）の研究への適切な



図I.1-1　研究の課題の取り組み方

適用等を進めながら，1）運動時の血流再分配と2）循環系に対するセントラルコマンドを中心とした神経性調節に焦点を当てた研究が遂行された．中心的課題である「運動時の血流分配に関する研究」と「運動時のセントラルコマンドが循環に与える影響に関する研究」はプロジェクトメンバー全員が参加する共同研究として行われた．さらに，特化したテーマについては，個別に研究を実施し，プロジェクト全体で討議して統合するという研究体制をつくった．これらに関する成果は，2006年11月の中間報告会で公表された．さらに，それらを統合した運動時の循環調節の機序については，2008年11月の国際シンポジウムで報告し，この分野で精力的に新知見を発表している海外の招待講演者や国内の研究者との議論を展開して，本プロジェクトの学術的成果を確認した．

プロジェクト最後の2年間（2007～2008年度）では，それまでの成果を様々な身体特性を持つ対象者で検証することと，運動の継続が循環調節に与える影響を横断的，縦断的に明らかにすることを中心課題とした．そして，それまでに得られたすべての知見をもとに，スポーツによる健康・体力づくりプログラムの構築に対して，循環調整の観点から提案を策定した．最終報告会（2009年2月）ではこれまでの成果とそれに基づく提案を，研究者だけでなく，一般の人々にも公開した．

以上のように，本テーマに関して学術的な貢献をすること，それをもとに，運動プログラム構築にむけた提案を行い，社会のニーズに応えることが本プロジェクトの学術面でのねらいであった．

3. 運動時循環調整研究の拠点整備

文部科学省学術フロンティア推進事業は，私立大学の大学院，研究所の中から，研究実績をあげ，将来の研究発展が期待される卓越した研究組織を選定し，内外の研究機関との共同研究に必要な研究施設，研究装置・設備の整備に対し，重点的かつ総合的支援を行うものとされている．したがって，本プロジェクトでは課題とする研究を推進して学術的貢献をすると同時に，運動時の循環調節研究の拠点となるようにハード・ソフト両面の研究環境の整備を行う

こともねらいの一つである．

本プロジェクトでは，初年度に脳の酸素動態を非侵襲的・連続的に計測する近赤外線分光法や解像度が高く，画像分析が自動化した超音波測定装置を購入した．2年目以降は既存の計測装置や運動負荷装置をシステム化して，ハード・ソフト面の整備が一段と進んだ．

多様な因子によって調節されている循環調節について，様々な様式・強度・持続時間の運動を用い，異なる姿勢や環境の影響等を考慮しながら，性・年齢・身体特性の異なる対象者で検証するには多くの研究者による共同研究が必要である．本プロジェクトでは本研究所と他の研究機関との共同研究や本研究所を拠点として学内外の若手研究者が参加する研究プロジェクトを実施し，本分野の研究拠点形成を目指した取り組みを行った．このような整備により，プロジェクト終了後も研究実施主体である日本女子体育大学の研究のさらなる研究活性化の中心となり，学内外の共同研究の拠点となるものである．

4. 研究組織および研究体制

4.1 研究組織と研究者の役割

平成16年度当初は8名の研究者と事務職員1名により，平成17年度からは，新たに基礎体力研究所助手佐藤耕平氏（後に助教）が加わり9名の研究者となり，事務職員1名，研究支援PDスタッフ1名（岩館雅子氏）を核とした研究組織を形成した．そして平成18年4月にPDスタッフの異動があり〔岩館雅子氏から笹原（上田）千穂子氏へ〕，さらに平成19年10月より澁谷顕一氏を新たなPDスタッフとして追加採用した．その後笹原（上田）千穂子氏が平成20年10月に辞職したが，その後も引き続き研究メンバーとして課題の遂行にあたった．

したがって，表I.4-1に示したようなメンバーが本プロジェクトの研究組織である．6名のメンバーは他機関に属するが，機関相互の合意のもとで実施する通常の共同研究組織ではなく，研究者個人が日本女子体育大学附属基礎体力研究所の研究グループに参画するという組織形態をとった．研究代表者および各研究者のプロジェクト内での役割・責任は表I.4-1のとおりである．その役割分担は明確であり，効率的なプロジェクトの推進を図った．

4.2 研究プロジェクトに参加する研究者・大学院生・PDの状況

本プロジェクトでは，各課題および共同研究課題につき，研究者（1～12名）と，研究支援PDスタッフ（1～2名），本学および他大学の大学院生（1～4名）の実験補助者を加えた研究チームを形成し，各プロジェクトを遂行した．また人的支援の必要な課題や医療施設で実施すべき課題では，必要に応じて，本学の教職員，他大学の研究者が参加した形で研究を実施した．学内の健康管理センター理学療法士 板倉尚子氏との連携，学外では女子美術大学 石田良恵氏，お茶の水女子大学 水村真由美氏，独立行政法人理化学研究所 生体力学シミュレーション　特別研究ユニット 小田俊明氏と連携した．さらに学内外の大学院修士課程および博士課程（日本女子体育大学大学院，お茶の水女子大学大学院，鹿屋体育大学大学院）の学生が実験補助スタッフとして参加した．小人数であるが，高い活動力の研究者・大学院生・PDが研究に参加する研究体制をとった．

4.3 研究チーム間の連携状況

本プロジェクトに参加する国内研究者の班員会議を平成16年度に2回，平成17～20年度において年3～4回開催し，これまでに14回の班会議を開催した．班会議では，研究計画立案の問題点，各課題に関する研究成果報告会等を開催し，逐次研究の進捗状況を確認し，相互に意見交換する場を設けた．この会は研究推進上の実務的意義もあるが，各研究者の専門性を統合できるような議論の場として機能した．循環調節にかかわる様々な因子を統合的に捉えて，生理的機序を解明するという本プロジェクトの趣旨を達成するために，極めて重要な位置を占めた．イタリアの研究者の参加は2回であったが，討議課題についてはあらかじめ電子メールで意見交換し，さらに随時連絡をとり，円滑な連携ができた．なお，平成16年度には国際シンポジウムを兼ねた班会議に出席し，平成17年度にはイタリア研究グループのPD研究者が約2週間基礎体力研究所に滞在し，国内研究者を含む13名と連携した共同研究を実施した．さらに平成19年度には国内メンバーが連携した共同

表I.4-1　研究組織および研究体制

研究者氏名	所属・職名	プロジェクトでの研究課題	プロジェクトでの役割
加賀谷淳子	日本女子体育大学名誉教授	骨格筋への血流分配と筋からの血液還流	運動特性と骨格筋への血流分配への関係解明，研究全体の統括と推進．平成16～18年度の研究代表者.
定本　朋子	日本女子体育大学教授	運動時の内臓器官および脳の血流動態とその調節機構	非活動組織血流からみた運動時の循環調節の解明，研究の実施に関する統括と推進. 平成19～20年度の研究代表者.
加茂　美冬	日本女子体育大学准教授	運動様式，運動強度，運動時間および筋代謝からみたモーターユニットの動員特性	筋疲労発現，運動特性，筋代謝との相互連関の解明
奥山（清水）靜代	慶應義塾大学体育研究所講師	運動時の心拍出量の変化と各種血管への血流分布	中心静脈と末梢循環のマッチングとミスマッチング
佐藤　耕平	日本女子体育大学附属基礎体力研究所助教	運動時の呼吸循環系変化に対する中枢性・末梢性の神経調節	呼吸循環応答にかかわる調節因子の解明
斉藤　　満	豊田工業大学教授	運動時の筋交感神経活動からみた中枢指令および反射性制御の調節機構	自律神経による運動時循環調節メカニズムの解明
長田　卓也	東京医科大学講師	有疾患者における運動および筋虚血に対する血流調節プロファイル	低体力者や有疾患者の循環調節メカニズムの解明と運動療法の基盤構築
Marco Ferrari	University of L'Aquila (Italy) 教授	脳循環・代謝測定用近赤外線分光法の開発	研究装置の開発
Valentina Quaresima	University of L'Aquila (Italy) 教授	近赤外線分光法による運動時の脳循環・代謝の変化	脳への血流分配にかかわる調節機構の解明
岩館　雅子	学術フロンティア支援スタッフ，ポスドク研究員	運動準備期のセントラルコマンドの働き	セントラルコマンドと循環応答の対応関係の解明，各研究プロジェクト実施のための補助や調整
笹原（上田）千穂子	学術フロンティア支援スタッフ，ポスドク研究員，東海学園大学講師	筋の酸素代謝特性と運動時循環応答との連関	運動強度と筋の酸素代謝特性との関係を解明およびプロジェクト実施のための補助や調整
澁谷　顕一	学術フロンティア支援スタッフ，ポスドク研究員	運動時における一次運動野の酸素化動態	筋出力調節時の左右半球間相互作用の解明およびプロジェクト実施のための補助や調整

（平成21年3月31日付）

研究を約3ヵ月にわたり実施した．このように，本プロジェクトでは，少人数の特性を活かした密な情報交換と連携により，高い活動レベルを維持することができた．

4.4　研究支援体制

学術フロンティア担当事務員として土井美由紀氏（派遣社員，週4日で16時間勤務）を平成16年度から採用した．また研究支援スタッフとして学術フロンティアPD研究員〔岩館雅子氏は平成17年4月～19年3月まで，笹原（上田）千穂子氏は平成19年4月～20年9月まで，澁谷顕一氏は平成19年10月～平成21年3月まで〕を採用し，支援体制が整えられた．研究経費や実験補助者への謝金支払い，また研究者間の連絡事項といった事務経理全般については，学術フロンティア担当事務員が行うこととした．一

方，研究内容に直接かかわる事務作業については研究支援スタッフとPD研究員が担当することにした．

基礎体力研究所技術職員（平成16～17年度大森芙美子氏，平成18年度森山真由美氏，平成19～20年度平澤　愛氏）が，実験装置の整備や実験補助者として，必要に応じて研究支援に加わった．また本プロジェクト事務・経理の全体管理は，基礎体力研究所事務長および本学の事務局が担当し，さらに経理的なことに関しては学校法人二階堂学園法人本部財務部が担当するという体制をとった．

5. プロジェクト達成目標と達成状況および優れた成果

5.1　プロジェクト達成目標

本プロジェクトの構想調書作成時に本プロジェクトの達成すべき数値目標を次のようにした．平成16～18年度には，運動時の循環調節の研究基礎を確立し，「学会発表25篇以上，レフリー付論文公表10篇以上，公開セミナー・シンポジウム2回，研究成果報告書の刊行1回，中間報告会（研究成果報告会）1回」とした．平成19～20年度には，応用的研究を展開し，エビデンスに基づく安全で効果的な運動のあり方を提言することを目標として，「学会発表20篇以上，レフリー付論文公表10篇以上，公開セミナー・シンポジウム1回，国際シンポジウム1回，最終研究成果報告書の刊行1回，最終成果報告会1回」とした．

5.2　優れた成果と特筆事項

本研究プロジェクトの目的は，「多数の因子が複雑に作用する運動時の循環調節機構について，運動特性と身体特性との関連から種々の循環動態を検討し，得られた成果を統合的に理解することにより，最終的には『安全で効果的な運動プログラムの構築に向けた提案』をすること」であった．5年間にわたる本プロジェクトは，多くの成果をもたらせた．またそれらのエビデンスに基づいた健康・体力づくりのための運動プログラム構築に向けた提案ができた点であった．5.1に示した達成目標に対応させると，公開シンポジウム3回，国際シンポジウム2回，中間報告会1回，年次研究成果報告書の刊行，学会発表130回，学術論文84篇，書籍10篇，その他の発表4回，その他の論文は35件と，すべての達成目標をクリアした．

公表された学会発表のなかで2演題が学会賞（アジアスポーツ医学会，日本体力医学会）を獲得した．さらにプロジェクトメンバーの加賀谷淳子氏が平成19年に第10回秩父宮記念スポーツ医科学賞（功労賞）を受賞した．これらの受賞は，プロジェクトの研究成果の質が評価されたこと，そして加賀谷氏を中心とする共同研究者の業績と社会貢献が広く認知され評価されたことを示していた．

また，本プロジェクトにより，関連分野の研究者および大学院生による活性化と研究拠点形成が実現し，定着した．多数の大学院生や若手研究者が公開セミナー，シンポジウム，大学院生・若手研究者を育成するためのセミナー，国際シンポジウム，公開フォーラムに参加し，新たな共同研究や研究会の開催も生まれた．特に2回の国際シンポジウムの開催（平成16年度および20年度）では，世界的研究リーダーでもある専門家を含むシンポジウムに多数の参加者があり，充実した情報交換と討論が行われた．その成果の一部は国際誌の論争課題において見解を表明することになった（Kagaya *et al*. 2008）．このような活動に加え，実験データの提供や取材協力（NHKためしてガッテン，2005年10月15日放映「寝たきり予防！自転車エクササイズ」，毎日新聞東京朝刊2009年4月10日，毎日新聞東京夕刊2009年4月11日等），日本学術会議公開シンポジウム，市民公開講座，一般誌での解説記事，学会シンポジウム等での発表など，研究成果の社会還元が積極的に行われた．

II. 本プロジェクトの研究成果の概要

5年間のプロジェクト成果を統合的に理解できるまとめをするようにした．その統合的視点として，「運動特性との関連からみた運動時の血流再分配」，「セントラルコマンドと反射性制御からみた運動時の循環調節機構」，「さまざまな対象者の身体特性からみた運動時の循環適応」の3点とした．そして，最終的に本プロジェクトの最終目標であるエビデンスに基づく，「健康・体力づくり運動プログラムの構築に向けた提案・留意点」をまとめた．

1．運動特性との関連からみた運動時の血流再分配

運動は，活動する骨格筋への血流量を増加させると同時に，運動指令を出す脳，運動を支援する心臓や肺への血液供給を適切に調節することが必要である．しかし，血液を循環させる心臓の拍出能力には限界があること，生命維持に必要な調節が不可欠であることなどから，これらの臓器への血流調節だけでなく，活動筋以外の臓器や組織への血流再分配が必要となる．逆に言えば，運動時の各器官・組織への血流量変化は，それら調節の結果として起こったものである．したがって，それらを把握することは，その背後にある調節機構を解明する有力な手がかりになる．一方，循環経路の動脈側と静脈側をつなぐ間に介在する骨格筋の活動は，循環に対して物理的あるいは代謝性に干渉する．そのため，骨格筋の活動特性が循環応答を修飾する極めて大きな要因である．そこで，運動特性と関連させながら，運動時の血流再分配を明らかにし，その背後にある循環機構についてまとめた．

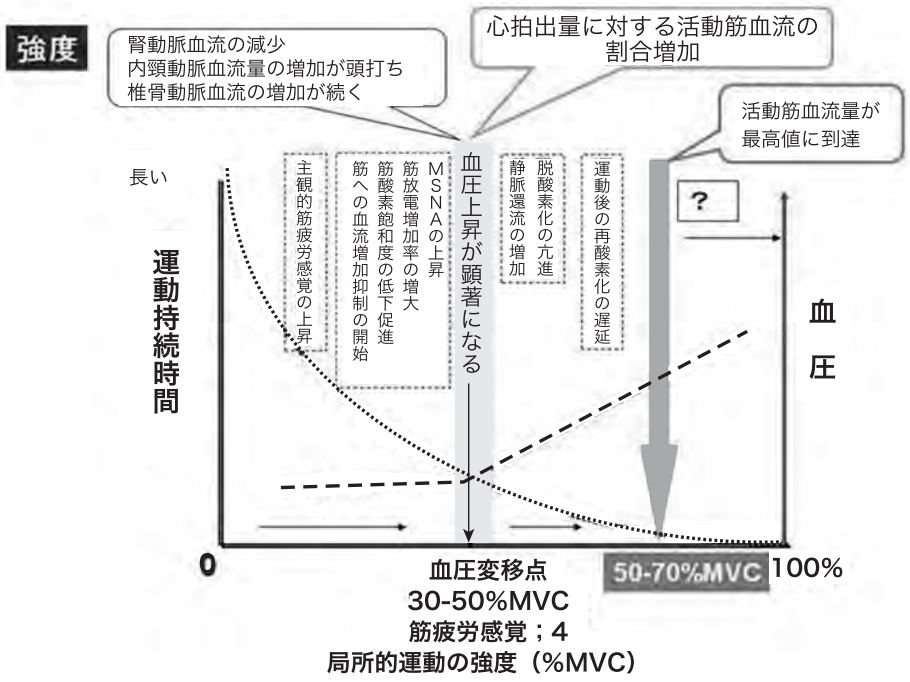
1.1　骨格筋，脳，腹部内臓への血流分配

一般的に心拍出量は運動強度や活動筋量の増加に連動して変化するとされている．しかし，本プロジェクトでは，局所的な小筋群の運動の場合は，両者が必ずしも連動した変化を示さず，骨格筋の血流需要に対して末梢的な対応をすることもあることが示された[5]（Shimizu and Kagaya 2004）．

運動指令を出す脳への血流再分配を，内頸動脈と椎骨動脈の2つの経路から調べたところ，内頸動脈経路では静的および動的運動時に動脈血圧および心拍出量が著しく上昇しても，血流量の変化は見られないのに対して，椎骨動脈経路では運動による血圧および心拍出量の上昇に伴い血流量が増加することが明らかになった[7]．活動筋への動脈血流は筋収縮時には阻害され，筋の弛緩期に増加する．一方，活動筋からの静脈血の流出は筋活動期に加速され，筋弛緩期には減速し，両者は，筋内圧の局所的変化により相互に関連しているが，一義的ではない[4]．また，筋の発揮張力が極めて低い場合であっても，ストレッチングのように筋線維が伸長すると，動脈側からの血流の逆行成分が増えて血流量は減少し，ストレッチング終了後には動脈側での加速，それに連動した静脈側の流出増加が起こることがわかった[3]．

骨格筋の血流がどこまで増えるかについてはなお議論が続いている問題である．この課題に関する先行研究は，主として代謝性の血管拡張能を調べたものが多かったが，酸素運搬系としての血流量の役割と考えると，運動中にどこまで増加するかが重要になる．本プロジェクトでは運動時最高値がどれくらいに達するかを知る前提条件として，最高血流量に達する運動条件を明らかにしようとした．その結果，動的運動時筋弛緩期の血流量については，運動強度とテンポの増加に伴って増加し，両者の組み合わせによって運動時血流量が最高になるのではないかとの知見を得た[4]．また，活動筋での血流増加は酸素需要に応えて酸素輸送を高めるためであるが，閉塞性動脈硬化症保有者に多段階負荷運動を実施した結果では，安静時には患側での血流量が低いのに対して，運動時には患側の血流量が健側より増加して，虚血に伴う骨格筋酸素消費量を代償する現象が見られた[6]．運動の物理的特性と代謝性特性の両面から，酸素供給系としての血流動態を捉えることが重要であることが示された．

運動に直接関与しない臓器である腹部内臓への血流量は，運動時に骨格筋へ血流を優先的に分配するために減少するとされてきた．しかし，静的・動的運動時の腎動脈と上腸間膜動脈の血流速度を調べると，腎動脈では血流速度減少が見られたが，上腸間膜動脈では顕著な変化は見られなかった．すなわち，運動時の腹部内臓器官への血流再分配は，一律の変化ではなく，本プロジェクトで調べた運動の範囲では，消化器官血流量は腎動脈血流量のような著しい減少がみられなかった[7]．



図II.1-1　血流変位点を基準とした運動強度と血流再配分

1.2　運動の時間経過に伴う循環・代謝応答の変化

静的筋活動開始直後には筋内圧の上昇により，動脈側からの流入が低下し，静脈側からの血液流出は加速される[4]．また，運動開始初期（約30秒程度）の動的運動では，心拍出量の増加に先行して活動筋への血流量が急速に増加するとされている．一方，運動開始初期の非活動肢の血流量変化をみると，強度依存で一過性の血流量の増加が見られ，それに続いて強度依存の血流減少が起こった（Yoshizawa *et al*. 2008）．すなわち，筋収縮開始と同時に起こる動静脈血流勾配の増加[4]等の作用によって，運動開始初期から活動筋での血流増加が素早く起こるものの，全身性の血管収縮作用は高まらずに，この時期には血流再分配は適切になされていないことが示唆される．非活動肢での血流量増加や，総末梢血管抵抗の減少により血圧が低下することは[1]それを支持する結果であると考えられる．

律動的な運動が持続すると，活動筋での血管拡張により動脈血流量の増加が起こり，筋血液量が増加する．そうなると，筋活動による静脈側の血液流出が，続いて起こる動脈血流入量と密接な関係を保つようになることがわかっている[4]．

運動が終了すると，静的筋活動後は急激な血流増加が起こり，運動後の血流は約3拍目の心周期で最高値に達する（Ohmori *et al*. 2006）．この時期には静脈血流は安静時以下に減速し，動脈血流量が最高値に達し，筋の血管床への血液再充満が起こってから静脈血流が安静レベルに復帰した[4]．

運動後の筋の酸素化動態の回復の速さは運動中の筋の代謝を反映しているので，筋線維組成の異なる深部と浅部において回復の速さ（$T_{1/2}$）が異なるかどうかを検討したが有意な差は見られなかった[8]．

1.3　運動強度と血流再分配

運動プログラムを考える上で，運動強度は極めて重要な運動条件である．本プロジェクトでは運動強度を筋収縮強度と収縮頻度から検討した．筋収縮強度がある強度を超えると筋交感神経の亢進が起こる（Saito *et al*. 1986）ことが知られているが，その結果，強度変化に対する血圧上昇が顕著になる（Kagaya *et al*. 2001）．そこで，血圧上昇が高くなる負荷（血圧変移点負荷）を基準として強度をとらえ，本研究の血流再分配の成果をまとめた（図II.1-1）．

活動筋への血流量が運動負荷強度の増加に伴って増加し，頭打ちになるかどうかは議論のあるところである．本プロジェクトでは動的膝伸展運動・足底屈運動や間欠的な静的掌握運動において検討し，前者では頭打ちが観察され，後者では筋弛緩期血流が負荷の増加とともに増加するという結果を得た[1, 4]．動的・静的

運動ともに，運動後血流量に対する運動中血流量の比は，血圧変移点負荷とほぼ類似の負荷強度で急激に低下し，運動中の血流需要を満たす割合が低くなることが確認された[1]．また，強度が高くなると，運動持続に伴う筋の電気活動漸増の割合が高くなり，筋疲労耐性の低い筋が動員されるようになることが示唆されたが，その強度は血圧変移点と類似であった[1]．筋の酸素代謝をみると，運動中の活動肢筋酸素化動態が負荷強度に対して低負荷とは異なる対応をする[1]ようになるのは，血圧変移点負荷よりやや低い負荷からであった[4]．さらに，運動中の有酸素性エネルギー機構関与の度合いを，運動後の筋酸素動態（再酸素化時間$T_{1/2}$）からみると，強度に対して指数関数的な延長を示し，有意な延長を示すようになるのは血圧変移点よりさらに高い強度においてであった[8]．

次に，運動中，活動筋での変化を中心に身体の様々な変化を統合して感知する主観的筋疲労感覚（10段階）は，血圧変移点より低い負荷（38％MVC）から急上昇した．血圧変移点に対応する値は4.0であった[4]．

骨格筋への血流量が心臓の拍出量とどう対応するかをみると，局所的な運動（足底屈運動）では，活動筋への動脈血流量が低負荷から増加を開始し始めるが，心拍出量（中心循環）は中等度負荷にならないと増加しなかった[5]．すなわち，低負荷では，心拍出量の増加を伴わずに活動筋への血流再分配が起こり，強度が高くなると心拍出量を増加させて骨格筋への血流再分配を行っていることが明らかになった．また血圧が上昇するような強度の高い負荷では，脳への血液を供給する1つの経路である椎骨動脈の血流増加が見られた．それに対して，腹部内臓においては腎動脈での血流減少が確認された[7]．

1.4　運動時の循環に対する重力の影響

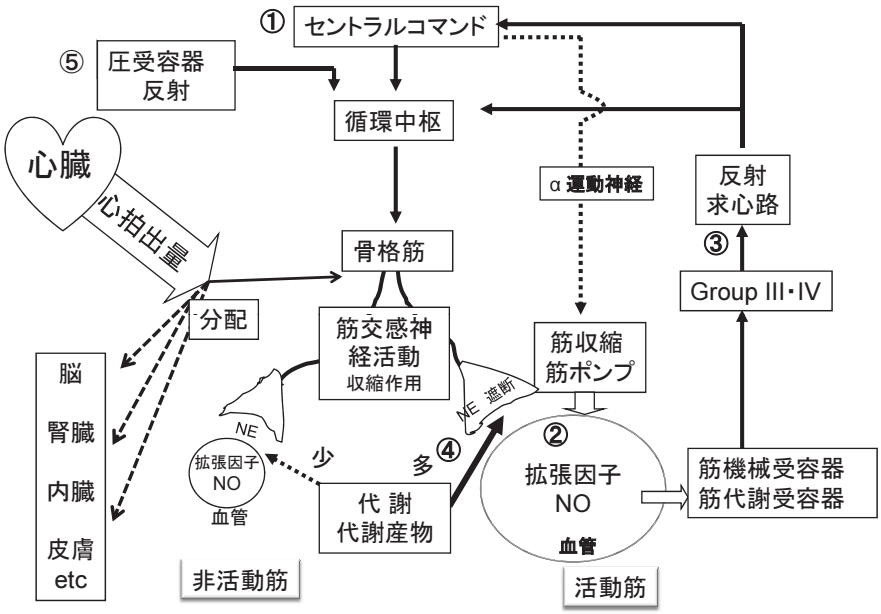
本プロジェクトでは，循環系に対する重力の影響を，活動体肢の位置を変化させて検討した[4]．掌握運動時の前腕を心臓より下にすると，筋活動中止期の血流量が有意に変化し，上腕動脈では増加，静脈では減少を示した．近赤外線分光法の総ヘモグロビン濃度変化からみた筋血液量は下垂で増加した．また，重力負荷を一定にして，血液貯留状態を変えた下肢の運動条件では，動脈静脈血流量には相違が見られず，30分程度では，貯留血液量レベルの差は影響しないことが示された．

2. セントラルコマンドと反射性制御からみた運動時の循環調節機構

運動時の適切な血流再分配には，局所性調節に加えて，神経調節が必要である（図II.2-1参照）．運動は，脳の運動中枢から出る運動指令がα運動神経を介して筋を収縮させることにより発現する．このような運動指令と並行して延髄の循環中枢に情報が送られる．この高位中枢から循環中枢に入力される情報をセントラルコマンドと呼び，運動開始に先行して起るフィードフォワード制御と考えられてきた．セントラルコマンドは運動に対する意思，頑張り，努力感といった主観的運動強度や筋疲労感覚を反映するといわれている．最近ではセントラルコマンドの概念が拡大され，筋収縮が伴わない運動想起や運動準備期に生じる循環反応もセントラルコマンドに起因すると考えられている．セントラルコマンドの発生回路と神経路および標的器官は部分的なデータがあるのみである．特に人における標的器官については，心臓，皮膚血管，腎以外はあまり調べられてはいない．また，運動（筋活動）が発現すると循環中枢に活動筋から反射性入力情報が伝えられる．これはフィードバック制御経路であり，活動筋に生じる機械的変化および化学的（代謝性）変化を刺激としてGroup III，IV求心性神経を介して循環中枢に連絡する．それらを筋機械受容器反射と筋代謝受容器反射と呼ぶ．さらに常時血圧調節に働く圧受容器反射がある．このような運動時の循環調節に関わる神経機構について，次のような新知見を得た．

2.1　運動発現にかかわる神経調節

運動発現にかかわる脳神経系の働きを理解するために，前頭前野の酸素化動態計測用の近赤外線分光計のセンサー，ホルダー，解析ソフトウェアの開発をした[9]．それらを用いて，運動時の前頭前野の活性を調べた結果，運動肢と同側半球の前頭前野が対側半球の前頭前野よりも高い活動があることを報告し，この活動が運動遂行に重要な役割を担うことを示唆した[10]．運動指令を出す一次運動野の活動についても両半球間で検討した結果，左右半球間が相互連絡をもち，対側一次運動野のみでは力発揮が不十分になる場合



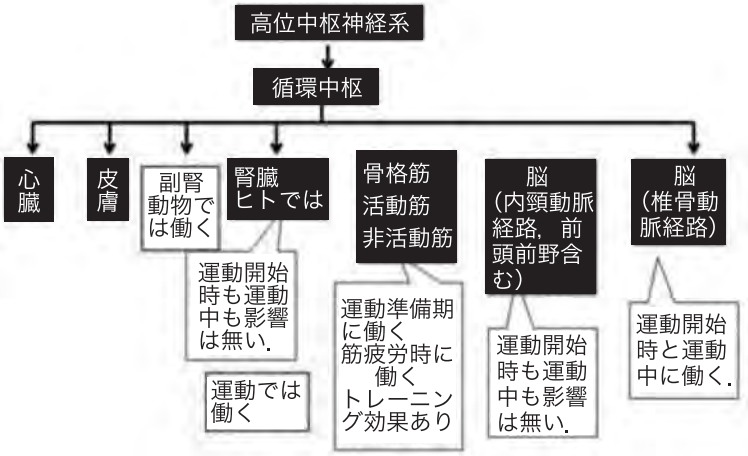
図II.2-1　セントラルコマンドと反射性制御からみた運動時の循環調節機構
運動指令が脊髄を下降しα運動神経を興奮させて活動筋が収縮する．この時にセントラルコマンドが生じる（①）．運動が開始されると，活動筋には血流増加が起こる．この血流増加には代謝性血管拡張および血流依存性血管拡張（ずり応力によるNOの増加が起因）が関与する（②）．運動強度が上がり活動筋の代謝が高まると，代謝産物が筋代謝受容器を刺激し（機械的刺激は筋機械受容器を刺激する），グループIII・IV求心性神経を介した反射性入力を循環中枢へ送る（③）．その結果，非活動筋や腎のように運動に直接関与しない部位では，交感神経活動が優勢となり，血流が減少する．一方，活動筋では代謝産物が交感神経活動の亢進を遮断するため〔神経伝達物質のノルエピネフリン（NE）が無効にされる（④）．これを機能的交感神経遮断と呼ぶ〕，血管拡張作用が優勢であり，血流増加が続く．このような活動筋と他の組織への心拍出量の血流分配を適正に保ち，一定の動脈血圧を常時維持するために圧受容器反射が働く（⑤）．

に，同側運動野の活性がそれを補完する役割を担うことが示唆された．さらに筋疲労時における対側半球の運動野の活動を，トップアスリートと一般人とで比較すると，アスリートは筋疲労時における活動が有意に低いことから，トレーニングが一次運動野の活動を変化させることが示唆された[11]（Shibuya *et al*. 2008）．運動指令に基づいて起こる運動単位の活動参加および放電間隔変化について検討した結果，一定筋力発揮時には運動単位の放電間隔時間の延長が観察されることを報告した[12]（Kamo *et al*. 2004）．

2.2　セントラルコマンドが働く標的器官

セントラルコマンドは，先行研究で示されている心臓および皮膚組織に加えて，①運動前と運動中の椎骨動脈経路の脳血流量調節に働くこと，②筋疲労時の活動筋と非活動筋の交感神経活動に働くこと，③セントラルコマンドの働きはレジスタンストレーニングで増大すること，④ヒトの腎血流量には働かないこと，という新しい知見が得られた（図II.2-2）．詳細は次のとおりである．

1）**運動準備期・開始直前**：運動準備期（約1分前から）の大脳皮質運動野周辺の脳酸素動態と心拍数，血圧および前腕屈筋群の酸素動態を同時計測し，運動準備に関連した皮質活動と循環応答の対応性を検討した．その結果，運動準備による大脳運動野周辺の活性は心拍数および筋酸素化ヘモグロビンの増加に対応することが示された（岩館と定本2008）．随意運動と他動運動に伴う脳血流量を，内頸動脈経路（主に大脳皮質側頭葉，前頭葉，頭頂葉，島皮質へ潅流）と椎骨動脈経路（主に延髄，小脳，後頭葉へ潅流）において比較した．その結果，椎骨動脈経路においてのみ，随意運動開始前の動作に先行する血管拡張がみられた．つまりセントラルコマンドは椎骨動脈経路が潅流する脳部位にのみ働くことが示唆された[7]．同様の実験を，腎動脈および上腸間膜動脈（主に消化器官へ血液を送る）において行ったが，両動脈経路には予測制御に伴う変化は見られなかった[7]．



図II.2-2　セントラルコマンドが働く標的器官

2）**運動中について**：一定負荷保持時の活動筋へ振動刺激（バイブレーション）を与え反射性張力発揮により運動指令を低下させ，ひいてはセントラルコマンドも低下させるという実験条件を設定した．この実験条件により，セントラルコマンドが運動時の心拍数，動脈血圧，心拍出量，筋疲労感覚，前頭前野の酸素化動態，内頸動脈経路，椎骨動脈血経路，腎動脈の血流調節にも低下をもたらすかどうかについて検討した．その結果，セントラルコマンド低下に伴う変化がみられたのは，心拍数，平均血圧，筋疲労感覚および椎骨動脈血流量のみであった．このことから，椎骨動脈経路の血流量がセントラルコマンドの影響を受けること，一方，動物とは異なり，ヒトの腎動脈血流がセントラルコマンドの影響を受けないことが示唆された[2]．

3）**筋疲労時**：最大ハンドグリップ張力を疲労困憊まで維持すると筋交感神経活動が亢進する．この亢進が活動筋からの筋代謝受容器反射の機構では説明できないため，筋疲労時における運動への意思・頑張り・努力感，すなわちセントラルコマンドがこの筋交感神経活動の上昇をもたらすことが示された．この交感神経活動の亢進は，抗疲労の役割を担うと示唆された[15]（Saito *et al*. 2007）．また筋疲労時にみられる筋交感神経活動の亢進は，短期間（4週間）の高強度レジスタンストレーニングにより増大することも明らかとなった[15]（Saito *et al*. 2009）．

2.3　反射性制御の働きと相互作用

筋機械受容器反射は反射性に心拍数を上げることが既に知られている．本プロジェクトでは，他動運動（セントラルコマンドや代謝受容器反射を刺激しない低負荷）で筋機械受容器反射の働きを調べた．その結果，脳，腎臓，消化器官といった血流量の調節には，低負荷では筋機械受容器反射が有意な作用をもたないことが示唆された[7]．一方，筋代謝受容器反射は，筋交感神経活動の亢進[15]（Saito *et al*. 2007）および腎血流量の減少[7]といった顕著な作用をもたらすことが示された．また消化器官の血流には作用しないことも明らかとなった[7]．

筋代謝受容器反射は運動時の血圧を上昇させるが，圧受容器反射はその上昇を抑制する働きがあることが知られている．本プロジェクトにより，代謝受容器反射は圧受容器反射と競合関係にあるだけでなく，むしろ圧受容器反射の働きを助長する作用（反射の反応時間を早め，反応の大きさも上げる）をもつことが示された．これにより，筋疲労時や高強度運動時のように代謝産物が蓄積され代謝受容器反射が働く場合には，代謝受容器反射自体が血圧の監視機能を高め循環破綻を防ぐ役割を果たしていることがわかった[15]（Ichinose *et al*. 2004）．

3. 身体特性の相違と適応からみた循環調節

身体活動・スポーツによる循環機能の向上策に必要な横断的研究および縦断的研究により，運動プログラム作成上に有意義な結果を得た．以下に主な知見を述べる．

3.1　発育に伴う脳血流の変化について

加賀谷らによる先行研究（Muraoka *et al*. 2002）では，心筋の形態と機能についてその発達が調べられた．このような心拍出量の発達に加えて，未知な部分であった脳循環の発達について検討した．特に，どの程度の心拍出量が脳へ分配されるのか（脳血流配分率）を，10～22歳の男女約300名について調べた．その結果，脳血流分配率は10歳で高く，その後徐々に低下し，15歳でほぼ発育が終了し，成人値に達することが示された．また心機能が脳循環より先行して発達するという新知見が得られた．さらに，心機能と脳循環の後に筋力（握力）が著しく発達する時期が出現することが示された[7]．

3.2　高齢者の心形態と血管形状の関連について

高齢者において心形態，筋厚および血管形状の変化がどのような関連を保っているのかを検討した結果，左室重量と大腿部筋体積との間には有意な正の相関関係が得られた．これまで，発育期の子どもでは，左室重量-大腿部体積の間に密な関係のあることが示されていたが，高齢者においても等しい関係性が認められたことは，身体運動による骨格筋量の保持が心臓の容量保持にも効果を与えるとの重要な知見を得た[5]．

3.3　有疾患者における運動および虚血に対する血流調節について

閉塞性動脈硬化症保有者は，下肢動脈血管の動脈硬化による血行障害のために運動歩行時に間歇性跛行を認める．しかしながら，疾病下肢運動中の血流動態についての報告は少ない．本研究では，閉塞性動脈硬化症保有者の患側肢と健側肢において多段階脚伸展運動時の下肢血行動態を比較検討した．その結果，運動時において，患側肢血流量が健側肢よりも顕著に増大することが確認され，末梢循環障害が安静時のみならず，運動中の骨格筋循環に大きな影響を及ぼすことが示唆された[6]．

3.4　テニス選手の利腕と非利腕の比較から

利き腕と非利き腕を各々トレーニング側，非トレーニング側と捉えて，テニス選手の筋厚と血管形状，上腕動脈血流量を比較した．その結果，利き腕の筋厚と血管径が非利き腕よりも大きく，漸増負荷運動時の最大血流量も利き腕が高いことがわかった．テニス選手の利き腕による運動時血流量が非利き腕の時よりも高くなるのは血管径の差によることも明らかになった[4]（Kagaya *et al*. in press）．このようにトレーニングが筋量，血管形状，活動筋への血流量を増加させることが示された．

3.5　トレーニングによる交感神経系の適応について

成人男性の利き腕と非利き腕における掌握運動を維持した時にみられる筋交感神経活動を比較した結果，トレーニング側と考えた利き腕運動時の筋交感神経活動が非利き腕運動より高くなった．このことを，筋疲労に抗して運動を持続させるには，交感神経活動を高いレベルに保つことが重要であること示すものである[15]（斉藤ら 2006a，2006b）．さらに，実際に，片側の腕によるハンドクリップレジスタンストレーニングを４週間行い，対照側と比較した結果，筋疲労時の筋交感神経活動が対照側の運動時よりも高くなることが示された．またこの交感神経活動の亢進は，活動筋からの反射性制御に起因するのではなく，高位中枢からのセントラルコマンドの増強に起因することも示された．したがって，短期間のレジスタンストレーニングは，活動筋というよりも，運動への頑張り・努力感にかかわる高位中枢に適応をもたらせ，その結果，抗疲労の役割を果たす交感神経活動の亢進をさせるという重要な知見を得た[15]（Saito *et al*. 2009）．

上記知見の得られた研究課題は以下のとおりであり，学術雑誌に公表されていない個別課題は本報告書の個別課題研究成果に詳しくまとめられている．
[1]「再分配」共同研究，[2]「セントラルコマンド」共同研究，[3] 若手研究者受け入れ「ストレッチング」研究，[4] 加賀谷担当個別課題，[5] 奥山（清水）担当個別課題，[6] 長田担当個別課題，[7] 定本担当個別課題，[8] 笹原（上田）担当個別課題，[9] Ferrari 担当個別課題，[10] Quaressima 担当個別課題，[11] 澁谷担当個別課題，[12] 加茂担当個別課題，[13] 岩館担当個別課題，[14] 佐藤担当個別課題，[15] 斉藤担当個別課題

4. 運動時の循環応答からみた提案ーエビデンスに基づく運動プログラムの構築に向けてー

運動プログラムは実施する運動特性と対象者の身

体特性を踏まえて作成する必要がある．本プロジェクトで得た知見をもとに次のような提案をする．

4.1　運動様式について

1）動的運動・静的運動

動的運動は心拍数や心拍出量を増加させ，血液循環を促進する運動様式といえる．また筋の収縮と弛緩がリズミカルに繰り返され（収縮期には静脈血が筋から流出し，筋弛緩期には動脈血の流入量が増加する反応をもたらす），活動筋の十分な血管拡張により，運動時の血圧上昇が低く，生体への負担度が少ないという特徴をもつ．また軽強度による脚の動的運動時（心拍数が110拍/分以下の強度）には，筋交感神経活動が安静時よりも低下することから，安静にするよりもゆっくり歩くほうがリラクゼーション効果をもつと示唆される．一方，筋収縮が持続する静的運動は，心拍数や心拍出量の著しい上昇はみられないが，活動筋での血液の流入・流出が制限されるため，動脈血圧を上昇させやすい運動様式となる．特に強度が高くなると，心臓や血管系への負担も大きくなりやすい．このような動的運動と静的運動の特徴を理解した運動プログラムの作成が必要である．

2）大筋群運動（全身的運動）・小筋群運動（局所的運動）

大筋群を用いた全身的運動による持久性運動は呼吸循環機能の維持向上のために有効であり，既に運動処方で広く活用されている．本プロジェクトでは，掌握運動のような小筋群の局所的運動であっても，活動筋のみならず非活動筋への血流量を増加させ，循環機能を活性化させることが示されている．運動強度が高くなると，脳血流増加の頭打ち，腎血流の減少，筋交感神経活動の亢進をもたらすことになる．また高強度負荷の掌握運動レジスタンストレーニングが運動時の頑張り・努力感にかかわる中枢指令（セントラルコマンド）を増強させる効果をもつことも示されている．したがって，対象者の特性を考慮した適切な運動様式や運動強度を選択することにより，小筋群の局所的運動も循環機能の活性に有効な手段となる．

3）上肢の運動・下肢の運動

上肢の運動と下肢の運動では，一定の酸素摂取量に対する動脈血圧，心拍数，毎分換気量などが異なり，いずれも上肢で高くなることが既に知られている．循環機能からみると，上肢の運動は，心臓との位置関係（重力作用）によって循環応答が変動することを考慮する必要がある．一方，心臓よりも低い位置で運動することが一般的である下肢の運動は，重力作用による血液貯留を避けるよう留意する必要がある．

4）一側性の運動

循環促進に有効なサイクリングやウォーキングのような両側性運動が運動プログラムの主体となっている．しかし，腕や脚の運動を片側だけで行った場合でも，運動を行わない対側や他の体肢（脚運動をしている時の腕など）の骨格筋血流量を一時的に変化させることから，一側性の運動も運動プログラムとして活用できると考えられる．

5）その他の運動や運動想起

ストレッチングのように筋の長さを変える運動も，筋内循環を促進させることから，ウォーミングアップやクーリングダウンに用いるだけでなく，要介護者や病床にある患者の筋循環の促進を目的とした運動プログラムとしても活用できる．

運動の準備・想起（イメージ）は，運動野皮質関連領域の脳活性，心拍数，活動筋の酸素化動態，脳血流量（椎骨動脈経路）を上昇させたことから，随意的に運動を準備し運動遂行のイメージをもつことは，運動開始後の循環調節および動作をスムーズにさせる手段となる．

4.2　運動強度の選定について

運動プログラムの作成において，適切な運動強度を選択することは重要課題である．全身運動における強度設定指標は確立されているが，局所運動については未だ確立されてはいない．本プロジェクトの結果から，次の二つの強度選定指標を提案する．

1）負荷増加に対して血圧上昇が顕著になる「血圧変移点」を指標とする．

「血圧変移点」を調べると（図II.1-1），随意最大筋力（MVC）の30～50％の運動強度に分布する．この血圧変移点の出現付近の負荷強度から，血液供給

が不足し，筋交感神経活動の亢進も起こる．そして，腎動脈および内頸動脈血流量の減少や頭打ちがみられる．なお，血圧変移点を超えて50～70％MVCまで上がると，活動筋代謝は有酸素系から無酸素系へとシフトし，活動筋中には代謝産物・局所性ホルモンが蓄積されることになる．

2）主観的筋疲労感覚を指標として活用する．

筋疲労感覚は筋交感神経活動を反映する指標であり，血圧変移点負荷に相当する筋疲労感覚は「4」であり，これは「疲れた」と「かなり疲れた」の中間の感覚である．この指標は誰もが容易に活用できることから，単独で，あるいは他の強度指標と併用して用いることを提案する．また，運動実施時には常にモニターすることを推奨する．

4.3　運動実施にあたっての留意点

本プロジェクトの成果に関連する運動実施上の留意点をまとめた．

1）運動時間の観点から

①運動開始前：運動への準備やイメージをもつことは運動開始後の循環調節および動作をスムーズにさせる有効な手段となる．

②運動開始時：運動に適した循環システムを再調整するには，運動開始後約30秒間は必要である．この調整がうまく運ばないと，血圧が低下することもある．したがって，運動開始時の急激な負荷上昇を避け，ゆっくりと徐々に運動強度を上げるようにする．

③運動終了前（疲労時）：運動持続時間とともに活動筋の疲労が始まる．筋疲労に抗して「頑張り・努力感」を働かせると，交感神経活動を介した力の維持が可能となる．しかし，運動経験の少ない人や低体力者の人は，無理のない時点で運動を終了させるようにする．その判断基準には主観的運動強度や筋疲労感覚を用いる（図II.1-1参照）．

④運動終了直後：運動終了とともに，身体の各部位の調節機能は運動前のレベルに戻ろうとする．しかし，活動筋では運動時に生じた血管拡張物質が洗い出されるまで，血流増加が続くことになる．この運動後の著しい血流増加が静脈還流量を低下させ，ひいては運動終了後低血圧を招く場合もある．そのため，軽い運動（クーリングダウン）を運動終了後にも行い，筋ポンプ作用により静脈還流の急激な低下を予防する必要がある．

2）対象者の身体特性の観点から

①発育期の子どもにおける循環機能の発達：心機能および脳循環が著しく発達する時期は，心機能（推定心拍出量）が10～12歳頃であり，脳循環（頸動脈血管内径）が12～15歳である（男女差がある）．したがって，このような心臓および血管機能が発達する時期を考慮した運動のプログラムが発育期には必要である．

②高齢者における筋量の保持：高齢者の心臓の形態（左室重量）は大腿部筋体積と密接に相関することが示された．このことから，高齢者においても骨格筋量の保持が心機能の保持に有効であるといえ，高齢者も筋量の維持に結びつく運動プログラムが必要である．

③末梢循環系有疾患者の運動：閉塞性動脈硬化症保有者は筋虚血を代償するために著しい血流量増加が生じる．しかし，運動時の心拍出量の増大には限界があることを考えると，健常人よりも運動時の血流および血圧調節が難しい．このことを踏まえたプログラム作成が必要である．

3）呼吸法との関連について

短時間の高強度レジスタンス運動時の脳血流応答から，息こらえは脳血流減少を，過呼吸は運動終了後の著しい血流増加（オーバーシュート）をもたらせることから，運動時の呼吸をコントロールすることに留意する必要がある．

4）運動時の姿勢（重力作用）について

活動筋と心臓との位置関係によって生じる重力作用が循環応答を大きく変動させることに留意する必要がある．活動筋が心臓よりも高い位置にある場合は，筋への動脈血流量が低下し筋から流出する静脈血流量が増加し，運動遂行には不利なことが多い（上肢の運動・下肢の運動参照）．

III. プロジェクトの個別課題における成果

1　骨格筋への血流分配と筋からの血液還流

加賀谷淳子[1)]

Distribution of blood flow to and outflow from skeletal muscles

Atsuko Kagaya

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1.1　研究の背景と目的

筋活動による静脈内の血液減少が，運動時の血流量増加に関与する要因となるとの報告はいくつかなされている．Magder（1995）は動物で，また，Leyk *et al*.（1994）やTschakovsky *et al*.（1995），Tschakovsky and Hughson（2000）は，ヒトにおいて活動筋の位置変化や静脈閉塞等を行って静脈側に血液が貯留する時には動脈側からの血液の流入は制限されるとし，血液循環の促進に対して，静脈内血液を空にして動静脈の圧勾配を高くすることの重要性を指摘した．そして，Shiotani *et al*.（2002）は，筋活動に伴う静脈圧の低下は座位での下肢血流量を少なくとも3倍に増加させるとしている．しかし，筋ポンプ作用は動脈側の血管拡張作用には貢献しないとする報告も見られる（Hamann *et al*. 2003; Valic *et al*. 2005）．Hamann *et al*.（2003）は，アデノシン注入により最大血管拡張を生じさせて筋活動を行っても血流はさらに増加しなかったことを根拠にあげている．しかし，ヒトを対象としたこれまでの研究では，静脈血流量を直接測定して検討しておらず，動脈血流量や筋内の血液量の変化（Kagaya *et al*. 1999; 市之瀬ら 1999）から推定されていることが多かった．

本研究では，筋が張力を発揮する筋活動や筋が主として形状を変える運動を取り上げて，運動時の動静脈血流バランスを中心に，骨格筋血流調節を運動特性との関係で明らかにすることを目的としている．そして，動静脈血流バランス，活動筋への最高血流量や骨格筋血流に対するトレーニング効果を運動条件と関連させて明らかにしようとした．

本課題に関連して行った研究は以下の通りである．

1. Venous and arterial blood flow velocity during static handgrip exercise at varying intensities with the forearm below heart level.
2. 前腕の律動的運動中の動静脈血流バランス
3. 受動的ストレッチングが循環・筋酸素動態に与える影響
4. Transient increase in femoral arterial blood flow to the contralateral non-exercising limb during one-legged exercise
5. Influence of combination of contraction intensity and frequency on attaining peak blood flow during exhaustive dynamic plantar flexion
6. 静的掌握運動時の主観的筋疲労感覚と血圧急上昇負荷との関係
7. Blood flow and arterial vessel diameter change during graded handgrip exercise in dominant and non-dominant forearms of tennis players
8. 運動時の末梢循環に対する重力の影響
   - 8.1 上肢垂下状態における掌握運動時の動静脈血流変化と酸素動態
   - 8.2 足底屈運動時の血液供給と酸素動態に対する血液プーリングの影響

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1.2 Venous and arterial blood flow velocity during static handgrip exercise at varying intensities with the forearm below heart level

Atsuko Kagaya, Shizuyo Shimizu-Okuyama, Fumiko Ohmori, Yoshiho Muraoka, and Mutsuko Yoshizawa

Abstract

The purpose of this study was to clarify the effect of contraction intensity on venous blood flow during short-term static muscle contraction and to test the hypothesis that the increase in venous flow accelerates arterial inflow in human subjects. Eight females performed 5-s handgrip contraction at 10%, 30%, 50% and 70% maximal voluntary contraction (MVC), with the forearm below heart level. Brachial venous blood flow velocity (Doppler ultrasound method) was accelerated at the onset of handgrip, and thereafter decreased to baseline during static phase of exercise. Further decrease in venous flow velocity was observed after cessation of handgrip contraction. The initial acceleration of venous flow was intensity-dependent ($P<0.01$). In contrast, the brachial arterial blood flow velocity was significantly reduced during exercise compared to baseline values, followed by intensity-dependent enhancement of post-exercise blood flow. Oxy-Hb concentration in forearm flexor muscles (NIR) was greatly decreased at higher intensities of 50% and 70% MVC. A significant relationship ($P<0.01$) was obtained between brachial venous velocity at the onset of exercise and post-exercise arterial velocity. In conclusion, muscle pump is effective at the onset of muscle contraction to induce intensity-dependent acceleration of venous outflow in humans and contributes to increase in arterial blood flow immediately after contraction of short duration intensity, whereas other circulatory parameters increased linearly.

● Purpose

The purpose of this study was to clarify the effect of contraction intensity on venous blood flow during short term static muscle contraction with the forearm below heart level and to test the hypothesis that an increase in venous flow accelerates arterial inflow in human subjects.

● Methods

Eight females participated in this study as subjects (25.5 ± 2.2 years old), after providing their written informed consents. Five-second static handgrip exercise was performed by dominant hands in upright sitting position with the forearm below heart level. Four exercise intensities were used; 10%, 30%, 50% and 70% of maximal voluntary contraction (MVC). Five trials were performed for identical intensity, with the order of the intensity at random. All the experiments were conducted in a room where the temperature and relative humidity were regulated at 26℃ and 60%, respectively.

Blood flow velocity was measured using Doppler ultrasound method (HP 8500, USA) in brachial artery and brachial vein at approximately 3 cm proximal from the level of elbow joint, and at a place where the clear vessel image was obtained. The pulsed wave transducer with an operating frequency of 7.5 MHz and sound beam angle relative to the flow direction was 60°. Blood pressure was measured (Finapres, Ohmeda, USA), muscle oxygenation was measured using

near-infrared spectroscopy (NIRS) (Niro 300, Hamamatsu Photo, Japan) on the flexor and extensor muscles of the right forearm. The distance between two optodes was 3cm.

Two-way ANOVA (intensity × phase) was used followed by Turkey's post hoc comparison when significant difference was obtained. A p value of less than 0.05 was considered statistically significant.

Results and Discussion

During baseline, venous blood flow velocity was significantly ($P < 0.01$) slower below heart level than that at heart level, whereas arterial blood flow velocity tended to be higher but not significant.

During handgrip contraction, the arterial flow velocity was significantly lower ($P < 0.01$) compared to baseline value. However, no significant difference was obtained among blood flow velocities of 4 different intensities. In contrast, post-exercise arterial blood flow increased significantly ($P < 0.01$) with increasing exercise intensities. It increased from 37.7 (± 2.8) cm/s at 10%MVC to 57.9 (± 2.9) cm/s at 50%MVC, and 59.5 (± 3.9) cm/s at 70%MVC.

Venous blood flow velocity increased markedly just before or upon initiation of tension development. Durations of the venous acceleration did not differ among 4 intensities, which indicated that venous blood flow was accelerated only during concentric phase of the muscle action, despite of contraction force. However, the magnitude of acceleration increased with increasing exercise intensity (Fig. III.1.2-1) and was negatively correlated with average arterial blood flow velocity during handgrip exercise ($r = -0.478$, $P < 0.01$), whereas positively correlated with that immediately after exercise ($r = 0.589$, $P < 0.01$).

Systolic, diastolic and mean blood pressure (SBP, DBP, MBP) were significantly elevated at the end of exercise at 50% and 70% MVC. The oxy-Hb and total Hb at the end of handgrip

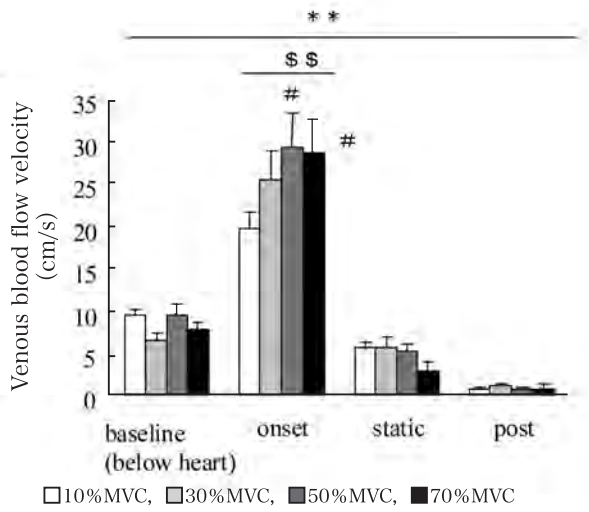

Fig. III.1.2-1 Comparison of venous flow velocity among exercise phases and exercise intensities. **; $P < 0.01$ among exercise phases, $$; $P < 0.01$ among exercise intensities at the onset, #: $P < 0.05$ vs 10% MVC.

became significantly lower with exercise intensity.

The results obtained in this study suggested that the blood was expelled when the muscle tension was developing, concomitant with the deformation of muscle fibers (shortening) and showed that the increasing contraction force made the outflow velocity higher on venous side and impede the blood flow inflow on arterial side. When muscle was relaxing, arterial blood flow velocity increased dramatically provably due to increased arterial-venous pressure gradient (Shiotani *et al*. 1996) and metabolic vasodilation (Tschakovsky *et al*. 1996). Thus muscle pump contributes to the increase in venous outflow at the onset of muscle contraction to empty blood vessel within the muscle and enhances arterial inflow during relxation phase of the exercise.

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1.3　前腕の律動的運動中の動静脈血流バランス

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An increase in venous outflow from exercising limb enhances arterial inflow during rhythmic exercise

Abstract

The aim of this study was to test the hypothesis that an increase in venous outflow due to muscle contraction enhances arterial inflow during exercise. Seven female subjects (aged 25.5 ± 2.4yrs) performed 60-s rhythmic handgrip in a sitting position with the forearm below heart level, following 2-minute rest with the forearm at heart level and 2-minute below heart level. The exercise consisted of 2-second handgrip (C) at 50%MVC, performed at 2-second interval (R). Arterial and venous blood flow velocities and minute flow volume were measured by Doppler and M-mode ultrasound method (HP8500). Muscle oxygenation was measured using near-infrared spectroscopy in radial and ulnar flexor muscles. Blood pressure was recorded on a finger by Finapres. Upon initiation of handgrip, the venous blood velocity was immediately and significantly accelerated from 6.48 ± 0.71 at baseline to 18.98 ± 3.21 cm･sec^{-1}, with no further increase through the entire period of exercise. Blood volume, during the first 16-20 seconds, decreased significantly in radial muscles. Thereafter, it gradually increased analogous to vascular conductance. When exercise was continued further, arterial inflow, venous outflow, and blood volume during C- and R-phases significantly increased. Significant relationships were observed between venous outflow during C- or R-phases and arterial inflow during successive R- and C-phases during the later period of exercise but not at the beginning of exercise. In conclusion, the augmented venous outflow due to muscle pump will increase arterial inflow when exercise-induced vasodilatation increases muscle blood volume. **Key words:** muscle pump, muscle blood volume, exercise duration

● 目　的

筋活動による静脈内の血液量減少が，運動時の動脈血流量増加の要因となるか否かについて，いくつか報告がなされているが，結果は一貫していない．本研究は，これまでヒトの運動時に実測されることの少なかった筋からの静脈血流量を実測し，静脈血流量の増加が，動脈血流増加を促進するか否かを明らかにすることを目的とした．

● 方　法

成人女性７名を被験者として，律動的掌握運動（活動２秒，活動中止２秒）を１分間行わせた．姿勢は，座位とし，活動体肢の前腕を心臓レベルより下位に位置させた．実験中，上腕静脈と上腕動脈の血流速度を超音波Doppler法（HP8500）で，血流量を超音波Ｍモード法で測定した．さらに，血圧（Finapres）と筋酸素動態（近赤外線分光法；NIRO300）の測定を行った．筋酸素動態は，前腕屈筋群の撓側と尺側の２カ所とした．

● 結果および考察

上腕動静脈血流速度は，筋活動期には静脈側が加速し，活動休止期には動脈側が加速し，筋活動期と休止期の血流速度の間には，動静脈とも，また，活動回数にかかわらず，有意差がみられた．

運動の時間経過に伴う活動期の静脈血流速度（Fig. III.1.3-1）には有意な変化が見られず，筋活動による血流は一定の高値を維持した．それに対して，筋活動間の静脈血流速度には，時間経過に伴う有意な変化（$P < 0.05$）が見られた．最初の１回の筋活動により静脈血流速度は安静時より有意に低下した後，徐々に増加し，24秒で１回めより有意に高くなった．

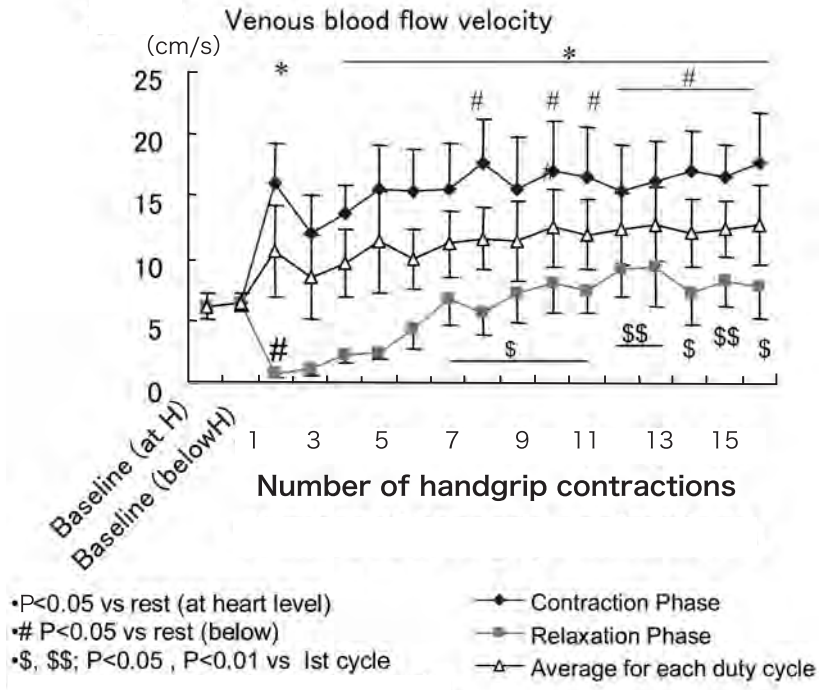

Fig. III.1.3-1　Venous blood flow velocity changes during rhythmic hand grip.

上腕動脈と静脈の血流速度を比較すると，運動開始と共に静脈血流速度は一気に加速され，中止期の動脈血流速度は徐々に加速されるが，活動中の動脈と活動中止期の静脈血流速度は一旦低下した後，安静時以上に増加するのに12～24秒を要していることがわかった．また，時間経過に伴う血流速度の変化は動静脈とも，活動期よりも，活動中止期に顕著であることが示された．

近赤外線分光法で得た筋血液量は開始初期に低下した後に増加した（掌握運動2回まで）．運動時全体における動脈と静脈の血流量の間には有意な相関関係が得られたが，開始初期約20秒までと，それ以後では循環応答が異なるので両時期に分けて両者の関係を調べた．

その結果，運動開始時には運動中止期の動脈血流量と次の活動期の静脈血流量の間，運動後半には，筋活動による静脈血流量の増加とそれに続く筋活動中止期の動脈血流量の間に有意な相関関係が得られた．したがって，運動開始による筋内血流の静脈への流出は，筋内血液量を減少させ（筋血液量の減少）るので，動脈側からの血流量が増えないと，筋ポンプ作用は有効にならないために，この時期にはむしろ，動脈血の流入量が静脈血流量を規定すると考えられる．それに対して，筋活動の持続に伴って血管拡張が起こり，筋血液量が増加するようになると筋ポンプ作用による静脈血流量の増加が動脈血流入を促進すると考えられる．

これまで，筋ポンプ作用は動脈側の血管拡張作用に貢献するか否かの観点で議論がすすめられてきたが（Hamann *et al*. 2003; Valic *et al*. 2005），本研究の結果は，少なくとも血管拡張が起こって，筋血管床が拡大する時期には，筋からの静脈血流出増加が，動脈血流入を促進することが明らかになった．

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1.4　受動的ストレッチングが循環・筋酸素動態に与える影響

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Effects of passive streching on circulation and muscle oxygenation

筋が張力を発揮しないで，筋線維が伸長・短縮するというように筋の形状を変えた場合，それに付随して筋内血管床の位置変化や血管の伸長・短縮を起こす．本プロジェクトでは，下腿筋のストレッチングをモデルとして，以下の課題について知見を得た．ストレッチングを取り上げた理由は，1）筋循環に影響する因子の一つである筋の形状変化から循環変化を明らかにすることと，2）ストレッチングは運動現場で実際によく行われている運動であり，その循環への影響を明らかにするためであった．

1.4.1 受動的ストレッチングによる末梢動脈と静脈の血流変化

1.4.2 受動的下腿ストレッチングによる膝窩動脈血流速度の変化－血流の順行成分と逆行成分からの検討－

1.4.3 受動的ストレッチング中の拮抗筋および協働筋における筋血液量と筋形状の関係

1.4.4 受動的ストレッチング時における下腿協働筋間への血流分配の相違

1.4.5 最大位までの多段階ストレッチングが筋の循環に与える影響

1.4.6 ストレッチングが筋血管容量に及ぼす影響

1.4.1　受動的ストレッチングによる末梢動脈と静脈の血流変化

加賀谷淳子，奥山（清水）靜代，大森芙美子，村岡　慈歩，水村真由美，
森　　曜生，鈴木早紀子

Regional blood flow changes in artery and vein during passive streching

Abstract

The purpose of this study was to test the hypothesis that stretching stimulates muscle circulation and also causes mechano-receptor mediated vasoconstriction. Blood flow in popliteal artery and vein were measured (ultrasound method) during passive stretching of the calf muscles with the angle of ankle joint kept at the maximally stretched position without pain. When calf muscle was stretched, blood flow velocity in the popliteal artery tended to decrease, whereas it deceased in brachial artery. When stretched muscle was restored to baseline position, the popliteal arterial velocity significantly increased, followed by an increase in venous blood velocity in 10-15 s. The results suggested that the muscle fiber stretching reduced blood flow to the muscles due to mechano-receptor mediated vasoconstriction and mechanically narrowing vessel diameter. However, immediately after stretching, the blood flow in the artery was accelerated and it pushed out blood in the venous side, resulting in increase in venous blood flow velocity.

● 目　的

ストレッチングによる筋線維の伸長（Kagaya and Muroka 2005; 横澤ら2002）は，血管径の短縮や筋機械受容器反射を起こし，動静脈血流を修飾すると考えられる（Fisher *et al*. 2005; Poole *et al*. 1997; Supinski *et al*. 1986）．しかし，ストレッチングによる当該筋への動脈血流量や当該筋からの静脈血流量の変化は明らかにされていない．本研究は受動的下腿ストレッチング（ST）によって，膝窩動脈血流速度が減少し，膝窩静脈からの血液流出が促進されるか否か，ストレッチング中止後に血流加速が起こるか否かを明らかにすることを目的とした．さらに，筋機械受容器反射による血管収縮作用を上腕血管における動静脈血流速度変化から検討することとした．

● 方　法

被験者は健康な成人女性10名（年齢21.6±0.8歳）とし，仰臥位で，膝関節角度を180°に伸展した状態で，痛みを伴わない最大角度まで足関節を背屈させてストレッチングを行わせた．実験では，4分間の安静状態を保った後，15秒で他動的に規定角度（痛みを伴わない最大角度）まで背屈して，1分間保持し，その後，15秒間で安静角度に復帰させた．回復期の測定は2分とした．循環系，特に静脈血流への呼吸運動の影響をコントロールするため，安静2分め経過後から，回復期まで，吸息1秒・呼息4秒の呼吸を行わせた．測定項目は，膝窩動静脈血流速度と上腕動静脈血流速度（超音波Doppler法，Vivid7pro，HP8500）であった．

● 結果および考察

ST中の膝窩動脈血流速度は減少傾向を，静脈血流速度は開始初期に増加傾向を示したがいずれも統計的に有意ではなかった（Fig. III.1.4.1-1）．ST終了10秒から動脈血流速度は有意に増加し，それに遅れて回復10～15秒で静脈血流速度の有意な増加がみられた．上腕動脈では，開始直後に有意な速度減少が起こり，上腕静脈血流速度も低下傾向を示した(Fig. III.1.4.1-2)．しかし，ストレッチング中，血圧には有意な変化は見られなかった．

ST中，当該筋より近位で測定された動脈血流速度は，ストレッチング中低下傾向を示し，ストレッチング終了により有意な増加を示した．静脈血流速度の変化が遅れて起こることは，動脈血依存の変化であると考えられる．このような変化が見られた第1の要因は，ストレッチングによる筋形状変化に伴う血管径の短縮と終了による拡大と考えられる．第2の要因は，上腕血管でストレッチング開始初期に血流速度減少が観察されたことから，開始初期には機械受容器反射も作用していたと考えられる（Welsh and Segal 1996)．それにもかかわらず，ストレッチング中の当該筋で，有意な血流速度低下が見られなかったのは，ストレッチングに関与する下腿の各筋群の循環応答が一様ではなかったことによると考え

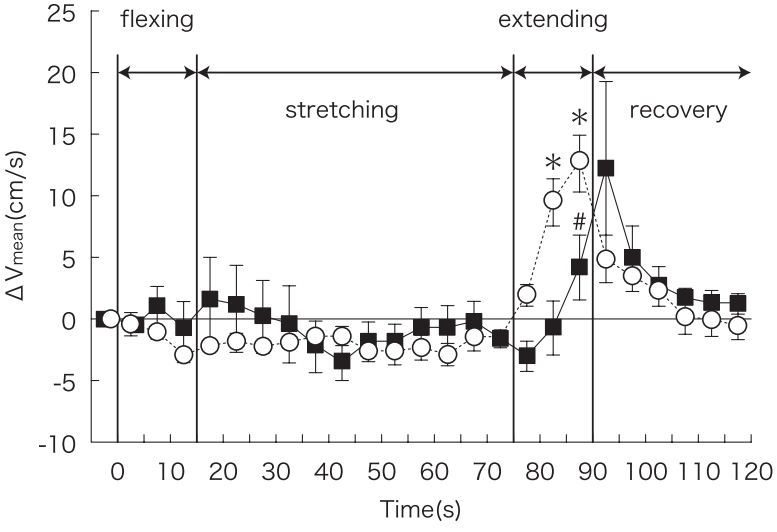

Fig. III.1.4.1-1　Arterial and venous blood flow velocity in popleteal vessels. ○: artery, ■: vein.

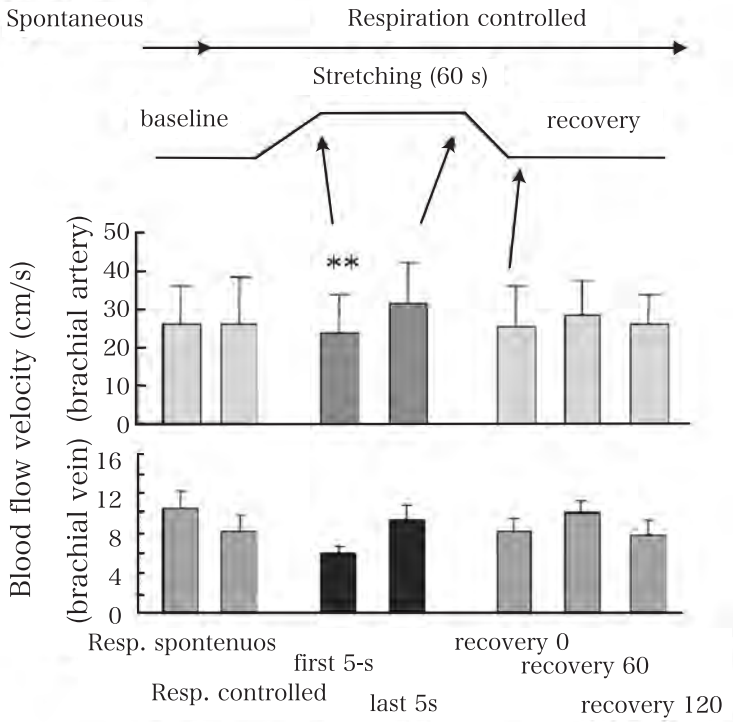

Fig. III.1.4.1-2　Blood flow velocity in brachial artery (upper) and vein (lower). **;P<0.01 vs baseline

られ，この点に関しては，血液量の変化から確認している．結論として，ストレッチングにより当該筋への血流，当該筋からの血流は動静脈とも修飾されるが，それは血管形状の物理的変化と筋機械受容器反射によると考えられる．

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1.4.2　受動的下腿ストレッチングによる膝窩動脈血流速度の変化 ー血流の順行成分と逆行成分からの検討ー

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Blood flow velocity changes in popliteal artery due to passive streching of calf muscle

Abstract

The flow pattern of antegrade and retrograde (Doppler ultrasound method) was studied in popliteal artery during calf muscle passive stretching in 10 female subjects. During stretching at anatomical position of the ankle joint, no significant changes were observed in mean blood flow velocity, antegrade and retrograde velocity. At maximal confortably streched position (CP), the retrograde diastolic flow was significantly accelerated, whereas the antegrade systolic flow and mean blood velocity did not change. Vascular resistance index increased during diastole at CP position ($P < 0.05$). The results suggest that the reduced diameter of the vessels in the stretched muscles increased vascular resistance during diastole and increased the retrograde diastolic flow.

● 目　的

動脈血流には中枢から末梢へ流れる順行（antegrade）成分とその逆に末梢から中枢に戻る逆行（retrograde）成分がある（Green *et al*. 2005）．これまでの報告では，antegradeとretrograde速度は，血管壁への刺激や血管拡張物質の放出などによって影響を受けること，またretrograde速度は，pulse-wave反射または筋収縮における血管圧迫などの抵抗のどちらかに起因し（Hoelting *et al*. 2001），血管抵抗の増加に反して動脈流入が増加したときに加速することが報告されている．一方，筋線維の伸長は筋内血管の地理的位置を変化させ，筋のサルコメアの伸長は血管径を縮小させる（Poole *et al*. 1997）ことが知られている．したがって，ストレッチングのように筋線維長が伸長すると，当該筋内の血管が引き伸ばされ，循環に影響を与えると考えられる．すなわち，血管径の短縮は血管抵抗を増加させ，当該筋へ流入する血流の速度成分を変えると考えられる．そこで本研究は，ストレッチングを行わせて，筋束長の伸長に伴い当該筋へ血液を供給している血管の速度成分にretrograde成分が増えるか否かを明らかにすることを目的とした．

● 方　法

成人女性10名を被験者とし，仰臥位での受動的ストレッチングを行わせた．ストレッチング角度には，足関節角度120°から解剖学的正位（AP）まで30°背屈させるAPと足関節角度120°から快適最大角度（痛みを感じる角度から3°減じた）まで背屈させるCPの2種類を用いた．安静4分の後，15秒で各角度まで背屈させ，1分間角度保持し，その後，15秒で底屈し，ベースラインに復帰させた．測定項目は，膝窩動脈血流速度と血圧であった．膝窩動脈速度は，平均血流速度，antegrade速度およびretrograde速度を計測した．

● 結果および考察

伸長度の異なる2種の角度のストレッチングにおける動脈血流速度（Fig. III.1.4.2-1）の中で，平均血流速度は一定角度保持中，CPで低い値を示したが，有意な変化ではなかった．また，antegrade速度も一定角度保持中に有意な変化はみられなかった，しかし，retrograde速度は，CP角度において，安静時より有意に速くなった．また，平均血流速度とantegrade速度では，角度間の血流速度に差が見られないが，

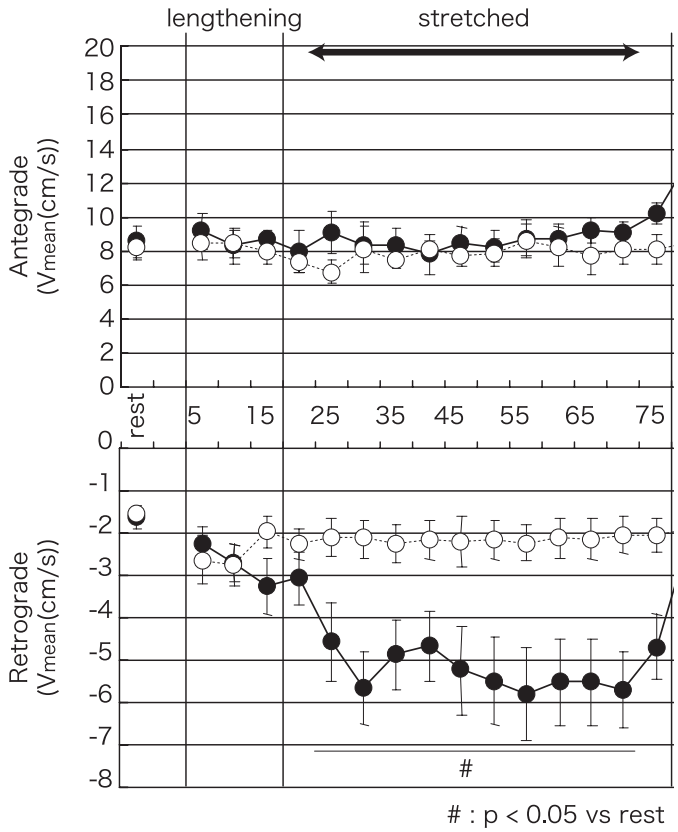

Fig. III.1.4.2-1 Antegrade systolic (upper panel) and retrograde diastolic (lower panel) blood flow during passive stretching. Passive stretching s at two positions were performed.
○; anatomical position, ●; maximal comfortable position.

retrograde速度では，AP角度より，CP角度で有意に高かった（P＜0.05）．一定角度保持中の血圧には有意な変化がなく，血管抵抗指数も心臓の収縮期には有意な変化が見られなかった。しかし，拡張期には増大し，それはCP角度で有意に高かった（P＜0.05）．したがって，筋束長の伸長度が高いCP角度では，ストレッチによって当該筋内の血管の伸長と血管径の短縮が顕著になり，血管抵抗が増加したことにより，血流の逆行成分が多くなったと考えられる．

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1.4.3　受動的ストレッチング中の拮抗筋および協働筋における筋血液量と筋形状の関係

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Relationship between blood volume and muscle structure in calf synergist and antagonist muscles during passive streching

Abstract

Changes in muscle structure in calf synergist and antagonist muscles were studied during passive stretching in 10 female subjects. Fascicle lengths of gastrocnemius medialis (MG) and soleus (SOL) muscles were lengthened, whereas shortened in tibialis anterior (TA) muscles. Percent increase in fascicle length was greater in MG than in SOL. These changes in fascicle length were closely related to muscle blood volume (total Hb) changes estimated by near-infrared spectroscopy, irrespective of synergist or antagonist muscles

● 目　的

ストレッチング（ST）中には筋線維と筋内血管の位置関係が変化し，それにより筋内循環の変化が生じることが報告されている．また，関節角度変化による筋線維長変化は筋によって異なるため，STによる筋線維長変化がもたらす筋内循環への影響は，協働筋間においても異なると考えられる．またSTの当該筋に拮抗する筋は受動的に短縮されるが，それによる筋内循環への影響については明らかにされていない．そこで本研究は，受動的ST中の筋形状と筋血液量変化との関係を協働筋（腓腹筋内側頭：MG，ヒラメ筋：SOL）と拮抗筋（前脛骨筋：TA）で明らかにすることを目的とした．

● 方　法

10名の成人女性に仰臥位・膝関節完全伸展位にて足背屈によるSTを行わせた．足関節角度120°で4分間の安静時測定を行い，引き続き15秒で関節角度を2種類の一定値（解剖学的正位，快適最大角度；痛みを感じる最初の角度から3°底屈した角度）まで変化させ，60秒間保持した後，15秒で120°に戻した．安静時から連続的に各筋の血液量（総Hb濃度；近赤外線分光法）を計測した．同様のプロトコルを用いて，筋形状（筋束長と羽状角；超音波Bモード法）を計測した．

● 結果および考察

ST中のSOLとMGの筋束長は伸長し，TAは短縮した（Fig. III.1.4.3-1）．筋束変化率はMGが有意に大きく（73％），続いてSOL（30％），TA（19％）の順であった．MGとSOLの羽状角減少率は同程度であった．ST中の筋血液量は，MGでは減少し，SOLとTAでは増加した．MGとTAにおいて，筋束長の伸長に伴い筋血液量が減少する傾向が見られ，SOLにおいては，これらと相反する傾向が見られた．

足関節底屈筋群について，一定関節角度のSTを行った結果，MGとSOLは協働筋であるにもかかわらず異なる筋血液動態を示した．SOLの筋血液量がST中に減少した理由については，MGとSOLの筋内血管の配置に差異が見られる可能性が考えられる．また，膝関節屈曲位で足関節背屈を行うとよりSOLをSTすることができるが，本プロトコルでは膝関節完全伸展位で行ったため，MGに比較してSOLのSTは十分ではなかった可能性もある．一方，拮抗筋であるTAは，足背屈方向のST中はMGと逆に筋束が短縮し，筋血液量が増加した．つまり，筋束長の変化と筋血液量変化の関係については，MGとTAは同様の傾向を示した．従って，受動的ST中は，拮抗筋においても，筋束長と筋血液量の関係は類似し，筋束長の短縮・伸長により血流量は増加・減少することが明らかになった．

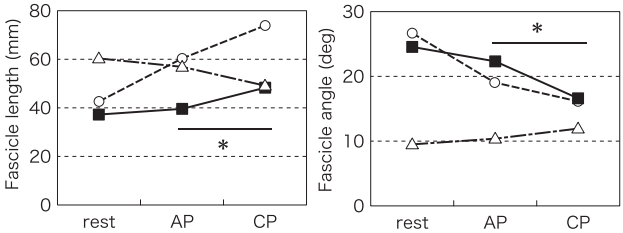

Fig. III.1.4.3-1　Fascicle length (left) and angle (right) of MG (○), SOL (■), and TA (△) during passive stretching. AP; anatomical position, CP; Maximal comfortable stretching without pain. *P < 0.001 vs rest.

1.4.4　受動的ストレッチング時における下腿協働筋間への血流分配の相違

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Heterogeneity of blood flow re-distribution during passive streching in calf muscles

Abstract

Purpose of this study was to clarify the heterogeneity of blood flow re-distribution during passive stretching in calf muscles. Ten female subjects were studied for muscle oxygenation in gastrocnemius medialis (MG) and solues (SOL) muscles using near-infrared spectroscopy. Angle of ankle joint was passively changed from resting position (120°) to anatomical position (AP; 90°) or maximal comfortable position without pain (CP). In MG, blood volume, oxygenated Hb and deoxygenated Hb decreased during stretching. In contrast, they increased in SOL muscles. The possible reasons to explain this different response include the difference in the ratio of fascicle lengthening and anatomical heterogeneity in vessel distribution among muscle fibers.

● 目　的

ストレッチング（ST）中に筋血管床血流量は減少するとされている．その要因には主に筋線維と平行に走行する血管が伸長し，血管径が縮小することが考えられるが，筋線維の走行と血管網との関係がストレッチングに関与する協働筋群において同じかどうかは明らかでない．それらの関係が異なるとすると，ストレッチングによる筋血液量の変化も異なると考えられる．本研究は，STによる血液量の変化が下腿協働筋群間で異なるかどうかを明らかにすることを目的とした．

● 方　法

被験者およびストレッチングの方法は1.4.1と同様である．安静２分後からは血液循環への影響をコントロールするため，吸息１秒・呼息４秒の呼吸をST終了まで行わせた．STには解剖学的正位（AP）と快適最大角度（CP）の２種類を用い，腓腹筋内側頭（MG）とヒラメ筋（SOL）の筋束長（超音波Bモード法），酸素化（OxyHb）・脱酸素化（DeoxyHb）・総ヘモグロビン（TotalHb）濃度（近赤外分光法），電気的筋活動（表面筋電図法）を測定した．

● 結果および考察

筋の平均活動電位はST中に有意な変化をしなかった．TotalHbは，MGではCPで減少し，SOLでは両角度で増加した（Fig. III.1.4.4-1）．OxyHb・DeoxyHbの増減はTotalHbの増減と一致した．筋束長の伸長率はAPよりもCPで，また両角度においてSOLよりもMGで高かった．ST中に筋の電気的な活動は変化しなかったので，OxyHbとDeoxyHbの変化はTotalHbに依存して起こったと考えられる．1.4.1で報告されたように膝窩動脈血流速度はST中に変化しなかったが，それはSOLのように血液量が増加した筋もあったためと考えられる．MGとSOLで血液量の変化が異なった要因の１つに筋束長の伸長率があげられる（1.4.3）．SOLの伸長率がMGよりも低かったことは，当該筋の血管の伸長・血管径の縮小・血管抵抗変化がMGよりもSOLで相対的に小さかった可能性を示唆しており，その結果SOLへの血液流入量が増加したとも考えられる．また，筋線維と血管の走行方向との関係のような構造的な違いも，もう一つの可能性としてあげられる．結論として，ST中の下腿協働筋群間では筋血液量の応答に相違があり，減少するだけでなく増加する筋も見られたことは下腿上位動脈の血流速度を必ずしも減少させない要因になると考えられる．

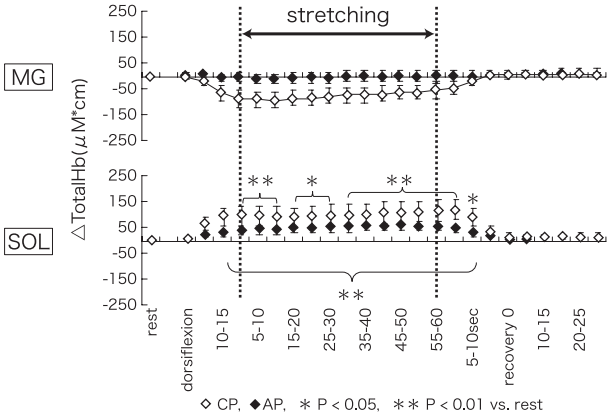

Fig. III.1.4.4-1　Blood volume (total Hb) changes in gastrocnemius medialis (MG) and soleus (SOL) muscles during passive stretching.

1.4.5　最大位までの多段階ストレッチングが筋の循環に与える影響

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Effect of maximal passive streching on muscle circulation

Abstract

Muscle blood volume and popliteal artery blood flow were determined during progressively increasing stretching calf muscles to find the extent of stretching to induce changes in muscle oxygenation and circulation in ten female subjects. Muscle blood volume (total Hb measured by NIRS) began to increase at 40% maximal stretched position in soleus muscles and to decrease at 80% max in medial gastrocnemius muscle. The latter corresponded to the ankle position of maximal comfortable stretching. However, no significant changes were obtained in popliteal arterial blood flow. These results suggest that submaximal muscle stretching larger than 40% could stimulate circulation within the muscles.

● 目　的

ストレッチング（ST）によって筋内血液量は減少する（横澤ら 2002）が，一定角度を保持した場合には上位血管の血流量低下はみられない（1.4.1）．そこで，本研究では段階的に最大位まで伸長させるSTにおいて，1）下腿の血液量変化を生ずるストレッチング角度，2）上位血管の血流動態と下位筋群での血液量との関係を明らかにすることを目的とした．

● 方　法

健康な成人女性10名に仰臥位で最大角度（max）の10，30，40，60，80，100％のストレッチングを漸増的に行わせ，各角度30秒間維持させた．測定項目は，腓腹筋内側頭（MG）とヒラメ筋（SOL）の酸素化（O_2Hb）・脱酸素化（HHb）・総ヘモグロビン（THb）濃度（近赤外分光法）と膝窩動脈血流速度（超音波法）とした．

● 結果および考察

THbは，MGにおいて80％max（52°底屈）から角度増加と共に減少した（$p < 0.05$）（Fig. III.1.4.5-1）．この角度は，痛みを伴わない最大角度（71.1 ± 1.5）に近似していた．しかし，SOLでは40％max（26°底屈）から角度増加ともに増加し（$p < 0.05$），協働筋であっても筋群間で応答は異なることが明らかになった．上位血管である膝窩動脈血流速度は，角度増加と共に減少傾向を示したが最大位まで有意な変化はみられなかった．以上のことから，1）下腿協働筋群間では40％max以降で筋血液量応答に相違がみられる，2）下腿協働筋群間で血液量が増加する筋と減少する筋があることから，上位血管である膝窩動脈血流速度では有意な変化がみられないことが明らかとなった．

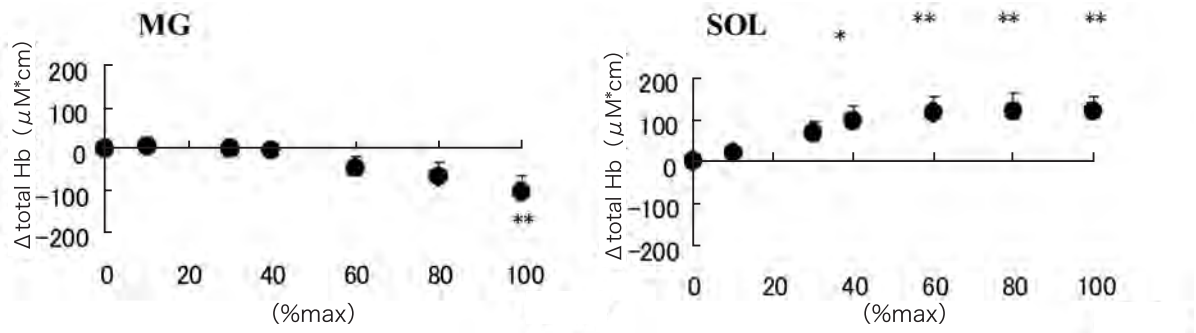

Fig. III.1.4.5-1　Blood volume changes (Total Hb, NIRS) during incremental passive stretching of calf muscles in medial gastrocnemius (MG) and solues (SOL) muscles. *, **; P < 0.05, P < 0.01 vs. baseline (0).

1.4.6　ストレッチングが筋血管容量に及ぼす影響（preliminary report）

小田　俊明，大森芙美子，森　　曜生，村岡　慈歩，奥山（清水）靜代，
水村真由美，加賀谷淳子

The effect of muscle streching on vessel capacity in muscle

Abstract

The effect of muscle fiber stretching on blood vessel shape was preliminary investigated using MR fresh blood imaging sequence. The image acquisitions with ECG gating were performed during resting, stretching to maximal comfort level without pain, and recovering phases. By modifying inversion time of imaging, each image of artery and vein was separately measured. The index of vein volume was decreased up to 0.75 by stretching. Then, the decreased index was gradually returned to the baseline after stretching. Additional analyses in detail are currently developing.

● 目　的

ストレッチングによる筋線維の形状的変化が筋内循環に与える影響に関して，これまでいくつかの知見が報告されているが，筋線維の形状的変化が筋内の血管形状をどのように変えるかについて明確に示した研究は人では見あたらない．これまでの我々の研究では，筋線維長が伸長する協働筋群間において，筋血液量が相反する方向に変化するという結果も得られているが，ストレッチングによる筋線維の形状変化の相違が各筋の血管形状を異なる方向に変えているか否かは明らかではない．そこで本研究では，MRを用いて，Flesh Blood Imaging法（FBI法）により，ストレッチング中の末梢血管像を取得し，筋血管容量の変化を明らかにすることを目的とした．

● 方　法

被験者は健康な女性5名であった．東芝メディカルシステムズ株式会社製EXELARTEを使用し，Flesh Blood Imaging法を用いて下腿の血管画像を取得した．被験者はMRIのガントリー内で仰臥位をとり，安静状態で撮像を行った後，最大快適ストレッチング角度で足関節底屈によるストレッチングを行った．対側のコントロール肢も同時に撮像した．心電図同期を用い，下腿横断面画像をecho time 80 ms, repetition time 2220 ms, スライス厚5 mmで計測した．撮影パラメータであるInversion timeを動脈撮像用と静脈撮像用に調整することで，心電図R波からの画像取得までの時間を制御し動脈と静脈の画像を分離して計測することとした．

● 結果および考察

Fig. III.1.4.6-1にFlesh Blood Image法による末梢血管の撮像写真を示す．これは，安静時と（左）とストレッチング中（中）と回復時（右）の画像変化の例を示したものである．どの図においても右がコントロール肢である．ストレッチングによって血管形状が変化し，ストレッチング終了によって安静時に戻ることが観察される．右側の静脈血index変化をみると，ストレッチング中に減少することが示された．ストレッチングによる筋線維の形状的変化が下腿のストレッチングに関与する協働筋の各筋において血管形状をどのように変化させるはまだ明らかにされていないので，今後はこの方法を用い，各筋別に検討していく必要がある．

Fig. III.1.4.6-1　The left figures demonstrate the examples of blood vein images over threshold, which were acquired by flesh blood imaging sequence and were conducted by maximal intensity projection. As shown in right graph, the vein area was decreased up to 0.75 by stretching with maximal comfort level without pain. Then, the decreased area was gradually returned to the baseline after stretching.

1.5 Transient increase in femoral arterial blood flow to the contralateral non-exercising limb during one-legged exercise

Mutsuko Yoshizawa, Shizuyo Shimizu-Okuyama, and Atsuko Kagaya

Abstract

We studied the effect of exercise intensity and duration on blood flow to the non-exercising leg during one-legged dynamic knee extension. Femoral arterial blood flow (FBF) to the non-exercising leg, blood pressure (BP), and heart rate (HR) were monitored during one-legged dynamic knee extension exercise at 15, 30, and 45% maximal voluntary contraction (MVC) in seven healthy females. There was an interaction between exercise intensity and duration for FBF and FVC ($P < 0.01$). During the initial phase of contralateral leg exercise at all intensities, FBF and femoral vascular conductance (FVC) of nonexercising leg increased, and the increase was larger at higher intensities ($P < 0.01$). After initial vasodilatation, FBF and FVC decreased to baseline, which suggests the vasoconstriction. However, FBF and FVC gradually increased during exercise at 15% MVC. We conclude that transient vasodilatation at the onset of exercise is followed by gradual change to vasoconstriction in non-exercising limb during dynamic one-legged exercise and these changes are exercise intensity- and duration-dependent.

● Purpose

Recent findings regarding blood flow to nonworking limbs are controversial. Several studies indicate that blood flow to the inactive forearm increases during leg cycling exercise (Ahlborg *et al*. 1975; Kagaya and Homma 1997; Tanaka *et al*. 2006; Taylor *et al*.1989). In contrast, Green *et al*. (2002a, b, c) found that leg cycling exercise at least at a low intensity decreases blood flow in the inactive forearm.

The purpose of this study, therefore, was to determine the effect of exercise intensity, duration of leg exercise, and the interaction between these two variables on the blood flow in the contralateral leg during dynamic knee extension exercises. The time course of changes in the blood flow to the femoral artery of the non-exercising contralateral leg was studied during one-legged knee extension exercise conducted at various intensities and continued to exhaustion.

● Methods

The subjects in this study were seven healthy females. The right leg maximal voluntary contraction (MVC) of knee extension was assessed by an "Action meter device" (VINE, Tokyo, Japan). On separate days, the subjects performed one-legged dynamic knee-extension exercise of the right leg in the upright position with the knee joint angle extended from 90° to 120° (180° = full extension). The exercise comprised contraction and relaxation for 1 s each, as indicated by a metronome. The exercise intensities corresponded to 15, 30, and 45% of the MVC. Following a 10-min rest period, the subjects performed the knee extension exercise at a given load until exhaustion. However, the activity was stopped after 15 min if the subjects could continue to exercise. B-mode ultrasound sonography was used to measure the diameter of the artery and Doppler-mode was used to measure blood flow velocity (HP 8500-GP, Hewlett-Packard, USA). A 7.5 mHz linear array transducer was placed on the skin over the femoral artery. Blood flow was obtained every 15 s for 90 s during exercise and at exhaustion.

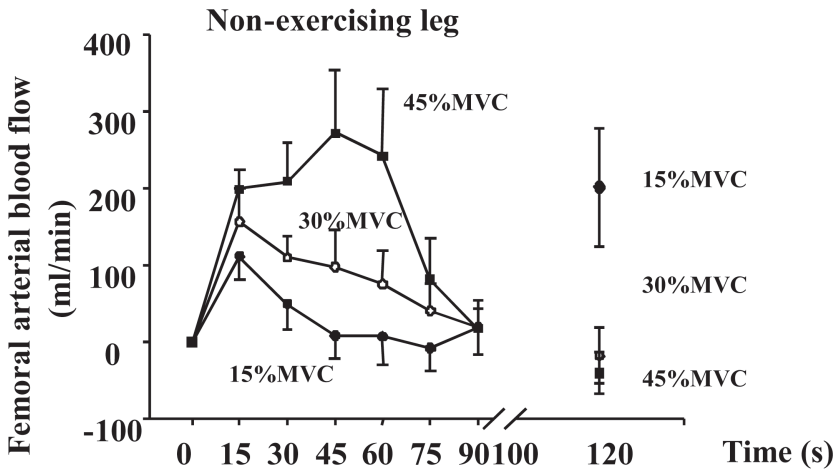

Fig. III.1.5-1 Femoral arterial blood flow to non-exercising leg during contralateral knee extension exercise at 15%, 30% and 45% MVC.

Heart rate (ECG) and blood pressure (BP) (Finapres model 2300, Ohmeda, USA) were measured on beat-by-beat basis throughout the experiment.

Results and discussion

At 15 s, FBF increased at all the intensities, and the changes in blood flow reached a maximum at 45% MVC. FBF remained elevated until 45 s (30% MVC) and 60 s (45% MVC), and thereafter it decreased toward the baseline, whereas at 15% MVC, the FBF returned to the resting level after initial increase and increased again at the end of exercise (Fig. III.1.5-1). Interaction was observed between the exercise intensity and duration ($P < 0.01$). An increase in the MBP was observed after 30 s of exercise at 15% ($P < 0.01$) and 30% MVC ($P < 0.01$), whereas it was observed after 45 s of exercise at 45% MVC ($P < 0.01$) The HR increased immediately at the onset of exercise and continued to increase throughout exercise. Femoral vascular conductance (FVC) increased at the onset of the exercise at all intensities ($P < 0.01$). The change in FVC was the highest at 45% MVC. At 15% MVC, the FVC increased again after having being reduced to the resting level, and high FVC values were observed at the end of exercise. At 30 and 45% MVC, FVC remained elevated until 30 s (30% MVC) and 60 s (45% MVC), and it thereafter decreased with time.

These results suggested that the vasodilatory response occurred in the non-exercising leg during the initial phase of exercise, and the magnitude of increase in blood flow was exercise-intensity dependent. Interestingly, it took 30-45 s to induce vasoconstriction in non-exercising regions. The mechanism to induce this biphasic response of blood flow should be studied further.

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1.6 Influence of combination of contraction intensity and frequency on attaining peak blood flow during exhaustive dynamic plantar flexion

Fumiko Ohmori, Takafumi Hamaoka, Shizuyo Shimizu-Okuyama, and Atsuko Kagaya

Abstract

We aimed to elucidate the effects of the contraction intensity and frequency on peak blood flow (BFpeak) during exhaustive dynamic plantar flexion exercise (EDPFEx) and to identify the conditions required for attaining BFpeak during EDPFEx. Seven women performed EDPFEx at intensities of 15%, 30%, 50%, and 70% of the maximal voluntary contraction (MVC) with 1-s contractions. EDPFEx was performed at 4 different intervals (10%, 30%, 50%, and 70% of the time required to attain BFpeak after a single contraction). The mean blood velocity and the vessel diameter of the popliteal artery were measured using Doppler and B-mode ultrasound. Beat-by-beat popliteal artery blood flow was calculated as follows: the flow integral × heart rate × area of the vessel. BFpeak immediately before and after the end of EDPFEx significantly changed with altering intervals and intensities. The BFpeak was obtained neither at the highest total work amount (30% MVC with 10% interval) nor at the highest work rate (70% MVC with 10% interval) but at 50% MVC with 10% interval ($p < 0.05$) both immediately before (618 ± 83 ml/min) and after (1246 ± 108 ml/min) the end of EDPFEx. This indicated that the combination of exercise intensity and frequency used in this study exerted a greater influence on the BFpeak during and after EDPFEx than those exerted individually by the total work amount and work rate per se.

Purpose

The blood flow to an active muscle changes depending on the exercise intensity, interval between contractions, contraction-to-relaxation duty cycle, etc. Blood flow markedly increases during the relaxation phase of dynamic exercise, whereas it remains at a lower level during the contraction period. Corcondilas *et al*. (1964) reported that the increase in the blood flow differed when the second contraction was performed 4 seconds and 10 seconds after a single contraction. An earlier study on contraction-to-relaxation duty cycle indicated that the blood flow to an active muscle during dynamic exercise reflected the influence of the alteration in the duration of the relaxation phase, rather than the effect of altering the duration of contraction phase (Hoelting *et al*. 2001). Therefore, the relaxation interval between successive contractions may be a causal factor that determines the blood flow during dynamic exercise (Ohmori *et al*. 2007).

Therefore, this study aimed to elucidate the effects of exercise intensity and interval, as determined by the blood flow response after a single contraction, on the peak blood flow during exhaustive dynamic plantar flexion exercise. Further, it aimed to determine the conditions required for attaining peak blood flow during dynamic plantar flexion exercise.

Methods

A total of 7 physically active women (age: 21.9 ± 0.7 years old) participated in the study after providing informed consent. In a supine position, each subject placed her respective right foot for 0.5 s on the pedal of the ergometer with the ankle and knee joints at 90° and 180°, respectively. The loads applied were adjusted to 15%, 30%, 50%, and 70% of the maximal voluntary contraction (MVC). The subjects continued plantar flexions until exhaustion or for a maximum of 10 min.

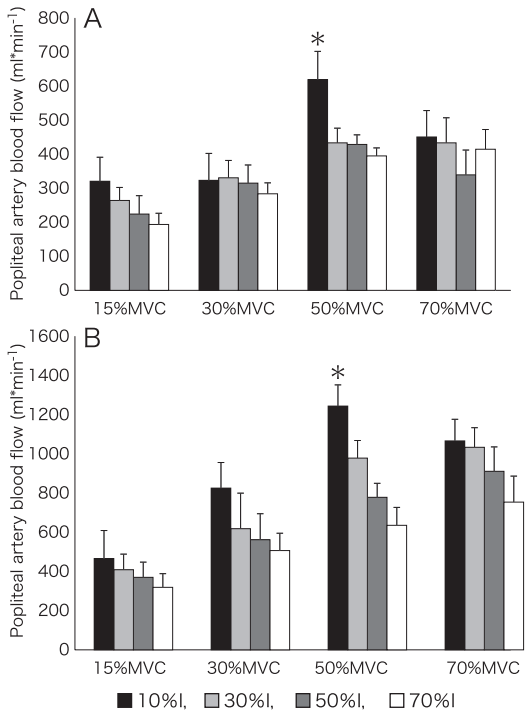

Fig. III.1.6-1 Peak blood flow immediately before (A) and after (B) the end of exhaustive exercise at 4 frequencies and intensities. * P < 0.05 (significant difference among intervals).

In the first experiment, we measured the popliteal artery blood flow after a single contraction during plantar flexion exercise to determine when peak blood flow was achieved. In the second experiment, dynamic plantar flexion until exhaustion was performed at 4 different intervals; these intervals were determined based on the results of the first experiment. They corresponded to 10% (10%I), 30% (30%I), 50% (50%I), and 70% (70%I) of the time required to attain peak blood flow. The blood velocity and the vessel diameter of the popliteal artery (Doppler and B-mode ultrasound method, HP8500GP, Hewlett-Packard Company, USA) and the blood pressure (Finapres, Ohmeda, USA) were measured.

Results and Discussion

The peak blood flow values immediately before and after the end of exercise until exhaustion are shown in Fig. III.1.6-1A and III.1.6-1B, respectively. Significant interaction was detected among 4 different frequencies and intensities for peak blood flow both immediately before and after the end of exercise. The highest blood flow values was obtained at the 50% MVC with 10% interval ($p < 0.05$) both immediately before (618 ± 83 ml/min) and after (1246 ± 108 ml/min) the end of exercise. A significant major effect on the mean blood pressure immediately after the end of exercise was observed among the 4 different frequencies and intensities.

In general, the increase in blood flow is influenced by the work rate and the total amount of work load, specifically after the end of exercise achieved (Gonzales *et al*. 2007; Osada and Rådegran 2002; Saltin *et al*. 1998). However, our results indicated that the peak blood flow was not always obtained during exercise at higher work load and work rate and that the combination of exercise intensity and frequency has a greater influence on the peak blood flow than that of either the total work amount or the work rate individually. The highest blood flow in this study was obtained at the intensity of 50% MVC and repeated at such a short interval as 10% of the time required to attain peak blood flow.

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1.7　静的掌握運動時の主観的筋疲労感覚と血圧急上昇負荷との関係

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Muscle fatigue sensation and critical blood pressure elevation during graded static handgrip exercise

Abstract

The purpose of this study was to clarify the changes in circulatory responses to graded handgrip exercise and its relationship to muscle oxygenation and muscle fatigue sensation in tennis players. Dominant hands of 10 tennis players were studied. Muscle oxygenation (NIRS), subjective muscle fatigue sensation, blood pressure (Finapres), brachial arterial blood flow velocity (Doppler ultrasound method) and vessel diameter (2-D ultrasonography) were determined during the muscle contraction and the relaxation phases of 30-s graded handgrip exercise. During this exercise, muscle oxygenation (NIRS), subjective muscle fatigue sensation, and blood pressure and blood flow increased linearly related to exercise load at lower intensities, and the former 3 parameters deviated from the initial linear relationship at higher intensities, whereas the blood flow continued to increase linearly. Critical load for blood pressure was significantly higher than that for muscle fatigue sensation, and did not differ from that for muscle oxygenation deviation.

● 目　的

局所的運動時の血圧応答は，低い負荷では負荷増加に対して直線的に上昇し，ある負荷以上の高い負荷になると急上昇する（Kagaya *et al*. 2001）．そのような変化は筋酸素動態についても確認されている（Grassi *et al*. 1999）．本研究では，静的掌握運動の負荷増加に対して，1）主観的筋疲労感覚が急上昇する負荷が存在するか否か，2）筋疲労感覚が急上昇するとすれば，その負荷と血圧急上昇の発現や筋酸素動態が顕著に変化する負荷との順序性を明らかにすることを目的としている．

● 方　法

被験者は大学のテニス部に所属して活動している女子テニス選手10名（平均年齢20.1 ± 1.0歳）であった．運動は，仰臥位の静的掌握運動であり仰臥位でハンドエルゴメータを用いて30秒間の静的掌握運動を，負荷を漸増して疲労するまで繰り返した．第一負荷は2kgとし，30秒の休息を挟んで2kgずつ負荷を漸増した．測定項目は，仰臥安静および運動時の血圧（オメダ：Finapres），上腕動脈血流量（循環器用超音波診断装置VIVID7 pro），前腕屈筋群の組織酸素飽和度（浜松ホトニクス：酸素モニターNIRO200）であった．また，Saito *et al*.（1989）による主観的筋疲労感覚を各負荷終了後に報告させた．この感覚は「0：疲れがない」から「9：疲れの限界である」まで10段階になっている．

● 結果および考察

血圧および主観的筋疲労感覚は運動負荷の増加に対して非直線的上昇を示した．それに対して，前腕屈筋群（RAD, ＵＬ）の酸素化指標は非直線的な低下を示した．3種のパラメータが負荷に対して非直線的に急増あるいは急減する変移点負荷をFig. III.1.7-1に示した．前腕屈筋群の尺側および橈側の筋酸素動態変移点負荷は，主観的筋疲労感覚とは有意差が見られなかったが，血圧急上昇負荷（右：14 ± 1kgw, 左：13 ± 1kgw)は筋疲労感覚急上昇負荷（右：11 ± 1kgw，左:9 ± 1kgw）よりも高い値（右：$p < 0.05$, 左：$p = 0.051$）を示した．血圧変移点負荷に相当する筋疲労感覚は4.0 ± 0.6であった．これらのパラメータに対して，上腕動脈血流量は，左右共に筋活動

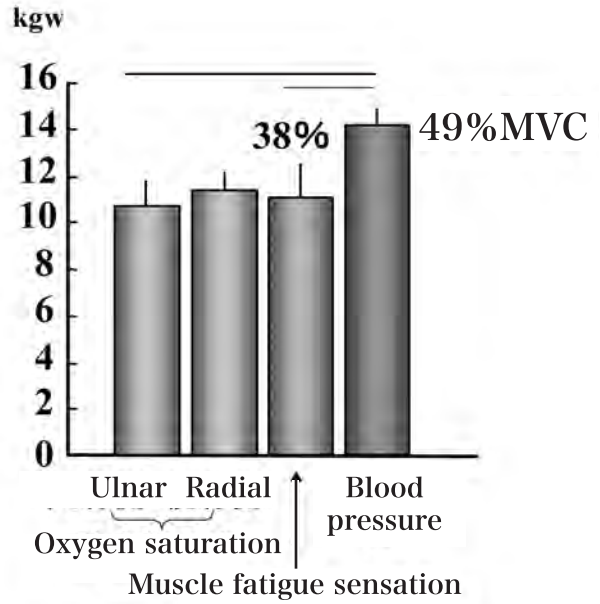

Fig. III.1.7-1　Critical loads for muscle oxygenation, muscle fatigue sensation and blood pressure.

時・活動中止期ともに，負荷増加に対して直線的増加を示している．しかし，筋活動中止期（筋内圧の除去）時の血流量に対する筋活動中の血流量の割合は，左右共に非直線的に低下した．

負荷増加に対する各パラメータ応答の関係には左右の相違は認められなかった．すなわち，主観的筋疲労感覚，筋酸素動態および血圧は非直線的変化を示すのに対して，活動肢への血流量は直線関係を保って増加した．しかし，運動中の血流量は，筋活動による機械的血管圧迫による血流制限が起こり，組織の血流需要を満たすものではない（Kagaya and Homma 1997）．需要に対して供給がどの程度満たされるかの指標として筋活動時中止後の血流に対する筋活動時血流の割合を求めると，それは負荷強度に対して指数関数的に低下した．すなわち，負荷増加に対する血流需要が低下し，それが筋酸素飽和度の低下，筋疲労感覚の急上昇を起こし，それに続いて血圧の上昇が起こったと考えられる．以上の結果は，負荷強度の選定に血圧変移点負荷を用いる生理的意義を示唆するものである．

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1.8 Blood flow and arterial vessel diameter change during graded handgrip exercise in dominant and non-dominant forearms of tennis players

Atsuko Kagaya, Fumiko Ohmori, Shizuyo Shimizu-Okuyama,
Yoshiho Muraoka, and Kohei Sato

Abstract

The training effect on exercise-induced maximal blood flow is still unclear. The purpose of this study was to clarify the difference of exercise-induced blood flow, blood flow velocity and vessel diameter of brachial artery in dominant and non-dominant forearms of tennis players during graded handgrip exercise. Ten female tennis players aged 20.1 ± 0.1 yrs. (mean ± SD) performed 30-s static handgrip exercise in a supine position with either the dominant or non-dominant hand by increasing load at 30-s intervals until exhaustion. Brachial arterial blood flow velocity (Doppler ultrasound method) did not differ between both limbs, whereas the vessel diameter (2-D method) was significantly larger in the dominant limb during diastole both at baseline ($P < 0.01$) and after exercise ($P < 0.05$), but no difference was found during systole. As a result, the blood flow was significantly higher ($P < 0.05$) in the dominant limb during post-exercise condition. Muscle thickness of the forearm muscles and maximal handgrip strength were significantly higher in the dominant limb. Thus, the effect of training on exercise-induced blood flow specific to the dominant limb was confirmed during post-exercise due to the enlarged vessel diameter during diastole of cardiac cycle. The dimensional change in the vasculature specific to the dominant side will be included in the training effects associated with the dimensional muscular changes in the dominant forearm.

Purpose

Despite that structural adaptation of vasculature has been reported at baseline, a training effect on vascular dimension during exercise remains to be studied. The purpose of this study was to clarify the effects of training on blood flow and structure of the conduit artery during static exercise (muscle action). For this purpose, the blood flow velocity and vessel diameter of the brachial artery were determined in dominant and non-dominant forearms of tennis players during and after each load of graded handgrip exercise.

Methods

Subjects; Ten female tennis players aged 20.1 ± 0.1 (mean ± SD) years old participated in the study. They were recruited from the collegiate tennis team, which won 4th place in the national inter-collegiate tennis tournament that year. Following 3-minute baseline measurements, the subject performed 30-s static handgrip exercise in a supine position with either the dominant (right side) or non-dominant hand on different days. The static handgrip exercise was repeated at 30-s intervals with increasing load by 2 kgw until exhaustion. Brachial arterial blood flow velocity (V) and diameter (D) were obtained continuously using ultrasound Doppler and 2-D methods (GE, Vivid7 Pro), each at diastole (Dd) and systole (Ds). Brachial arterial blood flow was calculated as $V^* \pi (D/2)^2$ ($D = 2Dd/3 + Ds/3$). Blood pressure (BP; Ohmeda, Finapres 2300) and maximal voluntary contraction (MVC) of forearm muscles, and radial and ulnar forearm flexor muscle thickness were measured (Aloka, SSD1000).

Results and Discussion

Muscle thickness of Rad and UL, MVC, highest load attained by each subject and total work index performed until exhaustion were significantly higher in the dominant limb.

The blood flow velocity during exercise and immediately after exercise increased significantly

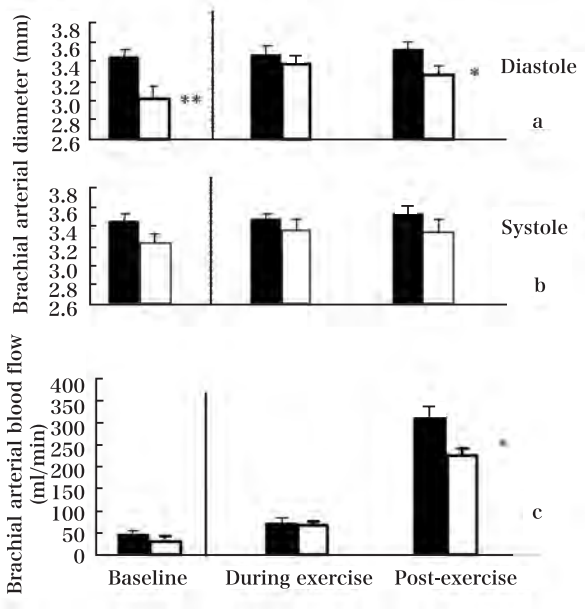

Fig. III.1.8-1 Diastolic (a), systolic (b) vessel diameter and brachial arterial blood flow (c) at baseline, during, and after exercise at the highest loads in dominant (■) and non-dominant (□) limbs. *, ** $P < 0.05$, $P < 0.001$ between limbs.

($P < 0.01$) with loads both in dominant and non-dominant limbs, though no significant difference in velocity was found between both limbs. The diastolic and systolic vessel diameters, during exercise and immediate post-exercise, gradually increased with time and increasing loads. The diastolic diameters were significantly larger in the dominant limb at baseline (dominant; 3.4 ± 0.1, non-dominant; 3.0 ± 0.1 mm) and after exercise at the highest load (dominant; 3.5 ± 0.1, non-dominant; 3.2 ± 0.1 mm) (Fig. III.1.8-1). In contrast, systolic diameter did not differ either during exercise or post-exercise between both limbs. The brachial arterial blood flow in both limbs increased linearly related to exercise load both during ($P < 0.01$) exercise and post-exercise ($P < 0.01$). Interaction was significant ($P < 0.05$) and higher post-exercise blood flow was obtained in the dominant limb after exercise at the highest load ($P < 0.05$).

The first finding of this study was that the trained forearm showed higher exercise-induced blood flow increase during post-exercise phase, (or relaxation phase of dynamic exercise). Our second finding was that the luminal vessel diameter of the brachial artery during systole did not change significantly between limbs, whereas the diameter during diastole was larger in the dominant limb. The latter finding is consistent with the study of Huonker *et al*. (2003), who studied thoracic, abdominal, subclavian and common femoral arteries in trained athletes including professional tennis players, but not with the study of Schmidt-Trucksäss *et al*. (2000). The discrepancy might be due to the difference of subjects compared in the respective studies. The possible mechanism to explain an increased blood flow with training involves structural remodeling of the vasculature (Miyachi *et al.* 1998). Other underlying mechanisms for the increased blood flow with training will include a change in vasoactivity because of an increased flow-mediated dilation after training (Allen *et al*. 2003; Clarkson *et al*. 1999). The contribution of NO to the effect of exercise training on vascular responses in human subjects remains undecided (Green *et al*. 1996).

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1.9　運動時の末梢循環に対する重力の影響

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村岡　慈歩，森　　曜生

Effects of gravity on peripheral circulation during exercise

地球上では，重力の影響を受けて血液循環が変化する．その結果，活動体肢と心臓との相対的位置関係が，骨格筋への酸素供給を行う動脈側血流を修飾して，筋の酸素供給-消費バランスを変えると考えられる．実際，上肢を挙上・垂下して，心臓との相対的位置関係を変えたとき，挙上時には，垂下時に比較して上腕動脈血流量が減少し，酸素化ヘモグロビン濃度の低下，脱酸素化ヘモグロビン濃度の上昇度は大きくなった（加賀谷ら 2001）．体肢が心臓より下に位置する場合は，重力の影響により筋血管床での血液プーリング（貯留）が起こる（加賀谷ら 2001）．それは，動脈血流入にも影響を及ぼす（Tschakovsky and Hughson, 2000）と考えられる．一方，血液プーリングは動静脈バランスにも依存するので，静脈血流量に変化があると，筋の酸素ダイナミクスにも影響を及ぼす可能性がある．しかし，運動時の静脈血流量の変化と血液プーリングおよびその動脈側への影響については，これまで明らかにされていない．

本研究は，活動体肢位置を心臓より下に位置させて，血液プーリングが起こるような状態で動的運動を行わせ，それが活動筋の血流変化と酸素ダイナミクスに与える影響を明らかにすることを目的としている．特に静脈血流量の変化に着目して活動体肢を心臓レベルにおいて運動した時の変化と比較検討した．

1.9.1　上肢垂下状態における掌握運動時の動静脈血流変化と酸素動態

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熊谷　真奈

Venous and arterial blood flow, and muscle oxygenation during hand-grip exercise with the arm below heart level

Abstract

The purpose of this study was to test the hypothesis that venous return from exercising muscles was enhanced under the condition that it was placed below heart level. Thirteen young females performed rhythmic handgrip exercise with the forearm at heart level or below heart level. Brachial venous blood flow was significantly larger with the forearm at heart level than that below heart level at the beginning of exercise. In contrast, the brachial arterial blood flow was higher with the forearm below heart level. The blood volume (THb) estimated by NIRS increased gradually with exercise duration and the increase was significant during exercise below heart level. These results suggested that the venous outflow and arterial inflow during the rhythmic handgrip became out of balance toward the arterial inflow, due to an increase in vascular bed and blood pooling in the muscle.

● 目　的

本研究は，活動筋からの静脈還流は，活動体肢を心臓レベルに置くよりも，心臓より下においた場合の方が運動による変化が大きく，それが動脈血流に

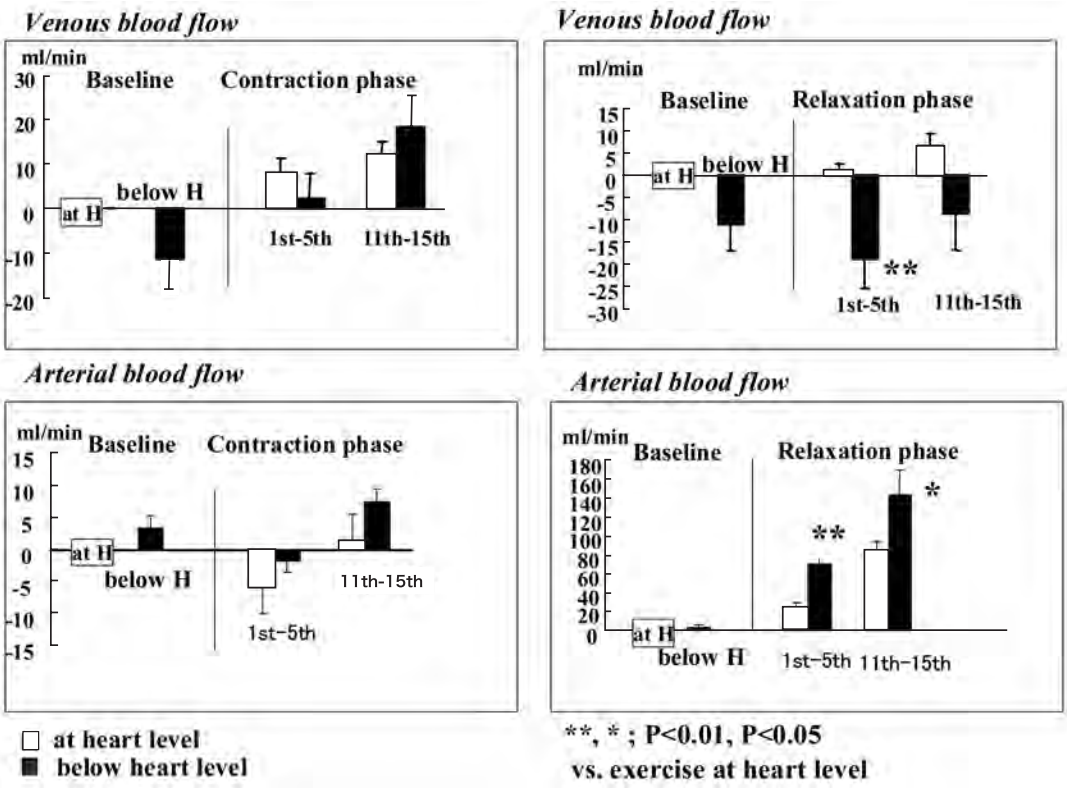

Fig. III.1.9.1-1　Venous (upper) and arterial (lower) blood flow changes during the contraction (left) and relaxation (right) phases of handgrip exercise. Handgrip exercises were performed with the forearm at heart level (at H) or below heart level (below H).

も影響するとの仮説を検証しようとした．その目的のため，上肢を下垂した状態で行う律動的掌握運動時の循環・酸素代謝変化を，心臓レベルでの運動時と比較した．

● 方　法

若年女性13名を被験者として，心臓レベル（6名）と心臓より下位（7名）に体肢をおいて，椅座位で，律動的掌握運動（50％MVC強度，1分間，活動・休止各2秒）を行わせた．測定項目は，上腕動静脈の血流速度（超音波Doppler法），血流量（M-mode法），血圧（Finapres）および近赤外線分光法（NIRO300）による前腕屈筋群の酸素化ヘモグロビン（O_2Hb），脱酸素化ヘモグロビン（HHb），総ヘモグロビン（THb）濃度であった．

● 結果および考察

律動的掌握運動を，心臓レベルと心臓以下のレベルで実施した時の血流量（M-mode法）は，心臓レベル運動時では時間経過に伴って静脈血流量は徐々に増加するが，心臓レベル以下での運動時には増加しなかった．また，NIRSによって得られたO_2Hb，HHb，THbはいずれも開始初期に一旦減少し，その後，O_2Hbは漸減，HHbとTHbは漸増した．次に，心臓レベルでのベースライン値を基準として，血流量の変化分を筋活動期と活動中止期に分けて体肢の位置間で比較すると，Fig. III.1.9.1-1 のようになった．静脈血流量は，心臓レベル以下の運動の方が有意に低く，それは，筋活動開始初期の筋活動中止期において認められた．それに対して動脈血流量は，筋活動中止期に心臓レベル以下の運動時の方が有意に高くなった．このような，動静脈血流量のバランスの変化は，心臓レベル以下で行われている活動体肢への血液プーリングを促進する結果になった．このことは，血液量（THb）の増加にも反映されており，運動に伴う血管拡張により，筋内血管床が増大したこと，筋からの流出血液量の減少が血液プーリングをより大きくしたことを示唆している．

1.9.2　足底屈運動時の血液供給と酸素動態に対する血液プーリングの影響

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村岡　慈歩，森　　曜生

Effect of blood pooling on blood supply and oxygenation during plantar flexion exercise

Abstract

Arterial and venous blood flow responses to rhythmic plantar flexion exercise were compared before and after 30-min upright sitting rest to determine the effect of pooling. Eight female subjects participated in this study. During 30-min upright rest, the blood volume (total Hb) in the calf muscles estimated by near-infrared spectroscopy increased significantly, suggesting blood pooling in the calf muscles. Either venous or arterial blood flow change did not differ significantly before and after pooling. Further study should be conducted to clarify the effect of pooling on venous and arterial blood flow changes during exercise.

● 目　的

運動時の動脈血流入に対して，活動筋からの血液流出（静脈血流）が規定因子になるか否かに関して，上肢を下垂した実験モデルで検討したが，上肢では心臓と活動体肢との高低差が小さい．また，筋ポンプ作用は血液貯留量と関連しているとされており，その点からも前腕の運動は静脈貯留・筋ポンプ作用の影響の可能性が小さい．そこで，本実験では，活動体肢をさらに低い位置に置くことができ，筋量も多い下腿の運動を対象として検討した．本実験では，血液貯留の影響が顕著になるよう下肢下垂状態を30分保持した．このような血液プーリングが起こるよ

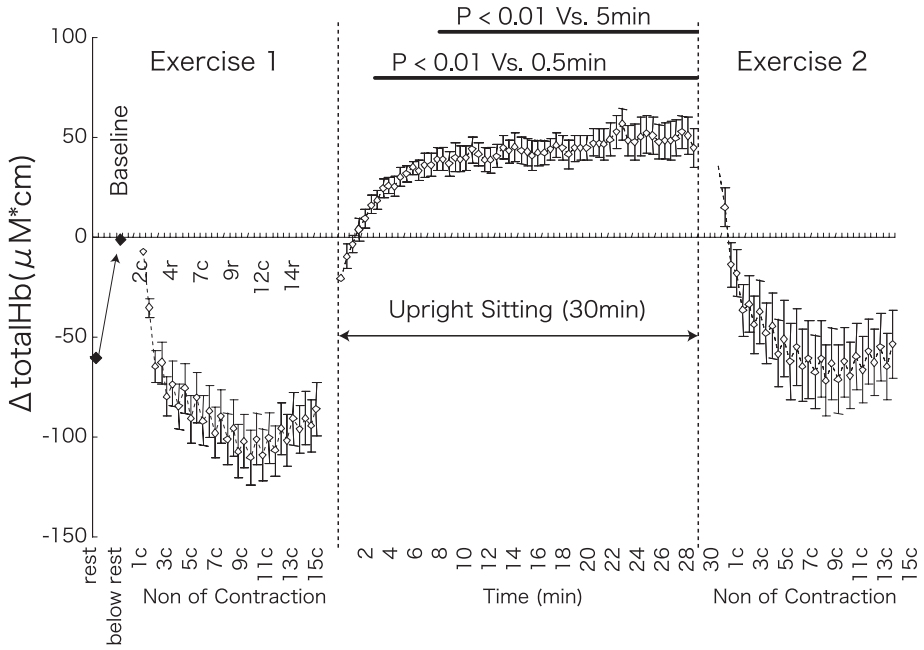

Fig. III.1.9.2-1　The muscle oxygenation changes during upright sitting rest and during dynamic plantar flexion exercise before and after 30-min upright rest. ◇ : O_2Hb.

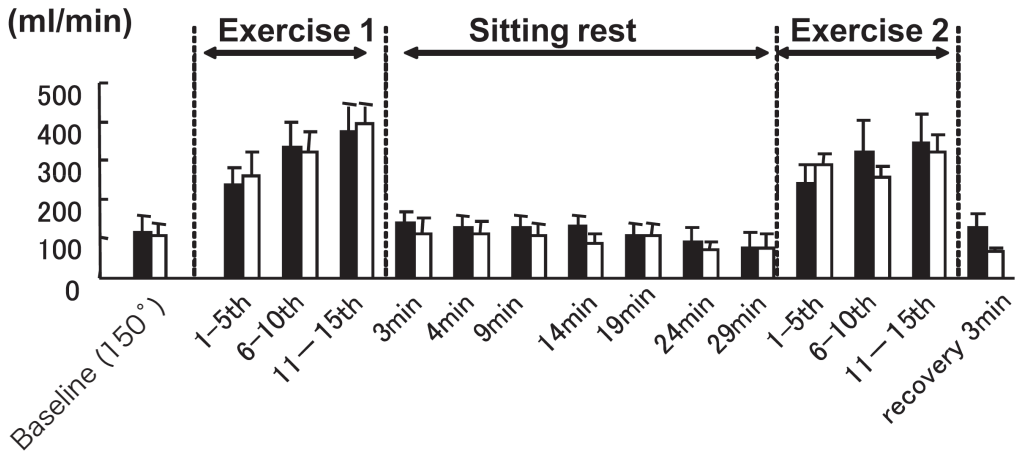

Fig. III.1.9.2-2　Venous (□) and arterial (■) blood flow in popliteal vessels during upright sitting rest and during rhythmic plantar flexion exercise. Significant difference was found between arterial blood flow and venous blood flow, whereas no significant difference was found those parameters between 1st and 2nd bout of exercise.

うな実験条件を設定し，運動時の動静脈血流バランスがプーリング前後で異なるか否かを明らかにすることを目的とした．

● 方　法

若年女性８名を対象に，椅座位で安静状態を保った後，60秒間の律動的（活動２秒，休止２秒）な足底屈運動を行わせた．引き続き，30分間の椅座位安静を保持して血液プーリングを行った後，最初と同様の足底屈運動を実施した．運動の強度は，あらかじめ漸増負荷運動によって得られた負荷-血圧関係式から，血圧が急上昇する負荷を求め，その＋20%（高負荷）と－20%（低負荷）に相当する負荷を用いた．測定項目は，腓腹筋内側頭（MG）の筋酸素動態（近赤外線分光法，NIRO200），膝窩動脈血流速度（超音波ドップラー法，Vivid7pro）であった．

● 結果および考察

Fig. III.1.9.2-2は安静状態から実験終了までのO2Hb，HHb，THbの変化を高強度運動の例で示したものである．30分間の椅座位姿勢保持によって，MGのTHbが増加し，血液プーリングが確認された．律動的足底屈運動時の膝窩動静脈血流量は，高強度・低強度運動共に，プーリング前に比べてプーリング後はやや低い値を示したが，統計的に有意な変化ではなかった（III.1.9.2-2）．逆に筋酸素動態の変化は，プーリング後やや大きかったが統計的に有意ではなかった．

● 文　献

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1.10　まとめ

本研究で明らかになった結果を，運動特性（特に，運動持続時間，運動強度）と関連させてまとめると以下のようになる．

1.10.1　時間経過に伴う骨格筋への血流調節

本研究の結果から筋活動の開始時には筋ポンプ作用により静脈血の流出が起こり，動脈血流入は開始初期に一旦抑制されるものの，続いて起こる活動筋の血管拡張によって血流量が増加した（Fig. III.1.10-1）．一方，運動開始初期の非活動肢の血流量変化をみると，強度依存で一過性の血流量の増加が見られ，それに続いて強度依存の血流減少が起こった（Yoshizawa *et al*. 2008）．すなわち，筋収縮開始と同時に起こる動静脈血流勾配の増加等の作用によって，運動開始初期から活動筋での血流増加が素早く起こるものの，全身性の血管収縮作用は高まらずに，この時期には血流再分配は適切になされていないことが示唆される．非活動肢での血流量増加や，総末梢血管抵抗の減少による血圧の低下はそれを支持する結果であると考えられる．

律動的な運動が持続すると，活動筋での血管拡張により動脈血流量の増加が起こり，筋血液量が増加する．そうなると，筋活動による静脈側の血液流出は，続いて起こる動脈血流入量と密接な関係を保つようになることがわかったが，運動が終了すると，急激な動脈血流増加が起こり，運動後の血流は約3拍目の心周期で最高値に達する（Ohmori *et al*. 2006）．この時期には静脈血流は安静時以下に減速し，静脈血流が安静レベルに復帰したのは，動脈血流量が最高値に達し，筋の血管床への血液再充満が起こってからであった．

このように運動開始時や運動終了直後のように身体が劇的に変化する状況においては，局所的運動の開始や中止に対する局所的対応と循環システム維持のための調節が急速に起こるが，両者の対応は必ずしも同時ではなく，運動実施上留意すべき循環応答も見られる．

また，動静脈血流には重力の影響が強く，心臓と活動体肢の位置関係が循環調節に影響を与えていることが示唆された．運動条件との関係についてはさらに検討を進める必要があろう．

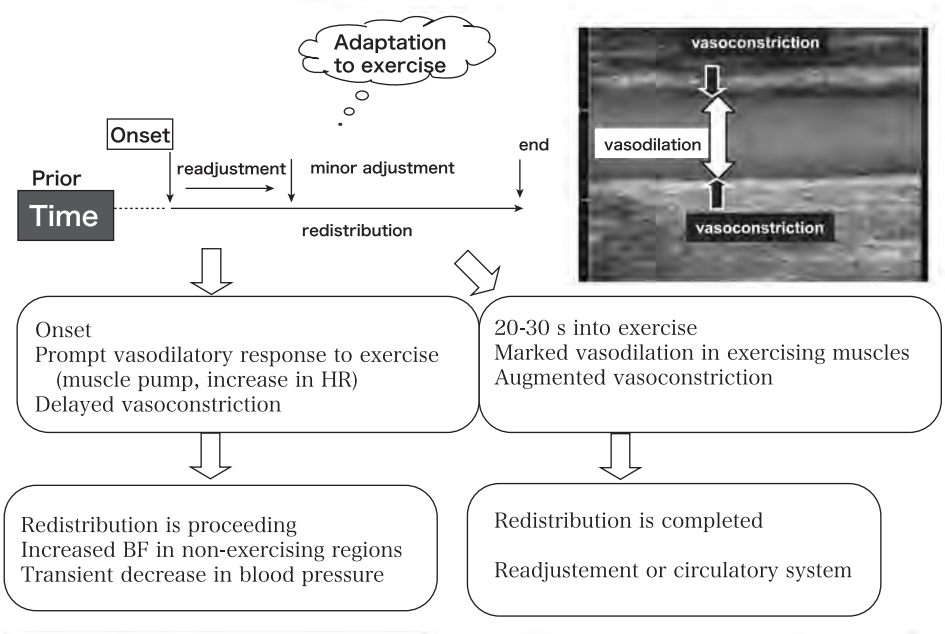

Fig. III.1.10-1　Regional and central circulatory adjustment to exercise.

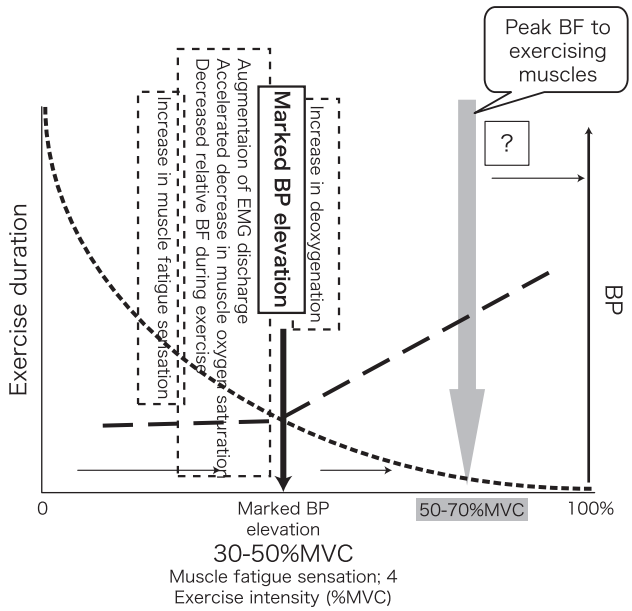

Fig. III.1.10-2　Deflection loads of circulatory and metabolic responses to exercise in relation to exercise intensity, exercise duration and blood pressure. Muscle fatigue sensation is also indicated.

1.10.2　運動強度と血流再分配

運動プログラムを考える上で，運動強度は極めて重要な運動条件である．本プロジェクトでは運動強度を筋収縮強度と収縮頻度から検討した．筋収縮強度がある強度を超えると筋交感神経の亢進が起こる（Saito *et al*. 1986）ことが知られているが，その結果，強度変化に対する血圧上昇が顕著になる（Kagaya *et al*. 2001）．そこで，血圧上昇が高くなる負荷（血圧変移点負荷）を基準として強度をとらえ，本研究の骨格筋への血流再分配の知見をまとめた（Fig. III.1.10-2）．

活動筋への血流量が運動負荷強度の増加に伴って増加し，頭打ちになるかどうかは議論のあるところである．本プロジェクトでは動的膝伸展運動・足底屈運動や間欠的な静的掌握運動において検討し，前者では頭打ちが観察され，後者では筋弛緩期血流が負荷の増加と共に増加するという結果を得た．動的・静的運動共に，運動後血流量に対する運動中血流量の比は，血圧変移点負荷とほぼ類似の負荷強度で急激に低下し，運動中の血流需要を満たす割合が低くなることが確認された（IV．プロジェクトの共同研究における成果 p. 139）．また，強度が高くなると，運動持続に伴う筋の電気活動漸増の割合が高くなり，筋疲労耐性の低い筋が動員されるようになることが示唆されたが，その強度は血圧変移点と類似であった（IV．プロジェクトの共同研究における成果 p. 139）．筋の酸素代謝をみると，運動中の活動肢筋酸素化動態が負荷強度に対して低負荷とは異なる対応をするようになるのは，血圧変移点負荷よりやや低い負荷からであった．そして，これらの負荷は主観的筋疲労感覚の急上昇より高い負荷であり，筋疲労感覚では10段階中の４に相当することがわかった．

血流量が最高値に達する運動負荷強度について，最終的な結論を得るには至っていないが，現段階では，負荷強度が50％MVCで比較的テンポの速い運動においてであった．この点については，さらに多くの負荷強度・運動頻度・持続時間を組み合わせた実験によりデータを蓄積する必要がある．

1.10.3　活動筋血流量に効果的なトレーニング条件

本研究では，先行研究と同様に，長年トレーニングを行っているテニス選手の利き腕の血流量が非利き腕に比べて高い値に増加することを確認した．そして，それが，心臓の拡張期に当たる時期の血管径の拡大によるという新しい知見を報告した．しかし，これまでの研究でも，また，本研究でも，最も効果的なトレーニング条件を明らかにするには至らなかった．本研究者らは，上記1.10.2で示した生理的な運動強度を用いて，血圧変転負荷以下とそれ以上の負荷によるトレーニングが末梢循環系と骨格筋に対する効果が異なるかどうかを明らかにする研究を本プロジェクトで開始した．このトレーニングによって，これまで別々に行われてきた筋肥大を起こすトレーニング条件と循環系に効果を及ぼすトレーニング条件を総合的に検討して，両者の関係を明らかにしたいと考えている．本学術フロンティア事業を契機に多くの研究者が参画する共同研究に発展して，トレーニングに関する指針の得られることが望まれる．

2　運動時の内臓器官および脳の血流動態とその調節機構

定本　朋子[1)]

Control of renal and splanchnic circulations during exercise

Tomoko Sadamoto

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2.1　運動時の内臓器官血流動態とその調節

定本　朋子，佐藤　耕平，平澤　　愛，島田奈央子

Control of renal and splanchnic circulations during exercise

2.1.1　静的運動時における腎動脈および上腸間膜動脈の血流応答

Renal and splanchnic vascular responses during static exercise and postexercise muscle ischemia

Abstract

Since visceral regions are consisted of functionally different organs such as kidneys and gastrointestinal tracts, it was hypothesized that blood flow regulation induced by the autonomic activation during exercise is different among arteries supplying to specific organs. To verify the hypothesis. We studied blood flow responses in renal artery (RA) and the superior mesenteric artery (SMA) during static handgrip exercise and the postexercise muscle ischemia (PEMI). Ten healthy female volunteers performed a sustained static handgrip exercise at 30 % of maximum voluntary contraction for 2 min followed by a 6-min recovery period (control condition). Subjects also underwent the occlusion condition, in which arterial blood flow in the upper arm was arrested immediately after the handgrip exercise. Mean arterial blood pressure (Finapres), heart rate (ECG), and blood flow in RA (RABF) and SMA (SMABF) were measured by Doppler ultrasound technique. Vascular resistance in RA and SMA (RAVR and SMAVR) were calculated. During handgrip exercise, RAVR significantly increased and sustained at the higher level during PEMI in occlusion condition, whereas RAVR in control condition returned to the resting level. On the contrary, SMAVR in both conditions slightly increased during exercise and returned to the resting level during PEMI. These results supported the hypothesis that blood flow regulation among different visceral organs is differential during exercise and PEMI. RA appeared to be more sensitive to exercise stimulus and the reflex signals arising from muscle metaboreceptors than SMA. The artery supplying to the digesting gastrointestinal tract such as SMA might be to some degree exempt from flow-reducing participation during exercise.

● 研究目的

安静時には心拍出量の20％もの血流配分がある内臓器官であるが，運動時には骨格筋血流への配分を増大させるために，血流減少の対象となるといわれる（Osada *et al*. 1999）．しかし，運動に対して個々の内臓器官の血流が画一的に血流減少を示すのかどうかについては明らかではない．本研究では，内臓器官の中でも消化器官（主に小腸）への血液を送る上腸間膜動脈（superior mesenteric artery：SMA）と腎臓へ血液を送る腎動脈（renal artery：RA）の2つを取り上げ，静的運動および運動後筋虚血に対するSMAとRAにおける血流動態を比較検討することにした．

● 研究方法

腎動脈（RA）および上腸間膜動脈（SMA）の2つの実験に10名の健康な成人女性〔年齢：22±1歳，体重：54±5kg，身長：158±7cm，随意最大筋力（MVC）：32±5kp〕が参加した．各実験では随意最大筋力（MVC）の30％の負荷で2分間握力発揮運動を維持する対照条件（Control）と，同一の運動の後に，上腕部血流を3分間阻止し運動後筋虚血（PEMI）

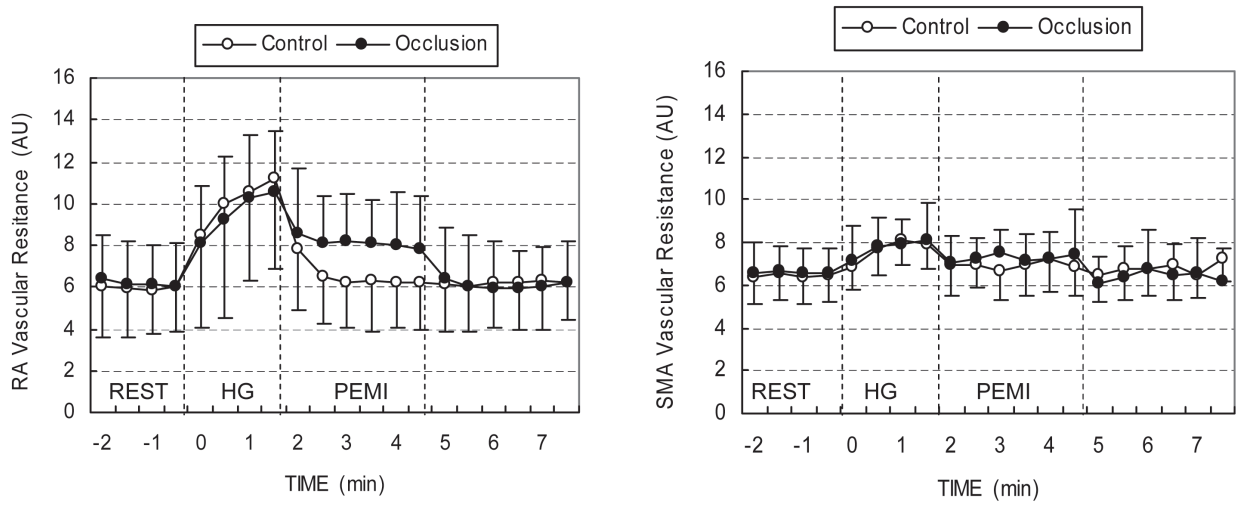

Fig. III.2.1.1-1　Renal artery (RA) vascular resistance and superior mesenteric artery (SMA) vascular resistance during rest, static handgrip (HG) exercise and postexercise muscle ischemia (PEMI) in control and occlusion conditions.

を実施する虚血条件（Occlusion）の２条件が実施された．RA 実験は食後４時間以上，SMA 実験は８時間以上を経過した後に行った．RA および SMA の動脈血流（BF）は平均血流速度および血管径（MCA は平均血流速度のみ）を超音波ドップラー法（Logic 3, Logiq5 GE Medical systems）により計測し，各動脈の血流量（BF）を算出した．平均動脈血圧（MAP, Finapress の指動脈圧波形計測）および心拍数（HR, ECG 法）により測定した．また RA および SMA 血管抵抗を MAP／RABF または MAP／SMABF の式から算出した．

● 結果と考察

（1）RA 実験：静的運動時には MAP および HR が有意に上昇し，それらの上昇量は Control と Occlusion の条件間で等しかった．PEMI 時には，Occlusion 条件の MAP だけが高値を示し HR は安静時値に戻った．腎動脈血流（RABF）は両条件ともに運動時に有意に低下し，PEMI 時に安静時値に戻った．このため RA 血管抵抗（Fig. III.2.1.1-1）が運動時に顕著に増大し，PEMI 時には Occlusion 条件が Control 条件よりも有意に高い値を示した．このような静的運動時および PEMI に対する RA 血管抵抗の応答は先行研究に一致していた（Momen *et al*. 2003）．また PET を用いて腎皮質の組織血流量を測定した Middlekauff *et al*.（1997）における成果ともほぼ一致していた．

（2）SMA 実験：静的運動時および PEMI 時における MAP と HR の反応は RA 実験と同様の結果を示した．しかし上腸間膜動脈血流（SMBF）は RABF とは異なり，静的運動時には両条件の値が安静時値に等しく，有意な変化を示さなかった．また PEMI 時には，Control 条件が安静時値に戻るのに対し，Occlusion 条件は著しく上昇した．そのため PEMI 時の SMA 血管抵抗は条件間の相違はなく，両条件ともに安静時に近い値を示した．本研究の SMA 実験における結果は，大筋群による動的運動を用いた研究（Perko et al. 1998; Puvi Rajasingham *et al*. 1997; Qamar MI and Read AE 1988）の成果とは異なっていた．これらの先行研究では，運動時の SMBF の低下あるいは SMA 血管抵抗の上昇が報告されていた．しかし，本実験と同様の掌握運動による静的運動を用いた Waaler *et al*.（1999）の研究では，本研究と同様に SMA 血管抵抗の有意な上昇は見られないことを報告していた．

これらの結果から，腹部内臓器官の血流は運動に対して画一的な反応を示すのではなく，腎動脈のように運動刺激および筋代謝受容器からの反射性入力に顕著に反応する組織（器官）と上腸間膜動脈のように反応の低い組織（器官）があり，そのために運動時の血流調節に関わる機構も異なることが示唆された．

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2.1.2　多段階の動的運動時における腎動脈および上腸間膜動脈の血流応答

Renal and splanchnic vascular responses during dynamic exercise with graded worklord

Abstract

From our previous report observed during static exercise it was hypothesized that the blood flow in the renal artery (RA) decreased more than the blood flow in the superior mesenteric artery (SMA) during dynamic exercise. To verify this hypothesis, we studied the blood flow responses in RA and SMA during dynamic exercise with graded workloads. Nine healthy female volunteers participated in the present study. After 10-min resting, the subject performed a 15-min bicycling exercise including three workloads of 30%, 50%, and 70 % of peak oxygen uptake for 5 min for each workload. During dynamic exercise, the responses in oxygen uptake, minute ventilation, mean arterial blood pressure, cardiac output, and heart rate, respectively, increased linearly with three workloads from rest to 30%, 50%, to 70% of the peak oxygen uptake. The conductance in RA, however, demonstrated a significant reduction during three workloads, by 19 ± 11 (SD) %, 29 ± 13 %, 45 ± 13 % of the value at rest for 30%, 50%, and 70% of the peak oxygen uptake, respectively. In contrast, the conductance in SMA showed no significant change from the resting level. The percent reduction of the conductance in SMA during exercise was 5 ± 15 %, 11 ± 16 %, and 19 ± 16 % for the three workloads, respectively. Thus, the present data supported the hypothesis that the renal blood flow decreased more than that in SMA during dynamic exercise with graded loads.

● 研究目的

安静時の腹部内臓器官には，心拍出量の約20％の血流が配分されるが，運動時には血流量が減少するといわれている．しかし，その減少量が，個々の腹部内臓器官により異なるのかどうかについては十分な検討がなされていない．著者らは，一定負荷（随意最大筋力の30％）の静的運動時における腎動脈血流と消化器官へ連絡する上腸間膜動脈血流の検討を行った．その結果，腹部内臓器官の血流は運動に対して画一的な反応を示すのではなく，腎動脈は運動による血流減少が顕著であるが，上腸間膜動脈では運動刺激に対する有意な変化が見られないことが示された．しかし動的運動時におけるこれらの腹部内臓血流動態に関する研究は数少ないといえる．Endo *et al*.（2008）は，若年女性が一定負荷強度（40 W）の自転車運動をした際における上腸間膜動脈および

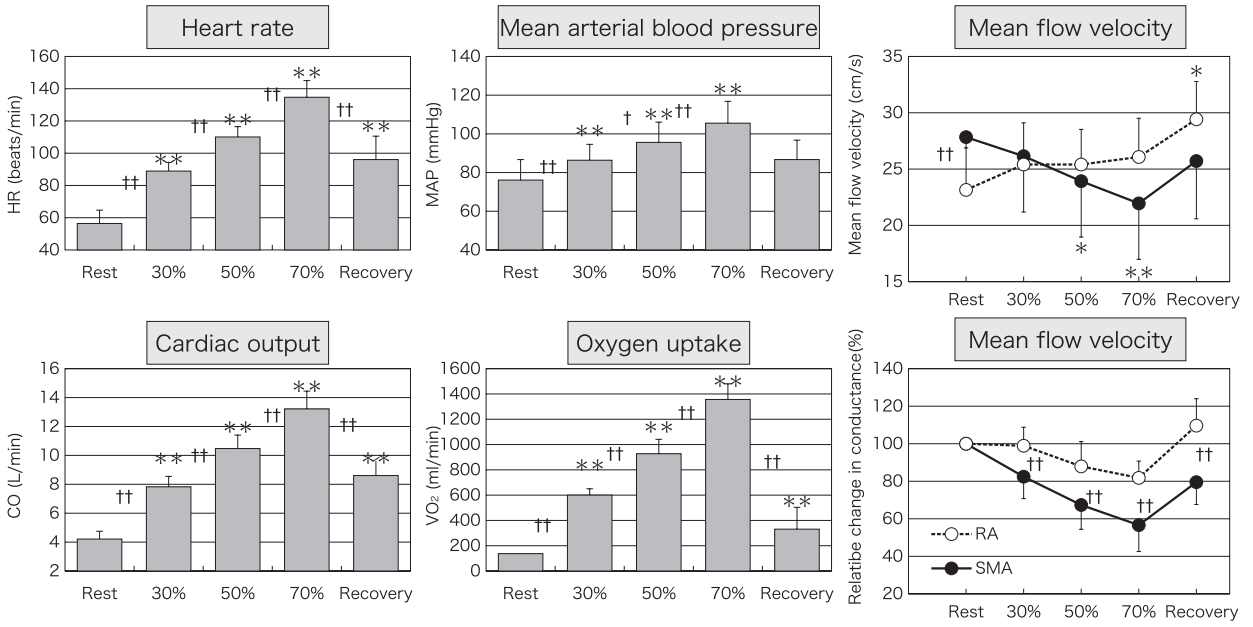

Fig. III.2.1.2-1 Heart rate, cardiac output, mean arterial blood pressure, oxygen uptake, mean flow velocity and peripheral conductance in renal artery (RA) and superior mesenteric artery (SMA) at rest and during exercise with intensity of 30%, 50% and 70% of peak oxygen uptake.

腎動脈の血流応答が異なることを報告している．彼らは種々の強度における動的運動時について比較検討してはいなかった．このようなことを踏まえ，本研究では，多段階負荷による自転車運動時における上腸間膜動脈（SMA）および腎動脈（RA）の血流応答を比較検討し，静的運動時で得られた同様の結果が示されるのかどうかについて検討することにした．

● 研究方法

健康な女子大学生９名（年齢：23±3歳，身長：162±5 cm，体重：58±5 kg，最高酸素摂取量 $\dot{V}O_{2peak}$：36±6 ml／kg・min^{-1}）が実験に参加した．5分間の安静後，30％，50％および70％ $\dot{V}O_{2peak}$ の負荷で各5分間，計15分間の自転車運動を行った．SMAおよびRAの平均血流速度を，超音波ドップラー法により（Vivid7pro，GE Medical systems）により測定した．測定には3.0 MHzのコンベックス型プローブを用いた．SMAは腹部大動脈分岐部より遠位1～2 cm，RAは右腎への流入部から近位1～3 cmの部位で測定した．心拍数（HR，心電図法），動脈平均血圧（MAP，Finometer，Finapres Medical systems），心拍出量（CO，圧波形からModel flow法により算出）および酸素摂取量（$\dot{V}O_2$，ARCO-1000，Arco System）は，3段階の各負荷の最後の1分間のデータを平均した．SMAおよびRAの血管コンダクタンスを，平均血流速度/平均血圧の式から算出し，SMAとRAの血管コンダクタンス（CSMA，CRA）とした．また安静時値を100％とした時の変化率（％）で表示した．

● 結果と考察

Fig. III.2.1.2-1にみられるように，SMA平均血流速度は運動により有意な変化が見られないが，RAでは運動強度とともに大きく減少した．また血管コンダクタンスでみると，RAの低下率がSMAに比較すると著しく大きかった．これらの結果は，静的運動時でみられたRAおよびSMAの血流応答の相違と等しい結果となった．また先行研究の報告とも一致していた（Endo *et al*. 2008; Flamm *et al*. 1990）．しかし，動的運動時のSMA血流応答についてみると，中高齢者を被験者としたPuvi-Rajasingham *et al*.（1997）の結果よりも本研究の低下率がやや少なかった．これは被験者の年齢の相違によると考えられた．このようなSMAとRAにみられる同一運動に対する応答の相違をもたらす要因として，アンギオテンシンII（Tidgren *et al*. 1991），エンドセリン-1

(Maeda *et al*. 2002)，交感神経活動の地域差等が考えられる．また交感神経活動の地域差をもたらす要因として圧受容器（Collins *et al*. 2001），筋代謝受容器や筋機械受容器（Momen *et al*. 2003）からの反射性制御が腎と消化器官では異なるということも考えられる．今後の詳細な検討が必要である．

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2.2　運動時の脳血流動態とその調節

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Cerebral blood flow regulation during exercise

2.2.1　静的運動および運動後筋虚血に対する脳血流動態

Cerebral blood flow responses to static exercise and postexercise muscle ischemia

Abstract

To elucidate the cerebral blood flow responses to static exercise, we measured arterial blood flow responses in three sites of “the carotid artery root” and one site of “the vertebral artery root”. Ten healthy female volunteers performed a 3-min sustained static handgrip exercise with ramp load increasing from 10% to 30% of maximum voluntary contraction followed by a 3-min postexercise muscle ischemia (PEMI). The blood flow (BF) in left common carotid artery (CCABF), the left internal carotid artery (ICABF), and the left vertebral artery (VABF) was measured by ultrasonography. Mean flow velocity in the left middle cerebral artery (MCAV) was also recorded. Mean arterial blood pressure (MAP; Finapres) and heart rate (HR; ECG). The vascular resistance (VR) was calculated from the ratio of MAP to the CCABF, ICABF, VABF, or MCAV. During static exercise (Fig. 1) the vascular resistance in all arteries increased from the resting level in parallel with the increase in MAP, but the magnitude of increase was greater in the “carotid artery root” than the “vertebral artery root”. During PEMI, CCABF-VR, ICABF-VR, and MCA-VR were significantly higher than the resting level, whereas VABF-VR returned to the resting level. These data suggested that the static exercise produced greater vasoconstriction in the “carotid artery root” than the “vertebral artery root” and that the muscle metaboreflex played an important role in vasoconstriction in the “the carotid artery root” but not in the “vertebral artery root”.

● 研究目的

脳への血流は左右の内頸動脈経路（主に大脳皮質側頭葉，前頭葉，頭頂葉，島皮質へ潅流）と椎骨動脈経路（主に延髄，小脳，後頭葉へ潅流）の２経路により供給される．しかし頸動脈経路における中大脳動脈の血流動態をみた研究は多いが（Jørgensen *et al*. 1999），椎骨動脈経路の血流動態に関する報告は数少ない．内頸動脈経路は大脳への血液供給が主体であるが，椎骨動脈経路の血流は，延髄，小脳，脳幹といった運動遂行に重要な部位への血液供給を担っている．この両経路が潅流する部位の違いを反映するような血流動態の相違が運動時にもみられるのかどうかについては不明である（Hellestrom *et al*. 1996; Pott *et al*. 1997）．このような点を踏まえ，本研究では静的運動時および運動後筋虚血時における頸動脈経路と椎骨動脈経路の血流動態を検討することとした．

● 研究方法

被験者は10名の健康な成人女性〔年齢：21 ± 1歳，身長：158 ± 7cm，体重：57 ± 9kg，随意最大筋力（MVC）：30 ± 5kp〕が，２分間の安静後，最大筋力の10％から30％まで上昇するランプ負荷を維持する静的握力発揮を３分間行った．その後，３分間の運動

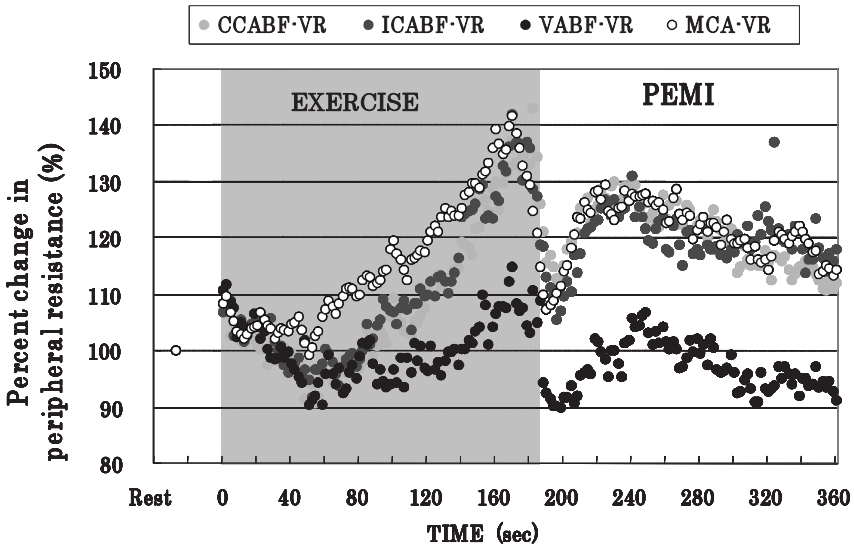

Fig. III.2.2.1-1 Percent changes in vascular resistance in common carotid artery (CCABF-VR), internal carotid artery (ICABF-VR), middle cerebral artery (MCA-VR) and vertebral artery (VABF-VR) during rest, static handgrip exercise, and postexercise muscles ischemia (PEMI). For the calculation of MCA-VR, mean flow velocity was used instead of volume blood flow. Resting vascular resistance was defined as 100%, and shadow area indicates exercise period in the figure.

後筋虚血（PEMI）を行った．平均動脈血圧（MAP, Finapress指動脈圧波形計測）および心拍数（HR, ECG法）により測定した．総頸動脈（CCA），内頸動脈（ICA）および椎骨動脈（VA）における血流量（BF）を，また中大脳動脈（MCA）では平均血流速度を超音波ドップラー法（Logic 3, Vivid 7）により計測した．各動脈の血管抵抗を平均血圧とBF（MCAは平均血流速度）の比として算出した．

● 結果および考察

HRおよびMAPは，運動後半にかけて著しく上昇した．そして，PEMI時にはHRは安静値に戻るが，MAPは安静値より高い値を示した．頸動脈経路におけるBFは，運動開始早期に増加するが，その後は一定値で維持された．そしてPEMI時には安静値まで戻った．一方，椎骨動脈経路におけるBFは，静的運動開始から終了まで漸増した．またPEMI時においても安静値よりも高い値を維持した．このため血管抵抗が（Fig. III.2.2.1-1），頸動脈経路では静的運動時の値が安静値から約50％も上昇したが，椎骨動脈経路では約10％程度の上昇にすぎなかった．PEMI時では，頸動脈経路の値は安静値に比べ有意に高いが，椎骨動脈経路ではほぼ安静値またはそれ以下の値を示した．このような結果は，運動負荷に対する頸動脈経路と椎骨動脈経路の血流動態が異なることを示していた．頸動脈経路では，血圧上昇に対して血管収縮作用により血流を制限するが，椎骨動脈では血管収縮作用が少なく血流の流入を許す経路という特徴がみられた．このような経路の相違をもたらす仕組みは，運動時に活性化する脳細胞代謝に起因するのか，両経路の脳血管の自動調節能の相違なのか，あるいは圧反射などの神経調節活動の関与の相違なのかは明らかではない（Querido and Sheel 2007）．

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2.2.2 Comparison of the blood flow responses between internal carotid and vertebral artery during dynamic exercise

Abstract

The development of the Doppler ultrasonography technique enabled the measurement of the change in the blood flow in the extra- and intracranial arteries at rest and during exercise. The purpose of the present study was to clarify the effect of exercise intensity on the cerebrovascular response in the ICA and VA during semi-recumbent bicycle exercise by using the Doppler ultrasound technique. A total of 10 healthy young adults (1 man, 9 women) [age: 22.5 ± 2.5 years (mean ± SD)] participated in this study. The exercise consisted of a 5-min baseline followed by levels of exercise load at 30%, 50%, and 70% of the power of the $\dot{V}O_{2peak}$ with 5-min duration of each stage. We continuously monitored cardiovascular (Model flow method with finometer), ventilatory (breathe-by-breathe method), internal carotid artery blood flow ($\dot{Q}_{ICA}$), and vertebral artery blood flow ($\dot{Q}_{VA}$) at rest and during exercise. $\dot{Q}_{ICA}$ and $\dot{Q}_{VA}$ was measured by a Doppler ultrasound system and cerebrovascular resistance index (CVR_{ICA} and CVR_{VA}) were also calculated as MAP divided by CBF. In this study, mean arterial pressure (MAP) and end-tidal partial pressure of CO_2 (P_{ET} CO_2) increased significantly with increase of exercise intensity. $\dot{Q}_{ICA}$ increased by 12 ± 2% during 30% $\dot{V}O_{2peak}$ and reached a maximum 8 ± 3% during 50% $\dot{V}O_{2peak}$. However, during 70% $\dot{V}O_{2peak}$, increase in $\dot{Q}_{ICA}$ had a level off, in contrast to a continued increase in CVR_{ICA} throughout exercise. On the other hand, $\dot{Q}_{VA}$ increase in proportion to the increase of exercise intensity (17 ± 3, 33 ± 4, and 40 ± 4% at 30, 50, and 70% $\dot{V}O_{2peak}$, respectively). In addition, CVR_{VA} did not change from the resting level throughout exercise. These data suggested that during dynamic exercise the blood flow responses in VA and ICA are different. The difference might be mainly explained by CVR responses.

● Purpose

The development of the Doppler ultrasonography technique enabled the measurement of the change in the blood flow in the extra- and intracranial arteries at rest and during exercise, i.e., the common carotid artery (CCA), internal carotid artery (ICA), vertebral artery (VA), and middle cerebral artery (MCA). Hellstrom *et al*. (1996) demonstrated using the Doppler ultrasound that the blood flow in the CCA, ICA, and MCA increases during graded dynamic exercise, indicating an increase in the blood flow in the carotid artery and a large part of the brain. Interestingly, they reported that compared with moderate exercise (60% maximal oxygen uptake ($\dot{V}O_{2max}$), heavy exercise (80% $\dot{V}O_{2max}$) tended to reduce blood flow in the ICA and MCA. However, the blood flow response in the VA during dynamic exercise has not been evaluated and the effect of exercise intensity on CBF during dynamic exercise is less clear. Therefore, the purpose of the present study was to clarify the effect of exercise intensity on the cerebrovascular response in the ICA and VA during dynamic exercise by using the Doppler ultrasound technique.

● Methods

A total of 10 healthy young adults (1 man, 9 women) [age: 22.5 ± 2.5 years (mean ± SD), height: 163.0 ± 5.9 cm, body mass: 57.6 ± 5.1 kg, and peak oxygen uptake ($\dot{V}O_{2peak}$): 37.3 ± 5.4 $ml/kg \cdot in^{-1}$] participated in this study. The procedure consisted of a 5-min baseline period (Rest), followed by exercise with loads of 30%, 50%, and 70% of the power at with $\dot{V}O_{2peak}$ occurred in the upright position, with each stage lasting for 5 min. The mean blood flow in the ICA ($\dot{Q}_{ICA}$) and the VA ($\dot{Q}_{VA}$) were measured with a high-resolution

ultrasound system (VIVID7 PRO and LOGIQ5, GE Medical Systems, Japan) equipped with a 10 MHz linear transducer. The mean MAP was measured non-invasively by photoelectric plethysmography with a Finometer (Finapres Medical Systems BV, Netherlands). Furthermore, the heart rate (HR), stroke volume (SV), and thus cardiac output (CO), were determined from the blood pressure wave form with the aid of the Modelflow software program, which incorporates gender, age, height, and weight (Beat Scope 1.1, Finapres Medical Systems BV, Netherlands). The CO was calculated as SV × HR. Ventilatory parameters were determined with an online system for the breath-by-breath method.

● Results and Discussion

Carotid blood flow studies using Doppler ultrasound measurements have been used to evaluate changes in the gCBF. Such measurements might be of value when estimating changes in the blood flow in the ICA. We observed that $\dot{Q}_{ICA}$ increased by ～12% during exercise with 30% $\dot{V}O_{2peak}$ and with a maximum increase of ～18% during exercise with 50% $\dot{V}O_{2peak}$. However, exercise with 70% $\dot{V}O_{2peak}$ did not further increase $\dot{Q}_{ICA}$ compared with the value at 50% $\dot{V}O_{2peak}$. In contrast to $\dot{Q}_{ICA}$ response that leveled off at 70% $\dot{V}O_{2peak}$, graded exercise significantly increased $\dot{Q}_{VA}$ with increasing exercise intensity. Thus, we considered that the blood flow responses during dynamic exercise should differ in responses between ICA and VA.

The differential responses of the ICA and VA blood flow during dynamic exercise should be mainly explained by the difference in the CVR responses. It is possible that there is little sympathetic and autoregulatory control of the blood flow and cerebrovascular in the peripheral branches of the VA as compared with the peripheral branches of the ICA. In this case, $\dot{Q}_{VA}$ passively increased with the MAP and CO during dynamic exercise. Nevertheless, this is speculation, given that there is no evidence to suggest regional differences in sympathetic and autoregulatory control in humans brain study. The other mechanism could contribute the difference in the CVR in the ICA and VA. First, the difference in the areas of the brain supplied by the ICA and VA may be a contributory factor. In a previous animal study, submaximal and maximal exercise induced small increases in the vascular resistance in the regions of the brain that were related to motor control and locomotion (spinal cord and cerebellum), maintenance equilibrium (cerebellum and vestibule), and cardiorespiratory control (medulla and pons), which are mainly supplied by the peripheral arteries of the vertebrobasilar sys-

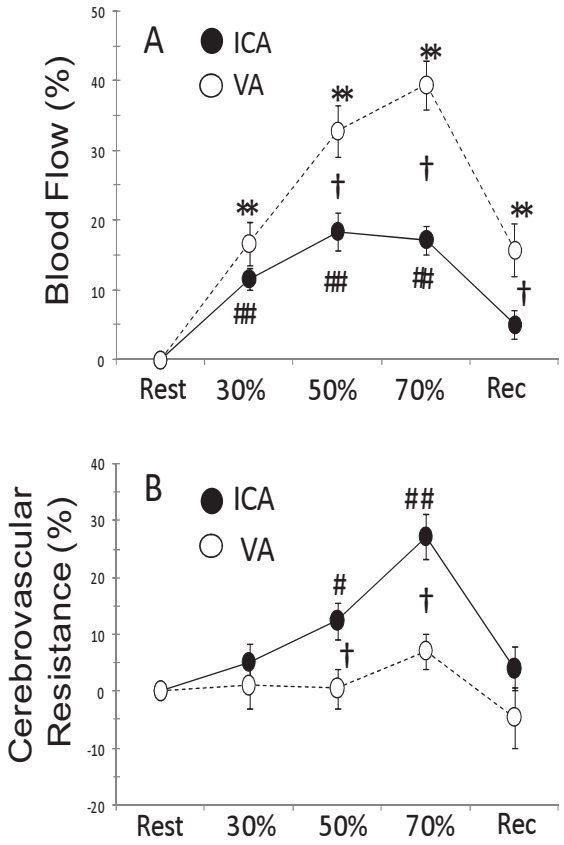

Fig. III.2.2.2-1 (A) Change (%) in blood flow in the ICA and VA during dynamic exercise and recovery. (B) Change (%) in the cerebrovascular resistance in ICA and VA during dynamic exercise and recovery. Values are means ± SE. 30%, 30% $\dot{V}O_{2peak}$; 50%, 50% $\dot{V}O_{2peak}$; and 70%, 70% $\dot{V}O_{2peak}$; Rec, Recovery. *, ##: significantly different from the Rest ($P < 0.05$). †: significant ($P < 0.01$) difference between ICA and VA.

tem, as compared with the cortical regions associated with motor and somatosensory functions (frontal cortex), which are mainly supplied by the peripheral branches of the ICA (Delp *et al*. 2001). A second, possibility is that two or more opposing and offsetting vasodilatory stimuli and substance are present in peripheral branches of vertebral-basilar system. There may be a sympathetic vasoconstriction in response to the increase in perfusion pressure, and simultaneously an equivalent vasodilatory stimulus resulting from increase neuronal metabolic release. In this case, the net effect is that vascular resistance remains unchanged as in our result of CVR_{VA}. Third, morphological differences in the two arteries might be directly connected with this phenomenon. Within the cranium, the two VA fuse into the basilar artery. In contrast, the two ICA independently run up to the brain. Accordingly, it is considered that several factors may contribute on the difference in the CVR in the ICA and VA. However, the detailed mechanism underlying the differential CVR responses of ICA and VA are unclear. Further investigation is required to clarify this.

In conclusion, during dynamic exercise, the increase in the $\dot{Q}_{ICA}$ had leveled off at 70% $\dot{V}O_{2peak}$, in contrast to a continued increase in the $\dot{Q}_{VA}$ increased with increasing exercise load. This difference might be induced by the difference in the CVR response to graded dynamic exercise.

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2.3　発育期の子どもにおける循環機能の発達

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Development of cardiovascular function in children

Abstract

To understand the development of cardiovascular functions, we studied age-related changes in cardiac output, total peripheral resistance, cerebral blood flow and the index of cerebral flow distribution in 207 healthy female children between 10 and 18 years of age. Mean arterial blood pressure (MAP) was measured non-invasively by photoelectric plethysmography with a Finometer. Heart rate (HR) and stroke volume (SV) and cardiac output (CO) were determined from the blood pressure waveform by using Model flow software program. The blood flow in left common carotid artery (BFCCA) was measured during sitting rest by ultrasonography. The index of cerebral blood flow distribution (%) was calculated as $BF_{CCA}/CO \times 100$. The total peripheral resistance, an index for changes in vascular growth, was calculated as MAP/CO. CO began to increase from 11 years and was nearly complete by 15 years. The increase in CO was due to a significant increase in SV since HR tended to decrease from 10 to 15 years. TPR decreased also from 10 to 15 years indicating a significant growth in the vascular beds of whole body. BF_{CCA} gradually decreased from 10 to 15 years and the index of cerebral flow distribution (18 %) was highest at 10 years and followed by a gradual decline to 15 % at 15 years of age. Over the age of 15 years, the values in CO, TPR, BF_{CCA} and the index of cerebral blood flow distribution were almost stable and identical to those in adult females. The present data suggested that the development in cardiovascular functions and cerebral flow distribution are accomplished by the age of 15 years in females.

● 研究目的

循環機能の発達について知ることは，発育期の子どもの運動を考えるために不可欠である．しかし循環機能の発育に関する研究は数少ない（加賀谷，2006）．本研究では，心臓および血管機能の発達という観点から，心臓のポンプ能力の指標となる心拍出量と血管床の成長指標として総末梢血管抵抗の変化を検討することにした．また中心循環と末梢循環の発達という観点から，心拍出量に対する脳血流量の比（脳血流配分）について検討することにした．末梢組織のなかから脳を取り上げる理由は，脳血流量の発育に関する研究が特に少ないからである（Schöing and Hartig,1996; 1998）．

本研究の目的は，10歳から18歳における発育期における心拍出量，総末梢血管抵抗，脳血流量，脳血流配分の変化を検討し，子どもの循環機能の発育過程を明らかにすることである．なお本報告では女子の結果について報告する．

● 研究方法

健康な小学生5年生（10～11歳），6年生（11～12歳），中高生（12～18歳）の合計207名の被験者とした．本研究では，座位安静時の循環変数として動脈血圧（MAP），心拍数（HR），1回拍出量（SV），心拍出量（CO）を測定した．また脳血流量の指標として，左総頸動脈の血流量（BF_{CCA}）を計測することにした．MAPはフィノメーター（Finapres Medical Systems BV）により測定し，またその指動脈波形からSVをModel Flow法を用いて推定し，同じく圧波形の間隔からHRを算出した．そしてSVとHRの積からCOを算出した．BF_{CCA}の測定には超音波画像診断装置（Logiq5，GE Medical Systems）を用いた．総末梢血管抵抗（TPR）はMAP／COの式から，脳血流量配分指標（%）はBF_{CCA}／CO × 100の式から算出した．

● 結果および考察

HRは小5（10歳）から高1（16歳）にかけて徐々に減少したが，SVが小6（11歳）から高1（16歳）

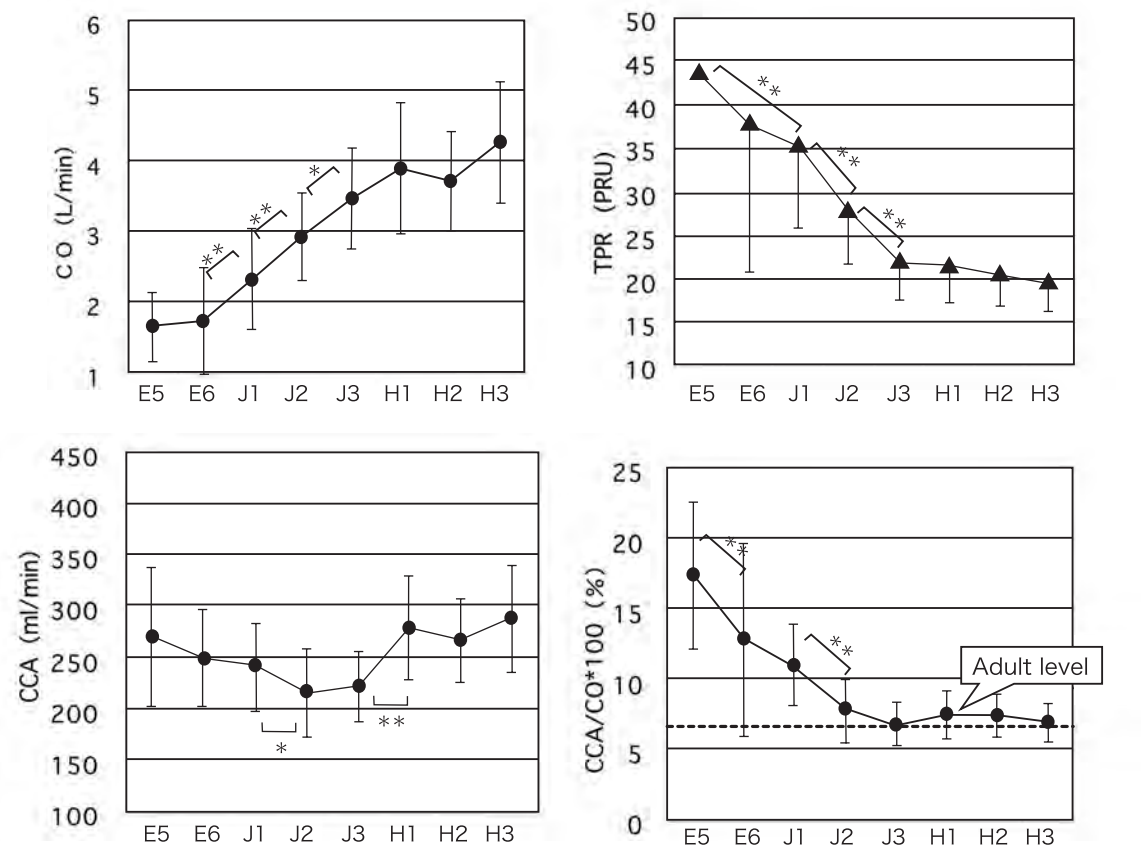

Fig. III.2.3-1　Developmental changes in cardiac output (CO), total peripheral resistance (TPR) and cerebral blood flow (CCA) and index of cerebral flow distribution (CCA/CO*100) from 10 to 18 years of age in female. The horizontal axis indicates the grade of elementary school (E), junior high school (J), and high school (H). *; $p < 0.05$, **; $p < 0.01$.

にかけて急激な上昇を示した．その結果，COが小6から高1間において著しく増大した．その後のCOには有意な変化はみられなかった（Fig. III.2.3-1）．同様に，全身の血管床の発達を示す指標であるTPRの低下は，小5（10歳）から始まり中3（15歳）にかけてみられた．このようなSVおよびCOの変化に関する結果は，心エコー法により8歳～18歳までの男女の左心室の拡張期内径と収縮期内径を計測した清水ら（1999）の結果とほぼ一致していた．またHRの低下についても先行研究（Malina and Roche 1983）と一致した．BF_{CCA}は小5から中2，3にかけて減少した．そして中3～高1間において有意な増加がみられ，高1以降には変化がみられなかった．このようなBF_{CCA}の変化は，ドイツ人の脳血流を検討した先行研究と類似していた（Schöing and Hartig, 1996; 1998）．上述したように，BF_{CCA}は小5から中2，3にかけて減少し，同時にCOが小6から高1間において著しく増大するため，脳血流配分指標は，小5で最も高く，中2にかけて低下し、中3（15歳）ではほぼ成人に近い値を示すことになった．

このように心機能（推定心拍出量），血管機能（総末梢血管抵抗），脳血流配分が小学高学年から中学生にかけて発達することが示された．このような結果から，最も発育するこの時期に循環機能を高めるため適切な運動や働きかけが必要であると考えられる．本研究は女子に関する知見であり，今後男子のデータを含めた検討が必要である．

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3　運動時の筋交感神経活動からみた中枢指令および反射性制御の調節機構

斉藤　　満[1)]

Analysis of central command and reflex regulation of cardiovascular system during exercise with respect to muscle sympathetic nerve activity

Mitsuru Saito

■本課題の共同研究者
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3.1　利き腕，非利き腕運動時の交感神経反応

斉藤　　満，相澤　清香，神谷　厚範

Comparison of sympathetic nerve activity responses between dominant and nondominant arm

Abstract

The aim of this study was to investigate whether muscle sympathetic nerve activity (MSNA) during handgrip exercise performed with the dominant (D) and nondominant arm (ND) was different. Intermittent static handgrip with maximal effort and rhythmic handgrip under the forearm circulation arrest with maximal effort followed by two 2-min post exercise arterial occlusion (PEAO) were used for test exercises. MSNA was recorded from the tibial nerve by microneurography. MSNA increased during intermittent static exercise while the response was not different between D and ND. During rhythmic handgrip and PEAO, MSNA increased 197% and 369% of resting value for D and 140% and 197% for ND respectively, and those differences between D and ND was significant. The different MSNA responses in D and ND may be due to the difference in size of muscle metaboreflex than that exercise effort.

● 目　的

左右の手の使い方には差があり，使用頻度は一般に利き腕で高く，大きな力発揮や調節が必要なときに用いられることが多い．このような手の使い方の違いは大脳皮質レベルでの差や前腕筋機能，運動時の交感神経活動反応の差としてみることができる．本研究では，神経性循環調節の中心的な役割を果たす筋交感神経活動（MSNA）を左右のハンドグリップ運動において比較検討することにより，循環調節に対する中枢性および末梢性の効果を明らかにすることを目的とした．

● 方　法

健康な右利き成人男子16名を対象とし，2種類の運動を行わせた．運動1として，中枢指令の左右差を確認するため，15秒間最大努力静的ハンドグリップ（HG）運動を15秒の休止を挟んで左右交互に20回繰り返す間欠運動．運動2として，代謝受容器反射の比較として動脈阻血下において律動的HGを1分間に40回，最大努力で実施し，運動後阻血（PEAO）のMSNAを比較した．

測定項目はMSNA，HG張力，心拍数，血圧であった．MSNAはバースト総面積として定量化した．HG張力曲線より運動時の作業量を計測した．

主効果および左右の比較は繰り返しのある分散分析で検定した．

● 結果および考察

利き腕，非利き腕の最大HG張力はそれぞれ48±2kg，44±2 kg（SD±SEM）（P＝0.056）であり，利き腕が高い傾向にあったが差は認められなかった．

1）運動1：間欠運動

間欠HG運動のピーク張力，作業量は運動回数とともに低下したが，MSNAは運動の1回から有意に増加し10回まで高値を維持した．心拍数は運動開始とともに増加したがMSNA反応と同様に1回から10回までほぼ一定値を示した（Fig. III.3.1-1）．HG張力，MSNA，心拍反応ともに左右差は認めなかった．

運動時のMSNA増加には中枢指令と活動筋反射が関係するが（Mitchell 1990），運動開始直後の活動筋反射の効果は小さい（Hashimoto *et al*. 1998）．従って，本研究で用いた15秒間の間欠的HG運動において，運動回数の増加とともにHG張力が低下し，筋

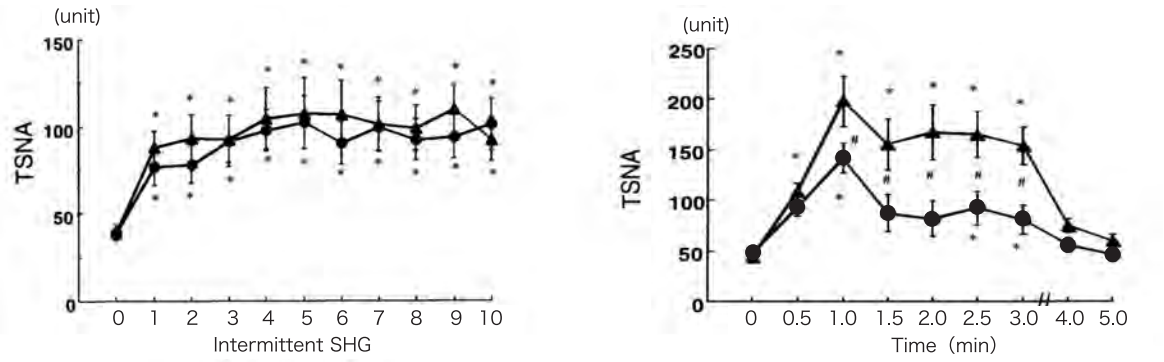

Fig. III.3.1-1　Comparison of muscle sympathetic nerve activity between dominant and nondominant arm during intermittent static handgrip exercise (left panel) and ischemic rhythmic handgrip exercise and post exercise arterial occlusion (right panel). ▲: dominant arm, ●: nondominat arm, * $p < 0.05$ compare to the resting control, # $p < 0.05$ dominant vs nondominantarm.

機械受容器の刺激が弱まったにもかかわらずMSNAが最後まで高値を持続した原因として中枢指令の効果が考えられる．他方，代謝受容器反射については，間欠運動休止期のMSNA活動が安静値に戻ったことから，代謝受容器刺激の効果は小さい．したがって，MSNA増加に対する中枢指令の効果は考えられるが，左右差はないといえる．また，心拍反応に関しても左右差はないと考えられる．これらの結果から，交感神経活動に対する中枢指令の効果は随意運動に共通する効果を持ち，活動肢の違いによる影響はないと考えられる．

2）運動２：動脈阻血下運動

動脈阻血下運動のピーク張力は利き腕，非利き腕がそれぞれ40 ± 2 kg，35 ± 1 kg，仕事量が880 ± 8 kg/分，760 ± 45 kg/分で，左右差は認められなかった．

運動の後半30秒間のTSNAは利き腕運動が安静値より344％，非利き腕運動が192％増加した．PEAO２分間のMSNAは利き腕，非利き腕がそれぞれ安静値より369％，197％増加した．運動およびPEAOのMSNA増加率は非利き腕より利き腕運動が高かった（Fig. III.3.1-1）．運動時の心拍数は高まったが，PEAOでは安静値まで低下した．心拍および血圧反応はともに左右差は認められなかった．

HG作業量は左右で差がなかったことから，運動時の代謝量に違いがあったとは考えられない．したがって，利き腕の代謝受容器反射が高くなった原因には，代謝以外の要因が考えられる．運動時のMSNA反応は速筋線維分布の高い筋の収縮時に高くなることから[3]，利き腕と非利き腕の筋線維組成が異なるのかもしれない．あるいは，利き腕調査の結果，「重いものを持つには利き腕を使う」という回答が多いことから（Saito 1995），速筋線維の動員が非利き腕運動より促進された可能性が考えられる．

左右運動時の代謝受容器反射の差には利き腕と非利き腕の日常的な手の使い方が反映され，この差は中枢より末梢レベルで生じる可能性の高いことが示唆される．

● 文　献

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3.2　運動時の筋交感神経活動に及ぼすレジスタンストレーニングの効果

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Effect of resistance training on the muscle sympathetic nerve activity during handgrip exercise

Abstract

To reveal the effect of resistance training on central and muscle reflex control of muscle sympathetic nerve activity (MSNA) during exercise, MSNA was investigated pre- (PRE), post-training (POST) and 4 weeks detraining after resistance training using fatigue-inducing handgrip exercise and post-exercise forearm occlusion (PEFO). Eighteen volunteers underwent forearm training, which contained 30 maximal effort, 10-s-duration static handgrips 4 days per week for 4 weeks. MSNA was recorded from the tibial nerve by microneurography. Maximal handgrip force increased at POST. The MSNA response during fatigued handgrip also increased at POST, as compared to PRE (52 ± 5 vs. 40 ± 4 bursts/min (mean ± SEM) respectively. However, at detraining, MSNA activity returned to PRE level (44 ± 5 bursts/min; $p < 0.0001$). The MSNA response during PEFO was constant throughout the experiment. The results indicate that an increased MSNA response after resistance training is likely to be the result of central command rather than the muscle metaboreflex.

● 目　的

身体トレーニングは心拍出量の増大や筋血流量の増加，運動時の心拍数や血圧の低下を伴う．これらの適応変化には交感神経活動の変化が関係すると考えられる．これまで，持久トレーニングに対する運動時の筋交感神経活動の反応は低下することが報告されているが，レジスタンストレーニング（RT）に関しては一定の見解は得られていない（斉藤 2004）．本研究では，RTは末梢活動筋だけでなく上位中枢からの中枢指令にも影響するとの仮説に基づいて，トレーニング前後の運動時の筋交感神経活動（MSNA）反応からレジスタンストレーニングの効果について検討した．

● 方　法

健康な成人男子18名を対象とし，9名は非利き腕を用いたRTを実施，残り9名は対照群とした．トレーニングは10秒間の最大努力静的ハンドグリップ（HG）運動を10秒間の休憩を挟んで10回繰り返す手順を，1日3セット，週5回，4週間実施した．

テスト運動：中枢指令と代謝受容器反射の効果を確かめる目的で最大HG張力（MVC）の33％張力が維持できなくなるまで持続する静的HGとこれに続く2分間の運動後阻血を用いた．運動テストはトレーニング前，トレーニング後，およびトレーニング停止4週後に実施した．

測定項目はMSNA，心拍数，血圧，HG張力であった．MSNAは脛骨神経より記録，1分間のバースト発射数（BF）で表した．心電図は胸部双極誘導により，血圧はフィナプレスにより測定した．

トレーニング前後の最大握力，仕事量，運動および運動後阻血下のMSNA，心拍数，血圧反応は繰り返しのある分散分析で検定し，下位検定にはWilcoxon testを適用した．

● 結果および考察

1）ハンドグリップ張力

トレーニング群の最大HG張力はトレーニング後17.6％（$P < 0.05$）増加し，トレーニング停止4週後も有意に高いHG張力が維持された．これに対し，対照群の最大HG張力はトレーニング前，後，トレーニング停止4週後の期間に有意な変化は認められなか

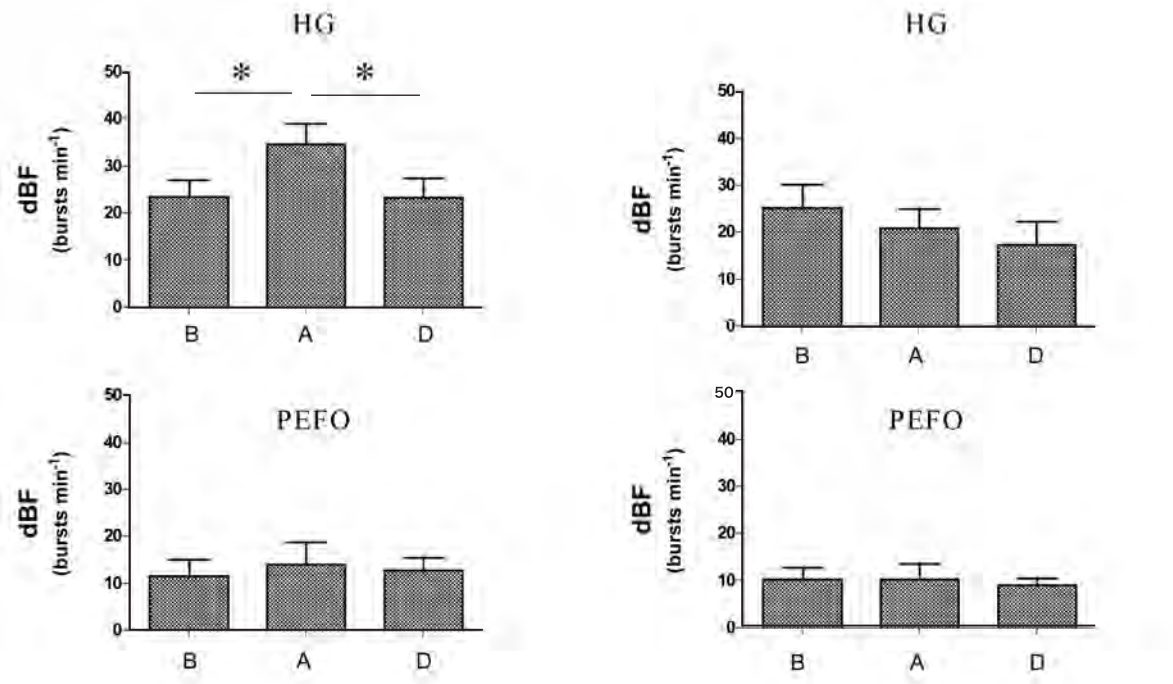

Fig. III.3.2-1　Comparison of the changes in burst frequency (dBF) during fatiguing handgrip exercise (HG) and post exercise forearm occlusion (PEFO) at pre-training (B), 1 week post-training (A) and 4 weeks post-training (D) in the trained (left panel) and control group (right panel). * $p < 0.05$ compared to the pre-training or 4 weeks post-training values.

った．

6週以下の短期間のRTに伴う筋力向上は筋収縮に動員される運動単位数の増加が主要因とされる（Sale 1988）．今回は4週間の最大努力HG運動を用いたことから，中枢指令を含めた運動神経機能の向上が筋力増加の主要因と考えられる．トレーニング停止後も高い張力が持続した背景には，高い運動神経機能が維持されたためと考えられる．

2）運動時の生理反応

Fig. III.3.2-1に33％MVC張力が維持できなくなるまで持続するHG運動とそれに続く動脈阻血時のMSNA反応の結果を示す．運動時のMSNA反応はトレーニング後有意に増加し，トレーニング停止4週後にはトレーニング前値に戻った．しかし，代謝受容器反射が反映される運動後阻血時のMSNA反応は研究期間を通して一定であり，トレーニング効果は認められなかった．対照群のMSNA反応は運動時および運動後阻血時ともに研究期間を通してほぼ一定であった．トレーニング群，対照群ともに運動時，運動後阻血時の心拍数，血圧反応は研究期間を通して変化は認められなかった．

筋反射が反映される運動後阻血時のMSNA反応がトレーニング期間を通して一定であったことから，運動時のMSNA反応の増大には中枢指令の効果が大きく関与した可能性が推察される．本結果は，MSNA反応はRTの影響を受けないか低下するとされるこれまでの結果（斉藤 2004）とは異なった．おそらくこの背景にはトレーニングに用いた運動強度の違いが影響したと考えられる．これまでのRT研究では30％MVC程度の負荷を用いているが，本研究ではより高強度の最大努力筋収縮を用いた．このことが，中枢指令に対する効果を有意にしたと推察される．

本結果から，高強度レジスタンス運動は運動時の中枢指令に影響を及ぼすが，代謝受容器反射への効果は小さいことが明らかとなった．

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4 Effects of Different Exercise Modalities on Skeletal Muscle and Prefrontal Cortex Oxygenation Monitored by Near Infrared Spectroscopy

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Effects of Different Exercise Modalities on Skeletal Muscle and Prefrontal Cortex Oxygenation Monitored by Near Infrared Spectroscopy

Valentina Quaresima

Abstract

The research activity has mainly been focused on the study of the vascular and metabolic mechanism regulating the cerebral and muscular oxygenation and metabolism by using near infrared spectroscopy (NIRS) and functional NIRS with a multidisciplinary approach. In particular, the results want to give a contribution for: 1) understanding the mechanism of the muscle fatigue during exercise and the kinetics of the transition rest-exercise, and 2) supporting the hypothesis that prefrontal/frontal lobe plays a role in maintaining strength of the forearm muscles and ensuring a correct execution of motor tasks which require a fine motor control and coordination.

4.1 Metabolic pattern of the leg skeletal muscle groups during very short and intense isometric exercise

The purpose of the study was to assess on heavy-resistance strength trained and untrained subjects the vastus lateralis (VL) muscle O_2 saturation (TOI) time course in response to a brief maximal voluntary isometric contraction.

● Methods

Trained (n = 10) and untrained (n = 10) subjects performed a trial consisting of: 1) a 1-min rest period, 2) a leg press exercise of about 3 s, and 3) a 2-min recovery period. The leg press exercise consisted of a static maximal voluntary contraction using only the dominant leg. The leg press strength was recorded using a load cell. The TOI was measured by NIRS (NIRO-300; 0.17 s sampling time).

● Results

Fig. III.4.1-1 left panel shows the VL oxygenation pattern observed in a athlete. TOI was unchanged over the 3-s exercise and started to drop immediately after the exercise end. Fig. III.4.1-1 right panel shows the typical TOI pattern of a sedentary subject. TOI was stable only over the first 1.5-2.0 s of the exercise; thereafter, TOI started to decline. The time to the onset of TOI decrease was consistently shorter in the untrained than in the trained subjects. In all the trained subjects, TOI started to decrease 0.5-1.0 s after the end of the contraction. After the end of the exercise, TOI transiently decreased reaching its minimum value in about 15 and 10 s in the trained and untrained subjects, respectively.

In conclusion, the results of this *in vivo* study demonstrated that the aerobic oxidative metabolic system occurs earlier in untrained than in strength power trained subjects upon a very short isometric high-intensity exercise. From this point of view, NIRS could be employed to: 1) profile in each muscle group the aerobic and, indirectly, anaerobic energy system contribution during even single brief maximal exercise, and 2) follow the

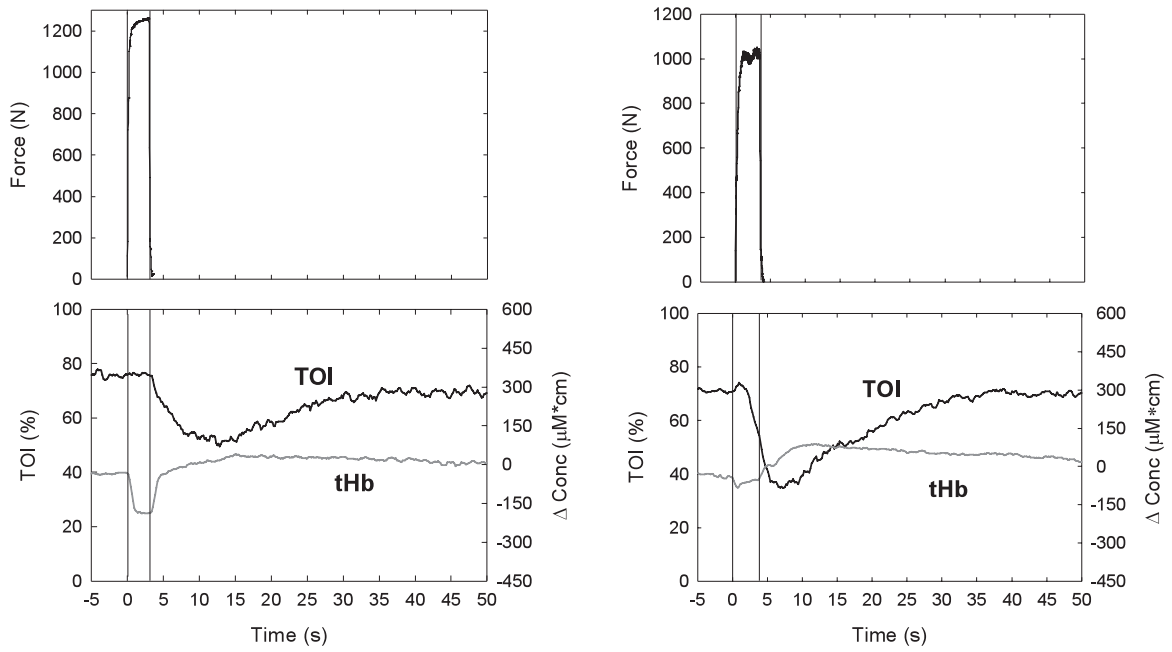

Fig. III.4.1-1 Left: Time course of leg force output (upper panel), and vastus lateralis TOI and tHb (lower panel) before, during, and after static leg press exercise. Right: Time course of leg force output (upper panel), and vastus lateralis TOI and tHb (lower panel) before, during, and after static leg press exercise.

alteration of the profile as function of specific aerobic or anaerobic training or rehabilitation programs.

The details of this study are reported in the previous study (Cettolo *et al*. 2007).

4.2 Acute effects of whole body vibration exercise (an alternative exercise intervention) on gastrocnemius medialis and vastus lateralis oxygenation

Whole body vibration (WBV) has been promoted as an alternative exercise intervention able to affect neuromuscular performance in young and old individuals. This new neuromuscular training method consists of squatting on specially designed plates producing sinusoidal oscillations of different frequencies and amplitudes. It has been suggested that the sinusoidal vibration generated by the plate oscillations elicits reflex muscle activity in the lower limbs mainly via monosynaptic pathways. Muscle activation during squat exercise on vibrating surfaces is still a controversial topic. Vibration exercise intensity can be determined by manipulating two parameters: amplitude and frequency. In most of the vibrating plates currently available on the market, vibration frequency is the only parameter that can be changed, and notwithstanding manufacturers' instructions, there is no real evidence to suggest the optimal training frequency to be adopted. Therefore, the determination of the effects of different WBV frequencies on muscle oxidative metabolism represents an important aspect to be analysed in order to provide guidelines for WBV training programs. Considering the lack of information regarding muscle oxygenation during WBV exercise, we aimed at investigating the effects of different WBV frequencies on oxygenation of VL and gastrocnemius medialis (GM)

muscles during static squatting in sedentary and physically active healthy males. We hypothesized that vibration would determine a decrease in muscle oxygenation in GM and VL greater than control condition, due to an increase in muscle activation. Furthermore, we hypothesized that the oxygenation of GM muscle, due to its proximity to the vibration source, would be more affected than the oxygenation of VL during WBV.

Methods

Ten subjects were sedentary individuals and ten were athletes practicing different sports. All subjects completed 4 trials (Control, 30 Hz, 40 Hz and 50 Hz WBV) in a randomised-controlled cross-over design. The trials consisted of static squatting on a vibrating platform for a total duration of 110 s. Muscle oxygenation status was recorded with NIRS (NIRO-300).

Results

The data analysis revealed no significant treatment by time interactions in both TOI and Δ total hemoglobin volume (tHb) in VL and GM muscles. A significant main effect of time in TOI of both VL and GM muscles was identified ($P < 0.001$). TOI significantly decreased from baseline in VL in control conditions after 90 s and 110 s ($P < 0.05$ and $P < 0.05$, respectively), in 30 Hz condition after 110 s ($P < 0.01$), in 40 Hz condition after 30 s ($P < 0.05$), and significantly increased after 30 s in 50 Hz condition. GM TOI was found to be significantly lower than baseline at 60 s ($P < 0.05$), 90 s ($P < 0.01$) and 110 s ($P < 0.01$) in control condition, and at 110 s ($P < 0.05$) in 30 Hz condition.

In conclusion, this study showed that WBV exercise with frequencies of 30, 40 and 50 Hz and small amplitudes does not affect muscle oxygenation of VL and GM muscles to a higher degree than a non-vibration condition.

The details of this study are reported in the previous study (Cardinale *et al*. 2007).

4.3 Biceps brachii myoelectric and oxygenation changes during static and sinusoidal isometric exercises

Surface myoelectric signal changes occurring during sustained isometric contractions have been extensively studied with quantitative surface electromyography (sEMG) and are described by means of some sEMG global variables in time and frequency domain (such as the median power spectral frequency).

The purpose of this work was to combine NIRS and sEMG techniques to analyze the relationship between modifications of sEMG parameters and the underlying metabolic status of the exercising biceps brachii muscle. This relationship was tested under different isometric contraction modalities, namely static (ST) at 20, 40, 60 and 80% MVC and sinusoidal (SIN) at 40 ± 20 and 60 ± 20% MVC.

Results

Results clearly indicate the presence of an initial fast phase of muscle O_2 desaturation followed by a slow phase, regardless of the contraction modality. Moreover, the initial rate of muscle O_2 desaturation was related to the level of force output ($R = 0.92$), but it was independent on the contraction modality ($P < 0.05$). Similarly, changes in sEMG parameters were related to force level (Conduction Velocity - CV vs. Force: $R = 0.87$; sEMG Median Frequency - MDF vs. Force: R =

0.86). The high correlation found between CV-MDF and Tissue Oxygenation Index (TOI) slope (R = 0.73 and 0.72, respectively) suggests a strong relationship between NIRS and sEMG data. Finally, this study indicates that muscle O_2 demand during isometric contractions from low to high force levels is influenced by the type of active motor units and not from the type of isometric exercise modality.

The details of this study are reported in the previous study (Felici *et al*. 2007).

4.4 Auxiliary muscles oxygenation during a rowing exercise

The aim of this study was to investigate the contribution of the auxiliary muscles, utilized to sustain the subject's position on the ergometer, to the oxygen uptake slow component phenomenon.

● Methods

Three tests were performed at the same severe relative intensity on a rowing ergometer: a standard rowing exercise test, a rowing exercise performed with the arms and one performed with the legs only. During the three exercise modalities oxygen uptake, local oxyhemoglobin saturation and surface electromyography signals of the trapezius and vastus lateralis muscles were measured.

● Results

The slow component amplitude, in absolute values resulted statistically lower for rowing (343.9 ± 232.2 ml · min^{-1}) than for arms (795.6 ± 405.6 ml · min^{-1}) and legs (695.8 ± 292.8 ml · min^{-1}) exercise modes. The same result was found when the slow component amplitude was calculated as percentage of $VO_{2\ peak}$ (7.1 ± 5.0 % for Rowing; 17.2 ± 6.6 % for Arms; 17.3 ± 6.4 % for Legs). The lower slow component amplitude measured for the rowing exercise mode with respect to both arms and legs modes, demonstrates that the auxiliary muscles involved in the exercise contribute to the increasing energetic cost due to the slow component.

The details of this study are reported in the previous study (Demarie *et al*. 2008).

4.5 Effects of handgrip exercise on frontal cortex oxygenation

Neuroimaging studies have reported a proportional relationship between cortical signals and exerted joint force in humans, indicating that brain signals are positively correlated to voluntary efforts, as a high level of effort is required for exerting greater muscle force. The effect of diverse skeletal muscle exercises on brain cortex oxygenation, and in particular on ipsi- and contralateral prefrontal cortex (PFC) has not been fully clarified yet.

The purpose of the study was to investigate the time course of the oxygenation of the frontal cortex (FC) during a handgrip task performed separately with right and left hand.

● Methods

Mean (± SD) age, height, and body mass of the 12 right-handed subjects were 27 ± 4 y, 177 ± 5 cm and 76 ± 12 kg, respectively. Participants completed two separate experimental sessions

performed at the same time of day and separated by a minimum period of 24 hours. In the first session each subject performed 5 maximal voluntary contractions (MVC) for each hand. The participant was instructed to squeeze a handgrip device with each hand to his maximum ability while staying in a supine position. Each MVC lasted approximately 2-s with a 120-s rest period between trials. In the second session, two identical rhythmic handgrip exercises at MVC were executed, one exercise for each hand. The exercise consisted of: a 5-min rest condition, a 5-min rhythmic exercise (100 MVCs; 2-s contraction and 1-s relaxation) and a 5-min recovery. Fifteen min later, the same exercise was repeated with the other hand. Handgrip force was measured by a system consisting of a handgrip device and a digital handgrip analyzer (MIE, Medical Research, UK). Subjects exerted handgrip contractions looking at a traffic light generated by the handgrip analyzer software. The visual stimulus was projected towards the ceiling over the subject by a video-projector. When the traffic light was green the subject had to exert his maximum force upon the transducer and maintain the force at his peak until the traffic light changed to red. Upon a red traffic light signal, the subject had to relax so that did not exert any force upon the transducer. The subject repeated this process for each cycle following the traffic light prompts. The sampling rate for force data was 33 Hz. Heart rate (HR) was measured by a pulse oximeter equipped with a ear lobe probe (Nellcor N600, USA).

A 8-channel fNIRS system (NIRO-200 with multi-fiber adapter, Hamamatsu Photonics K.K., Japan) was used to measure frontal changes in [O_2Hb] and [HHb]. Two optical fiber bundles (2.5 m length; 3 mm diameter) carried the light to the left and the right frontal cortex; whereas eight optical fiber bundles of the same size (4 for each lobe) collected the light emerging from the frontal areas. The two illuminating bundles and the collecting ones were assembled into a specifically designed flexible probe holder (Elastomer LCG20R, Chiorino S.p.A, Italy) ensuring that the position of the 10 optodes, relative to each other, was fixed. The probe holder consisted of two mirror-like units (10 × 8 cm each) held together by a flexible junction. The 8 fNIRS measurement points (channels) were defined as the midpoint of the corresponding detector-illuminator pairs (distance set to 3 cm). The optodes were inserted into the elastomer probe holder through fiber optical bundle socket connectors, and then placed over the forehead of both hemispheres. The probe holder was fixed to the head by a velcro brand fastener, adapting them to the individual size and shape of the different heads. This flexible probe holder and its position on the head allowed the creation of stable optical contact with the forehead's scalp for all optodes. The channels 8, 5, 4, and 1 corresponded to Fp1, AF3, Fp2, and AF4 respectively, according to the extended international 10/20 system of electrode placement. The quantification of concentration changes, expressed in $\Delta\mu$M, was obtained by including an age-dependent constant differential pathlength factor (DPF) ($5.13 + 0.07 \times age^{0.81}$). Data were acquired at 1 Hz and transferred online from the NIRO-200 monitor to a computer.

Statistical analyses were performed using the SigmaStat 3.5 package (Systat Software Inc., Richmond, CA). The average values were expressed as mean ± SD. The criterion for significance was $P < 0.05$. In order to determine the significance of [O_2Hb], [HHb] heart rate and force changes one way repeated measures analysis of variance (one way RMANOVA) and post-hoc Tukey test were performed. For [O_2Hb], [HHb] and HR the control condition was the mean value of the 30-s rest condition.

To examine the effect of the handgrip exercise on [O_2Hb] and [HHb] changes, areas under the curve (AUCs) were computed using the curves

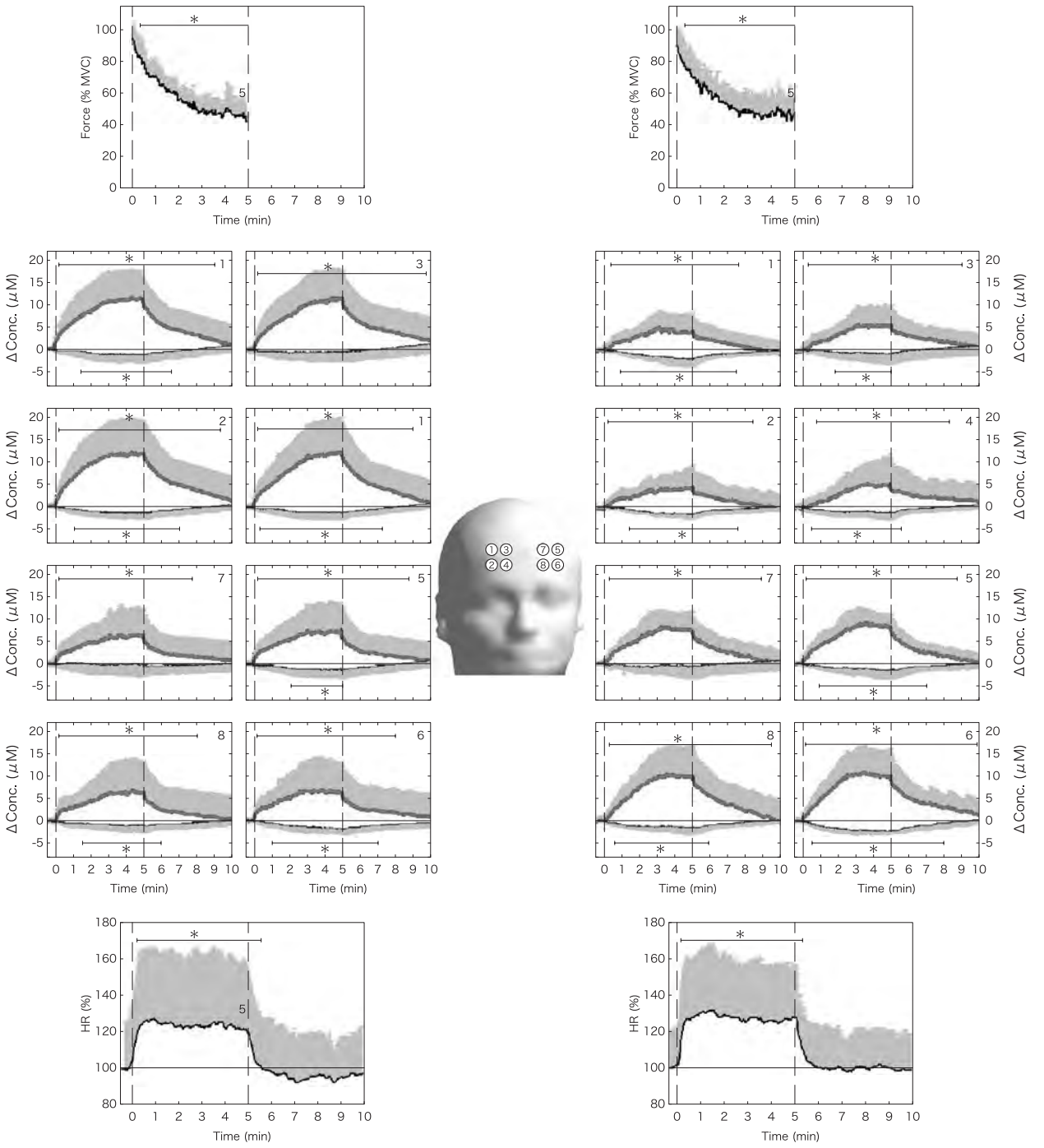

Fig. III.4.5-1 Force tracings; heart rate tracing and FC oxygenation changes during right and left handgrip exercise (left and right panels, respectively). Although the force was decreasing and the HR was constantly high during the exercise period, FC was found activated (increase in O_2Hb and a concomitant decrease in HHb) throughout the investigated frontal region. A higher activation was found ipsilateral to the exercising hand. The horizontal lines indicate the significance interval. Means ± SD.

over the time associated with the exercise. This analytic approach is well established in the quantification of concentration change over time and it would be maximally sensitive to task-related changes on [O_2Hb] and [HHb] regardless of the shape of the response profile.

The AUC of the rest period was subtracted to the AUC of the exercise period and resulting data were analyzed by using a three-way analysis of variance model using post hoc Tukey test to determine the significance of individual changes between three experimental factors[hemisphere

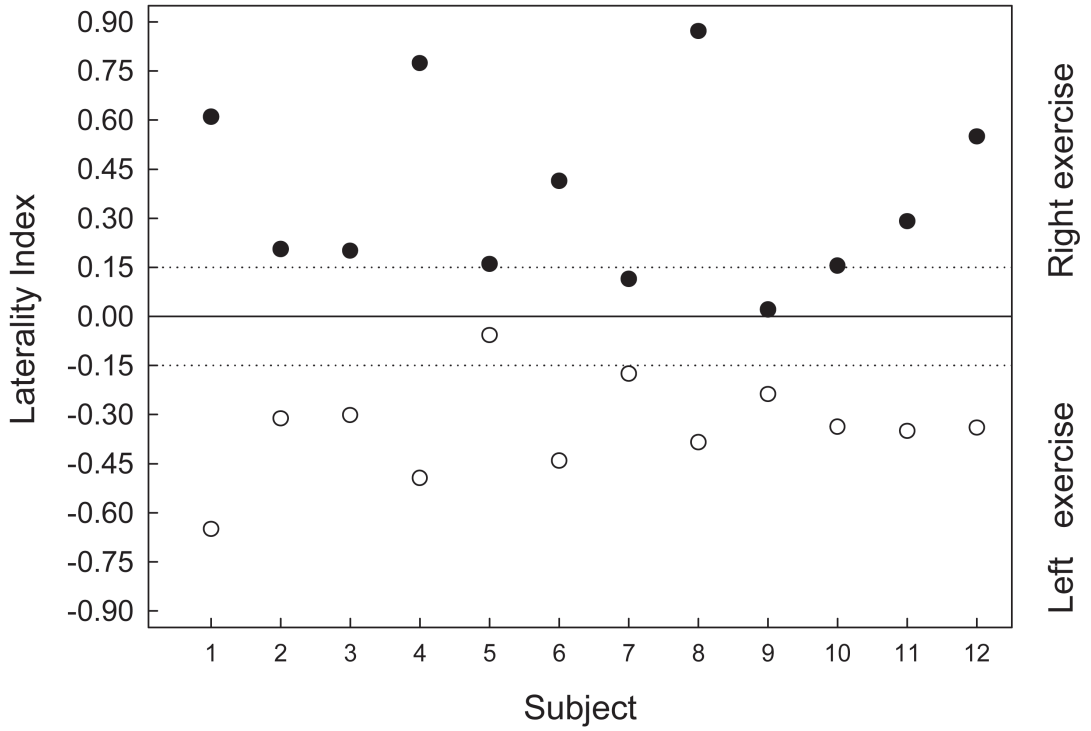

Fig. III.4.5-2 Laterality index for the [O_2Hb] and [HHb] changes of the 12 subjects for the right (filled circle) and left (empty circle) hand exercises. The two dashed lines indicate the significant thresholds for the two exercises.

(2)× channels (4)× task execution(2)].

In order to determine left/right asymmetry of FC activity during the handgrip task, a laterality index (LI) for the [O_2Hb] concentration changes was calculated using the formula (R-L)/(R+L), where R and L indicated the sum of the AUC values of the right side (channels 1, 2, 3, 4) and the left side (channels 5, 6, 7, 8). LI > 0 indicates greater activity of the right FC, while LI < 0 indicates greater activity of the left FC. When the activation of one side was 1.4 times greater than that one found on the other side, the absolute value of LI became greater than 0.15. One side predominance was arbitrarily defined as the absolute LI greater than 0.15.

The summary of the study is reported in Fig. III.4.5-1. A significant progressive decline (up to about 60%) of force was observed over the exercise duration. The so-called cortical activation of both frontal areas (ipsi and contralateral) was observed in all subjects during rhythmic maximal handgrip exercise. The mismatched patterns of HR and O_2Hb changes suggest that the observed FC oxygenation changes were task related. The laterality index for [O_2Hb] changes (the most sensitive parameter to cortical blood flow changes) is reported in Fig. III.4.5-2. The amplitude of [O_2Hb] changes was found greater in the FC ipsilateral to the exercising hand with respect to the contralateral one.

These results confirm the previous ones obtained by others using fMRI and provide further evidence that FC plays a role in maintaining strength of the forearm muscles and ensuring a correct execution of motor tasks which require a fine motor control and coordination.

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5 Technical Developments of Multi-channel Near-infrared Devices for Studying Oxygenation and Hemodynamics in Brain Cortex and Skeletal Muscle

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5.1 Test a 31-channel near infrared spectroscopy-continuous wave imager

5.2 Test a 8-channel near infrared spectroscopy-continuous wave imager

5.3 Test a 8-channel time-resolved imager

5.4 Prepare two review articles on NIRS technical developments and applications

5.5 Contribute to the refinement of NIRS muscle and brain measurements

Technical Developments of Multi-channel Near-infrared Devices for Studying Oxygenation and Hemodynamics in Brain Cortex and Skeletal Muscle

Marco Ferrari

Abstract

The research activity has mainly been focused on the development and application of near infrared spectroscopy (NIRS) or imaging (NIRI) in different fields of medicine including sports medicine, cognitive neuroscience and psychiatry. In particular, 1) specific probe holders were designed and realized for measuring oxygenation changes at cortical frontal lobe level of both hemispheres, 2) a software for data handling and statistical analysis was developed/tested, and 3) research efforts were made on the refinement of NIRS muscle/brain measurements and data analysis.

5.1 Test of a near infrared spectroscopy-continuous wave imager (NIRStation 16, Shimadzu)

Thanks to relatively low cost, simplicity and overall robustness, near infrared spectroscopy-continuous wave (NIRS-CW) systems have been widely used not only in basic research, but also in clinical applications including tissue oximetry and functional brain/muscle imaging. Recently, several groups began to use multi-channel NIRS-CW imaging systems that allow, with high temporal resolution (up to 10 Hz), the generation of images of a large area of the subject's head and muscle and, thereby, the production of maps of cortical and muscle oxygenation changes. Unfortunately few imagers are commercially available and they are quite expensive.

● Methods

In the framework of the project, two imagers produced by Japanese companies (Shimadzu and Hamamatsu), were tested. During a visit in Tokyo, the NIRS-CW imager (NIRStation 16, Shimadzu) (http://www.med.shimadzu.co.jp/products/om/01.html) was utilized for investigating the effect of an exhaustive handgrip exercise on the oxygenation of the frontal cortex. The subject (with eyes closed) was sitting and, when requested, exerted his maximum effort grasping a builder grip with the right hand.

● Results

A cortical activation (decrease in deoxy-hemoglobin (HHb) accompanied by an increase in oxy-hemoglobin (O_2Hb)) was observed over the 31 measurement points in the right and left frontal cortex (source-detector distance: 3 cm). The highest increase in O_2Hb was found in the measurement point #3 of the left frontal cortex. The NIRStation 16 is not commercially available outside Japan.

5.2 Test of a 8-channel near infrared spectroscopy-continuous wave imager (Hamamatsu)

A 8-channel-NIRS-CW imager (NIRO-200 with a multi-fiber adapter, Hamamatsu; http://jp.hamamatsu.com/resources/products/sys/pdf/eng/e_niro200.pdf) was installed in our laboratory in 2006. This is the only system operating in Europe.

Probe holders, dedicated for carrying out cortical oxygenation measurements over the frontal lobe of both hemispheres, were custom made. Two optical fiber bundles (2.5 m length; 3 mm diameter) carry the light to the left and the right frontal cortex; whereas eight optical fiber bundles of the same size (4 for each lobe) collect the light emerging from the frontal areas. The two illuminating bundles and the collecting ones were assembled into a specifically designed flexible probe holder (Elastomer LCG20R, Chiorino S.p.A, Italy) ensuring that the position of the 10 optodes, relative to each other, was fixed (Fig. III.5.2-1). The probe holder consists of two mirror-like units (10 × 8 cm each) held together by a flexible junction. The 8 fNIRS measurement points (associated to the 8 channels) are defined as the midpoint of the corresponding detector-illuminator pairs (distance set to 3 cm) (Fig. III.5.2-2). The optodes are inserted into the elastomer probe holder through fiber optical bundle socket connectors, and then placed over the forehead of both hemispheres. The probe holder can be fixed to the head by a velcro brand fastener, adapting them to the individual size and shape of the different heads.

A software was developed and tested for the data handling and statistical analysis. The possibility to adapt the software "Functional Optical Signal Analysis (fOSA)" developed by the "Department of Medical Physics and Bioengine ering of the University College" of London was also investigated.

This instrumental set up has been utilized in two cognitive neuroscience studies (Curcio *et al*. 2005; Quaresima *et al*. 2009) and in other ones as stated in the report by Quaresima.

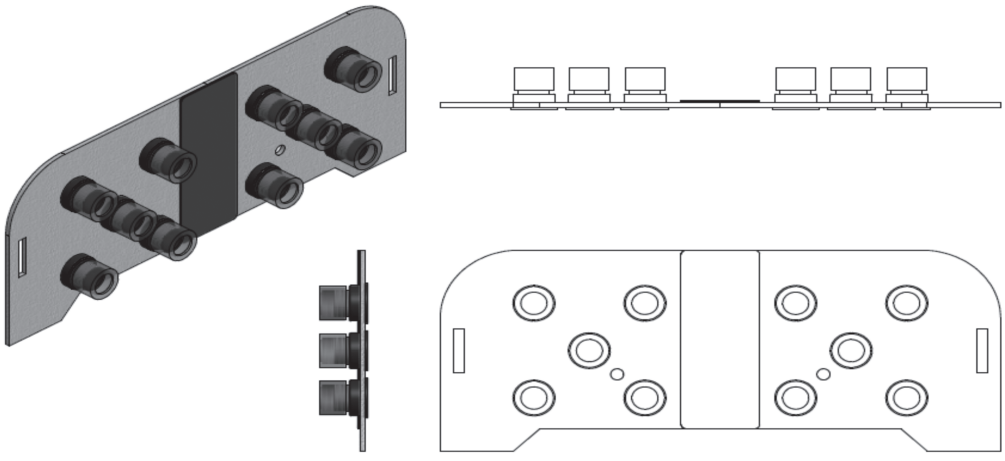

Fig. III.5.2-1 Schematic drawing of the flexible probe holder.

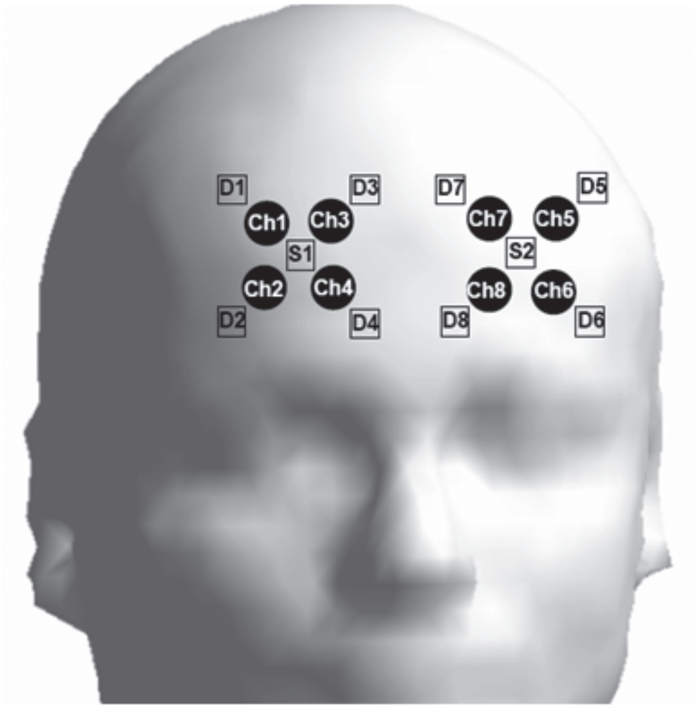

Fig. III.5.2-2 Eight measurement points (channels, Ch) over the frontal lobe. S: source; D: detector.

5.3 Test of a 8-channel time-resolved imager (Politecnico, Milan, Italy)

The key limitation of NIRS-CW is the coupling between the absorption and the scattering coefficient causing the lack of quantitative assessment. The simultaneous estimation of both absorption and scattering can be achieved by NIRS-time resolved (NIRS-TR) systems, which deliver ultrashort laser pulses into tissue and record the time distribution of diffusive photons. In the past, for both technological and financial constraints, NIRS-TR systems have grown on a complex laboratory scale, yet, in recent times, they have evolved towards compact and portable instruments. Up to now, such systems have not been commercially available either on the market or at the research and laboratory stage.

In collaboration with Politecnico of Milan (Italy), a compact eight-channel NIRS-TR system was developed for the non-invasive measurement of tissue oxygen saturation and total hemoglobin volume (tHb). The system has a high temporal resolution (200 ms) and a fast image reconstruction/data analysis. The instrument was used for monitoring spatial changes in calf oxygen saturation (SO_2) during dynamic plantar flexion exercise (Torricelli *et al*. 2004). The same system was utilized to investigate the bilateral PFC oxygenation responses to a letter-fluency task (Quaresima *et al*. 2005). The cross-subject mean values of PFC SO_2 were $68.8 \pm 3.2\%$ (right) and $71.0 \pm 3.6\%$ (left), and of tHb were $69.6 \pm 9.6\ \mu$M (right) and $69.5 \pm 9.9\ \mu$M (left). The typical cortical activation response to the cognitive task was observed at each measurement point. O_2Hb is the most sensitive indicator of increases in cerebral blood flow (neurovascular coupling) and the direction of the changes in HHb is determined by the oxygenation and volume of the venous blood.

The same system was used to monitor the optical response following a motor task (finger opposition, 3 Hz) (Contini *et al*. 2006). The Fig. III.5.3-1 (left

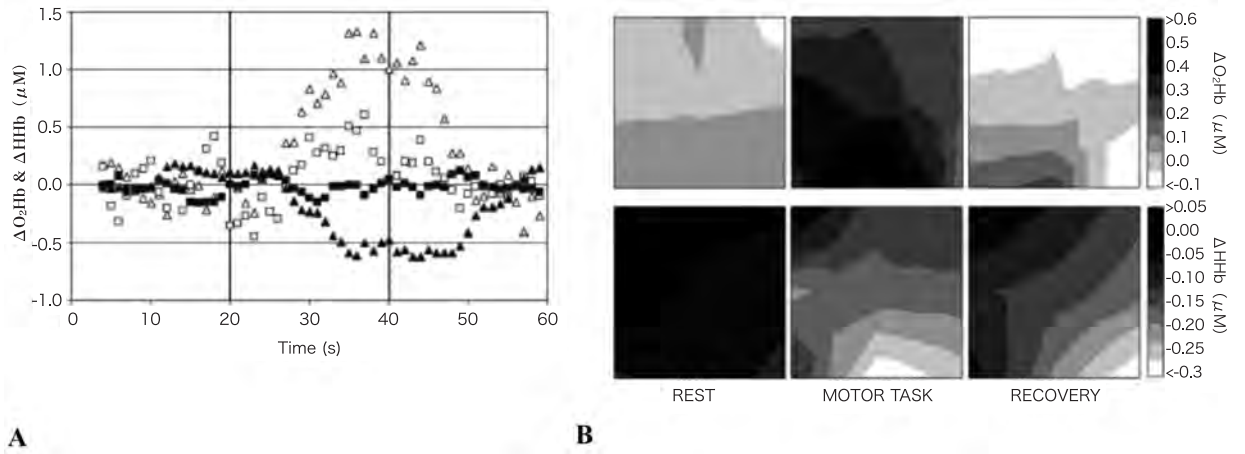

Fig. III.5.3-1 Panel A) Time course of changes in O_2Hb (open symbols) and HHb (filled symbols) of the left motor area during the exercise performed with the right hand (triangle) and with the left hand (square). The vertical lines represent the task interval.
Panel B) Grey level maps representing changes in O_2Hb (top row) and HHb (bottom row) over the left motor area cortex during the baseline period (left column), the finger opposition task performed with the right hand (middle column), and the recovery period (right column).

panel) shows the time course of the changes in O_2Hb and HHb for a single detection channel. The grey level maps of O_2Hb and HHb changes (obtained by interpolating the results from the eight collection points) is shown in the right panel. As it would be expected, during the task, the activated area is revealed by an increase in O_2Hb (black area in the central image of the upper line) and by a concomitant decrease in HHb (white area in the central image of the lower line).

The development of improved NIRS-TR systems and their application in functional imaging studies will serve not only to definitely set its potentiality, but also as a feedback to the development of improved NIRS-CW set-ups for next-generation optical imaging devices. In the future we want to continue in giving a contribution to the development of multi-channel NIRS systems for better studying oxygenation and hemodynamic changes in brain cortex and skeletal muscle during different challenges.

5.4 Preparation of two review articles on NIRS technical developments and applications

Two review articles (Hamaoka*et al*. 2007; Wolf *et al*. 2007) were written to give a contribution to the Special Section of the Journal of Biomedical Optics entitled: “Pioneers in Biomedical Optics for honoring Professor Frans F. Jobsis of Duke University” (Delpy *et al*. 2007).

The first one (Hamaoka *et al*. 2007) reports the progress of the *in vivo* NIRS and near infrared imaging (NIRI) instrumentation for brain and muscle clinical applications. The article summarizes the main characteristics of the present commercially available NIRS and NIRI instrumentation. Moreover, it discusses strengths and limitations.

The second one (Wolf *et al*. 2007) highlights the progress that has been made in developing and adapting NIRS and NIRI technologies for evaluating skeletal muscle oxygen dynamics and oxidative energy metabolism. NIRS measurements have

been extended to resting, ischemic, localized exercise, and whole body exercise conditions. In addition, the review article describes the application of NIRS to the study of a number of chronic health conditions, including patients with chronic heart failure, peripheral vascular disease, chronic obstructive pulmonary disease, varying muscle diseases, spinal cord injury, and renal failure.

5.5 Contribution to the refinement of NIRS muscle measurements

Unfortunately in several recent publications the presentation of the CW NIRS muscle or brain data is still confusing and inadequate. In order to give a contribution to the correct use of the NIRS instrumentation in skeletal muscle and brain studies, five letters were submitted to the Editor-in-Chief of different International Journals. All the letters, related to one of the following topics:

- the light source-detector spacing of near-infrared-based tissue oximeters and the influence of skin blood flow (Ferrari *et al*. 2006)
- the evaluation of skin blood flow contribution to the muscle oxygenation measurement (Quaresima and Ferrari 2006a)
- the quantification of quadriceps oxygen desaturation at the onset of exercise (Quaresima and Ferrari 2007)
- the quantification of calf oxygenation in paraplegic patients (Quaresima and Ferrari 2006b)
- the clinical significance of cerebral oxygenation during exercise in patients with coronary artery disease (Quaresima and Ferrari, 2009)

have been accepted for publication.

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6　運動様式，運動強度，運動時間および筋代謝からみたモーターユニットの動員特性

加茂　美冬[1)]

Discharge properties of motor unit with respect to the mode, intensity, duration of the exercise and muscle metabolism

Mifuyu Kamo

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6.1　反復電気刺激に対するヒト筋線維群の張力応答

加茂　美冬，森本　　茂

Force output of human muscle fibers during repetitive electrical stimulation using physiological rates

Abstract

This study examined changes in an evoked force of human muscle fibers by electrical stimulation using inter-stimulus interval within physiological range occur during submaximal contraction. Muscle fibers in vastus medialis muscle were percutaneously stimulated for 3min using constant inter-stimulus interval at 100 and 50ms. The evoked tetanic forces of muscle fibers initially appeared significant increment during the electrical stimulation. The initial increment force had two peaks; initial transient and following gradual slow increase during 100 ms and had one peak during 50 ms simulation. The results confirmed that increase in tetanic force of muscle fibers like potentiation is evident during repetitive activation within physiological rate in human. Therefore, spike interval elongation would be necessary to achieve a constant force during isometric contraction at low level.

● 目　的

筋力を決定するモーターユニット（MU）活動は，神経筋機能はもとより循環系機能との間にも相互に密接な関係をもつと考えられる．したがって，運動時の循環調節を統合的に理解するためには，MU活動およびその発現メカニズムを知ることが重要となる．等尺性一定筋力発揮において筋力発揮初期より活動するMU放電間隔は漸次延長する．この現象は，出現期が数秒から数分と強度に依存しているものの全ての筋力レベルで共通して観察されている（DeLura *et al*. 1996; Kamo 2002; Kamo and Morimoto 2001）．しかし，放電間隔延長の合目的性およびメカニズムについては未だ十分に明らかにされていない．本実験では，その合目的性を知るために，一定筋力発揮中に単一MUが発揮している張力の推定を行おうとした．すなわち，随意一定筋力発揮時のMU放電間隔の範囲内にある刺激間隔を用いて筋線維群に電気刺激を加え，その誘発張力変化を観察した．

● 方　法

被験筋は内側広筋とし，被験者は股関節および膝関節角度90度で椅座位姿勢をとった．電気刺激は，motor pointへ経皮的に加えた．刺激持続時間は1 msとした．収縮時間（contraction time：CT）が一定となる最低の強度を刺激強度として用いた．この強度は被験者の痛み閾値以下であった．刺激間隔には5 s，100 msおよび50 msを用いた．各間隔での刺激期間は3分であった．電気刺激中，誘発張力と誘発電位を記録した．

● 結果および考察

100 msおよび50 ms間隔刺激により誘発された張力は不完全強縮であり，3分間一定あるいは単調な変化を示さなかった．100 ms刺激においては非常に複雑な変化を示した（Fig. III.6.1-1）．まず，最初に一過性に増大，低下を示した．その後，約15秒目まで緩徐に増大し，低下に転じた．一方，50 ms刺激では100 msで観られた一過性のピークは出現せず，200　msまで急峻に張力が融合し，その後約10秒間緩徐に増大した後低下に転じた．誘発張力が，増減する複雑なパターンを示したことは，MUが一定間隔で放電する条件では，一定筋力を保持することは困難であることを示唆している．変化パターンのなかでも，特に，初期に増大するフェーズをもつことが特徴的であった．一般的に，MUの放電間隔延長は，張力融合の程度を低下させ発揮張力を低下させる．

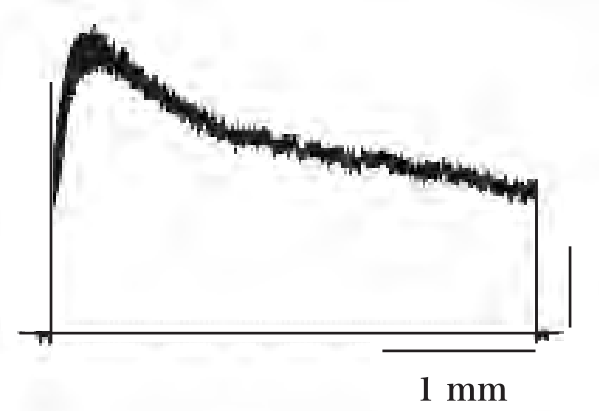

Fig. III.6.1-1 Representative changes pattern of evoked force during constant inter-stimulus interval stimulation at 100ms. Vertical line shows magnitude of peak force of twitch.

したがって，随意一定筋力発揮時の放電間隔延長はMU発揮張力の初期の増大を防ぎ，一定筋力保持に貢献している可能性が考えられた．また，刺激初期の誘発張力の増大率（最高張力/初期張力）は，100 ms刺激に比較して50 ms刺激で必ずしも大きい値を示さなかった．このことから，MU活動レベルが高い場合のみならず，放電間隔100 msという低活動レベルにおいても放電間隔延長が一定筋力保持に貢献していることが示唆された．

● 文　献

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6.2　最大下一定筋力発揮におけるモーターユニット活動を規定する要因

加茂　美冬

Mechanisms responsible for spike interval elongation of motor unit during submaximal contractions

Abstract

Discharge of motor units (MU) is well known to show elongating trends in the spike interval during voluntary constant-force isometric contraction, but neural mechanisms underlying those trends remain unclear. This study examined effects of peripheral afferent stimulation on MU activity during voluntary contraction. Some MUs were discharged at the longer interval without an elongating trend during involuntary constant-force contraction via tonic vibration reflex. Furthermore, irrespective of peripheral afferent manipulation, the spike interval's elongating trend did not disappear during the contraction after prolonged vibration and during the contraction with intermittent vibration. Results suggest that changes in neural input information to single MUs with peripheral afferent stimulation do not eliminate the spike interval's trend of elongation in the presence of voluntary drive.

● 目　的

運動時の循環調節を統合的に理解するためには，酸素需要の源となるモーターユニット（MU）活動およびその発現メカニズムを理解することも必要である．最大下一定筋力発揮初期に観られる特徴的なMU活動に数秒から数分にわたる“放電間隔延長”がある（DeLura *et al*. 1996; Kamo 2002; Kamo and Morimoto 2001）．先に，筋の収縮特性の変化と放電間隔延長の関係を調べ，放電間隔延長は反復収縮に伴い生じる筋張力増大（potentiation）を補償する効果をもつことを確かめた．続いて，本実験ではMU放電間隔延長発現のメカニズムを探るために，一定

筋力保持に必要とされる感覚情報のフィードバックに注目し，それらの情報と放電間隔延長の関係を調べようとした．

● 方　法

膝関節角度90度条件における内側広筋単一MUを観察対象とした．単一MU活動電位は直径5 mmの銀・塩化銀表面電極にて双極導出した．また，内側広筋，外側広筋，大腿直筋および大腿二頭筋から表面筋電位を導出した．感覚情報の操作は，腱へ振動刺激を与えることにより行った．振動刺激は膝蓋腱に経皮的に加え，条件は頻度75および100 Hz，振幅0.5～0.8 mmとした．弛緩筋に振動刺激を加える条件（緊張性振動反射），観察するMUの活動参加閾値張力直上の随意筋力をコントロール収縮とし，その前に持続的に振動刺激（10分以上）を加える条件およびコントロール収縮に間欠的に振動刺激を加える条件（10秒間隔で5秒間）において，単一MUの放電間隔変化を観察した．

● 結果および考察

随意収縮においては全ての単一MUが放電間隔延長を示すにも関わらず，弛緩筋に振動刺激を加え一定筋力を発揮した条件では放電間隔が延長するMUと延長を示さないMUが観察された（Fig. III.6.2-1）．随意筋力発揮前に持続的に振動刺激を加えた条件では，放電間隔の延長量は低下したが延長は消失しなかった．また，収縮中に振動刺激を加えた条件においても延長は観察された．これらの結果から，一定筋力発揮時のMU放電間隔延長発現には末梢興奮入力の低下とあわせて，central driveによる興奮入力の低下あるいは抑制の制御が重要な役割を果たしていると考えられた．

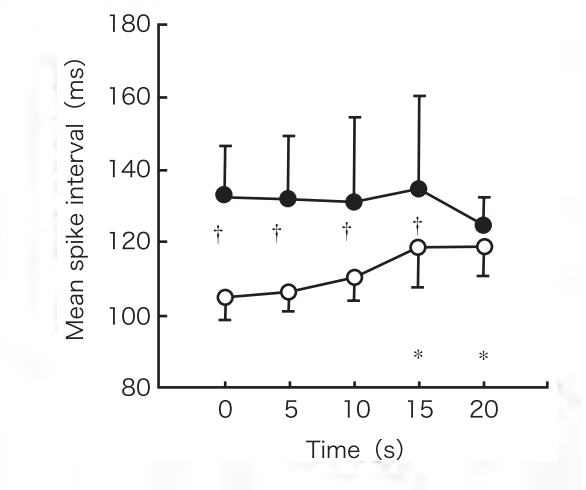

Fig. III.6.2-1　A typical change in the mean spike interval of a single motor unit during contractions. Filled and open points respectively represent the means (± SD) of results in vibration-induced response (Vib) and voluntary reproduction (Vo). Asterisks and daggers indicate statistically significant differences from value at 0min, and between Vo and Vib, respectively.

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6.3　等尺性筋力発揮におけるモーターユニット活動と循環系機能の関係

加茂　美冬

Effects of motor unit activity on circulatory responses and muscle oxygenation

Abstract

Motor unit activities and cardiovascular responses during voluntary ascending ramp contraction (30s, - 10% maximal voluntary contraction) were compared with those during involuntary via tonic vibration reflex. Heart rate and blood pressure changed immediately before and after the onset of the ascending ramp contraction, but no change occurred during vibratory contraction. Integrated value of electromyography and decreased oxygenated hemoglobin in the muscle during the voluntary contraction were larger than those during the reflex contraction. More efficient muscle oxygen consumption during voluntary contraction will result not only from cardiovascular regulation by central cardiovascular command, but also from motor unit activities by central motor command.

● 目 的

運動は，時間的，空間的に様々な組み合わせで起こるモーターユニット（MU）活動を基礎として成り立っている．すなわち，筋力は，筋を構成するMUの発揮張力の総和であり，筋力増大は，活動するMU数の増大と参加したMUの放電頻度の上昇により実現される．先に，緊張性振動反射による誘発収縮と随意収縮では同一筋力発揮時のMU活動が異なることを報告した．そこで，反射性収縮と随意収縮の比較を行うことにより，随意筋力発揮時の循環調節に

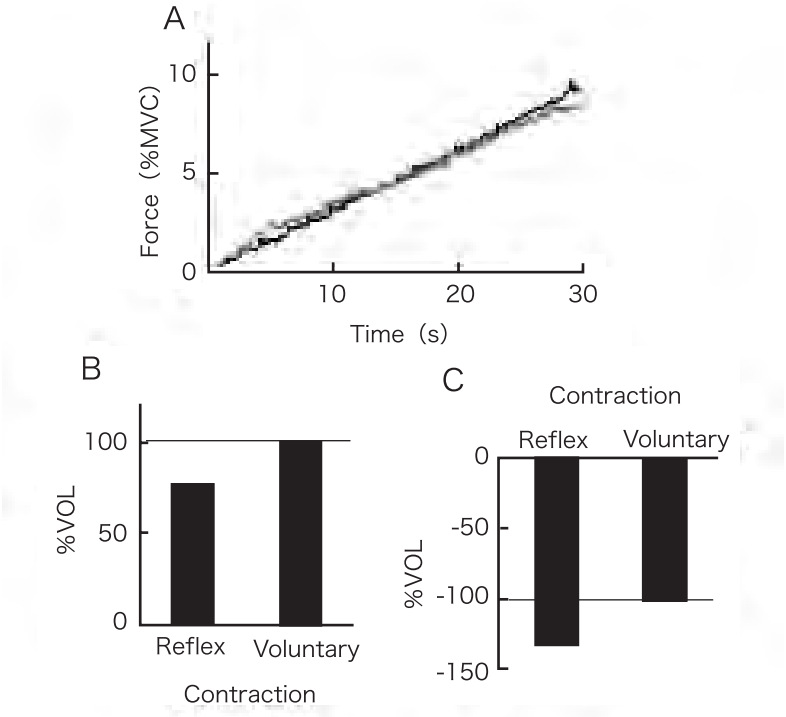

Fig. III.6.3-1　Motor unit activities and oxygenated hemoglobin during a representative experiment.
A: force, B: force impulse/integrated value of electromyogram, C: decrease in oxygenated hemoglobin. Black and gray lines represent value during voluntary contraction and during reflex contraction, respectively in A.

ついて検討を加えた．

● 方　法

筋力発揮様式および振動刺激の頻度・振幅は先の報告（2．最大下一定筋力発揮におけるモーターユニット活動を規定する要因）と同様であった．先ず，弛緩筋に30 s間刺激を加え誘発された張力（RC）を記録し，その後，十分な休息をとり，誘発張力と同様な張力を随意的に発揮させた（VC）．両条件におけるMU活動と循環系機能および代謝変化を比較した．MU活動は筋電位積分値（IEMG）により評価した．循環系機能および代謝変化の指標には心拍数，血圧および筋酸素化ヘモグロビンを用いた．

● 結果および考察

IEMGはVCよりRCにおいて有意に大きいあるいは大きい傾向にあった．VCにおいて心拍数と血圧はこれまでに報告されている随意筋力発揮におけるcentral cardiovascular commandの制御による変化（Matsukawa *et al*. 2007）と同様な傾向を示したが，RCでは観られなかった．筋酸素化ヘモグロビンの筋力発揮開始時からの低下量はVCに比較しRCで大きかった（Fig. III.6.3-1）．これらのことは，随意収縮では，central cardiovascular commandによる循環系機能制御とともにcentral motor commandによる筋力発揮効率のよいMU活動が効率のよい酸素利用に貢献していることを示唆している．

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6.4　膝関節前十字靱帯損傷再建術後の筋力回復に関する研究

板倉　尚子，加茂　美冬

Effect of exercise proguram on the recovery of mucsle strength after anterior cruciate ligament reconstruction

Abstract

To investigate how muscle strength is recovered after the reconstructing operation of anterior cruciate ligament (ACL), we examined the effects of two exercise programs, distal and proximal resistance exercise (DPRE) and proximal resistance with traction exercise (PRTE), in 7 female subjects. The peak force exerted during dynamic knee extension in low (60 deg/s) and high (180 deg/s) speeds was measured in the operated leg and the contralateral control leg before and 3 months after the operation. Both programs of DPRE and PRTE recovered the muscle force in the operated leg by 76-79 % from the pre operation level and by 98-100 % from the control leg in both speeds. These data suggested that both exercise programs of PRTE and DPRE are effective for recovering muscle force after ACL reconstructing operation.

● 目　的

膝前十字靱帯（以下，ACL）再建術後3ヵ月間は再建靱帯の力学的強度が脆弱であるため，大腿四頭筋収縮による生じる前方剪断力を制限し，また膝関節可動域を制動してACLへのストレスを回避しリハビリテーションを施行する．しかし，これにより膝関節30°屈曲位から伸展域での大腿四頭筋の収縮が制限されるため，この可動域で作用しやすい内側広筋が萎縮し改善しにくい症例が多い．当センターでは大腿四頭筋の筋力回復運動を実施する際に，抵抗を

Fig. III.6.4-1　Experimental setup

加える位置を脛骨粗面部とし大腿四頭筋収縮による脛骨前方変位を制動する方法（以下，DPRE）と，膝関節90°から60°でも内側広筋の筋収縮を誘発させられるとされるproximal resistance with traction exercise（以下，PRTE）を導入し，リハビリテーションプログラムを実施している．今回，手術前と手術後3ヵ月に筋力測定を行い当センターでのリハビリテーションプログラムを評価した．なお本研究は本人の同意を得て，本学「人を対象とする実験・調査に関する倫理指針」に基づき配慮し，また個人情報管理については責任者の管理のもと適正に実施した．

● 膝関節前十字靱帯損傷術後の膝関節伸展運動に対するプログラム（術後3ヵ月まで）

1）近位抵抗（DPRE）

椅子座位にて近位の脛骨粗面上にゴムチューブを強く二重に巻き，下腿遠位に軽く1本つけ膝関節を屈曲90～45°の範囲で伸展する．

2）PRTE

椅子座位にて下腿近位部に徒手抵抗をかけ膝関節屈曲90～45°の範囲で伸展する．その際，下腿内旋位をとらせ，遠位方向へ牽引力をかけることで内側広筋の収縮を促しやすい．

● 方　法

膝関節前十字靱帯再建術施行前および術後3ヵ月に筋力測定を下記の通り実施した．

1）測定機器

品名：バイオデックスシステム3（納品／平成16年10月20日）

型式：BDX-3C（製品番号：S61FX010）

2）対象者

・膝前十字靱帯再建術を施行（半腱様筋を採取）した本学女子体育大生7名

・平均年齢19.7歳

・右膝3件，左膝4件（受傷から手術施行までの平均期間3ヵ月10日）

3）プロトコール

・膝関節伸展運動を60 deg/secを5回，180 deg/

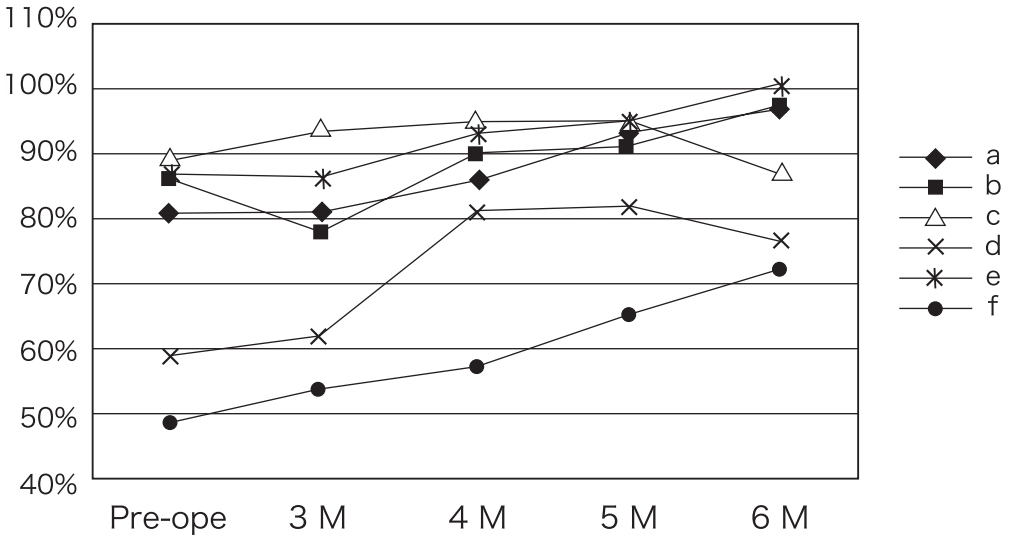

Fig. III.6.4-2　Peak force during dynamic knee extension at the speed of 60 deg/sec before operation and 3 month to 6 month after operation.
Pre-ope; before operation, 3M; 3 month after operation, 4M; 4 month after operation, 5M; 5 month after operation, 6M; 6 month after operation.

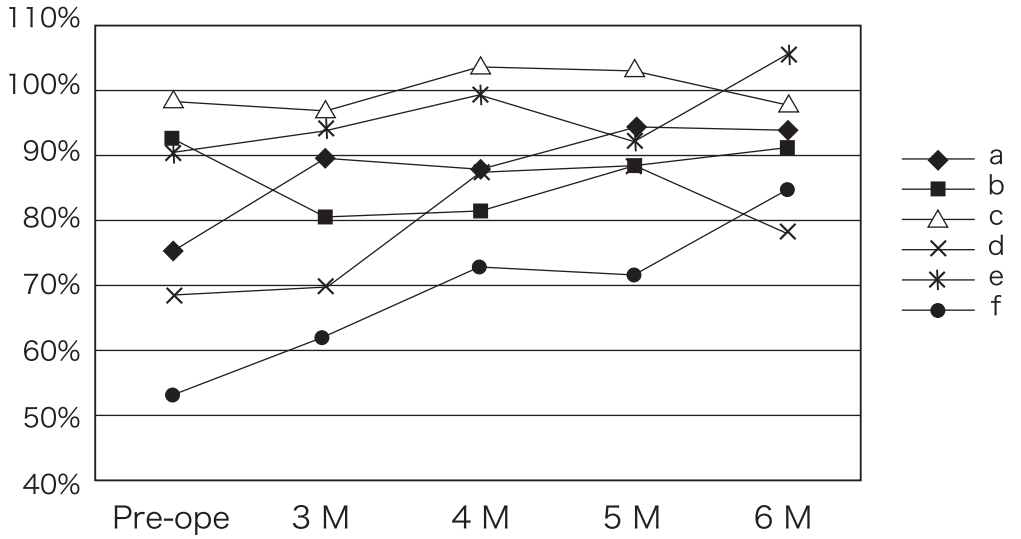

Fig. III.6.4-3　Peak force during dynamic knee extension at the speed of 180 deg/sec before operation and 3 month to 6 month after operation.
Pre-ope; before operation, 3M; 3 month after operation, 4M; 4 month after operation, 5M; 5 month after operation, 6M; 6 month after operation.

secを10回施行し測定（Fig. III.6.4-1）.

● 結　果

1）　手術後3ヵ月の膝関節伸展筋力ピークトルク健患比

角速度60 deg/sec：76.2％±10.4％（Fig. III.6.4-2），角速度180 deg/sec：78.6％±11.3％（Fig. III.6.4-3）.

2）　患側の手術前および手術後3ヵ月の膝関節伸展筋力ピークトルク比

角速度60 deg/sec：98.3％±11.6％（Fig. III.6.4-2），角速度180 deg/sec：99.8％±16.6％（Fig. III.6.4-3）.

● 考　察

近年，前十字靱帯再建術は複数の骨孔を移植腱の断面形状に応じて作製することにより，移植腱と骨孔の接触断面が拡大され，再建靱帯の治癒，再構築が期待されるものに進化されてきている．これに応じて術後のリハビリテーションも徐々に加速化が図られている．再建術後3ヵ月までのリハビリテーション期間は，再建靱帯が治癒，再構築するまでの期間であり，再建靱帯への伸張ストレスを回避したリハビリテーションプログラムが行われている．本センターにおいても，膝前十字靱帯損傷術後のリハビリテーションプログラムとしてDPREとPRTEを導入し，内側広筋の筋力回復を図っている．DPREとPRTEの効果を検討した本研究において，手術後3ヵ月における膝伸展筋力のピークトルク値の健患比が60 deg/secで76.2％±10.4％であり，180 deg/secでは78.6％±11.3％であり，患側の手術前と手術後3ヵ月の術前後比は60 deg/secで98.3％±11.6％，180 deg/secでは99.8％±16.6％となり，健側比率80％にまで回復することが示された．この結果は，ジョギングなどの運動を許可する条件を満たすものであり，リハビリテーションプログラムとしてDPREとPRTEが有効であることを示すものと考えられた．

7　運動時の心拍出量の変化と各種血管への血流配分

奥山（清水）靜代[1)]

Cardiac output during exercise and distribution of blood flow into the various vessels

Shizuyo Shimizu-Okuyama

■本課題の共同研究者
大森芙美子[2, 3)]，佐藤　耕平[3)]，村岡　慈歩[4)]，岩館　雅子[3, 5)]，加賀谷淳子[3)]

[1)] 慶應義塾大学，[2)] 鹿屋体育大学大学院，[3)] 日本女子体育大学，[4)] 明星大学，[5)] 日本大学

7.1　多段階静的足底屈運動時における心拍出量と膝窩動脈血流量の関係

奥山（清水）静代，大森芙美子，佐藤　耕平，加賀谷淳子

Cardiac output and leg blood flow during incremental plantar flexion exercise prolonged to exhaustion

Abstract

The purpose of this study was to determine central and peripheral hemodynamic responses to incremental exercise. Seven physically active women performed static plantar flexions until exhaustion. Exercise comprised of incremental 30-s static plantar exercise separated by 30-s recovery. The initial load was 5% MVC, and then the load was increased by 5%MVC until exhaustion. During exercise we measured stroke volume using a Doppler ultrasound method and the heart rate using an electrocardiogram (ECG). Cardiac output was calculated as products of SV and HR. The mean blood velocity and the vessel diameter of the popliteal artery were measured by using a Doppler and B-mode ultrasound method. Cardiac output began to increase from 50%MVC (3.8 ± 0.1 l/min). In contrast to popliteal arterial blood flow began to increase slightly from 25%MVC. These results suggest that popliteal arterial blood flow began to increase earlier than cardiac output at low intensity exercise during incremental exercise to exhaustion on the planter flexion. In addition, the percentage of cardiac output the popliteal arterial blood flow was increased with exercise intensity. In conclusion, peripheral blood flow was differentially regulated from central circulation, and the increase in peripheral blood flow demand did not always require the increase in cardiac output. Relationships between central and peripheral circulatory changes were intensity-depending.

● 目　的

循環の中枢である心臓の拍出量と末梢の血流量は互いに影響しあい，末梢循環のみで調節できる場合と，中心循環を促進させて調節する場合がある（清水ら 2001）が，活動する筋量が変わった場合，負荷増加に伴う活動筋の血流需要増加に心拍出量がどのように対応するかは明らかではない．そこで，本研究の目的は多段階静的足底屈運動時の心拍出量と膝窩動脈血流量関係を明らかにすることにより，負荷増加に伴う活動筋の血流需要増加に心拍出量がどのように対応するかを明らかにすることである．

● 方　法

健康な成人女性７名を対象とした（年齢22 ± 1歳）．被験者には椅座位姿勢にて30秒間の静的足底屈運動を30秒の休息を挟んで繰り返す運動を行わせた．負荷強度は初期負荷を５％MVCとし，以後５％MVCずつ増加して，疲労困憊まで運動を続けた．運動は椅座位姿勢で足関節伸展力を発揮させた．測定項目は心拍出量および膝窩動脈血流量で，超音波ドップラー法により測定した．

● 結果および考察

心拍出量は負荷増加が増加しても，50％MVC（3.8 ± 0.1 l／min）まで変化しなかったが，55％MVC（4.5 ± 0.3 l／min）では安静時に対して有意（$p < 0.05$）に増加した．一方，膝窩動脈血流量は負荷増加に伴い徐々に増加する傾向を示し，40％MVC（0.6 ～ 0.8 l／min）以上では，安静時（0.1 ± 0.01 l／min）に対して有意差（$p < 0.05$）が認められた．心拍出量を規定する要因である心拍数は，負荷増加にともなう有意な変化はみられなかったので，一回拍出量の負荷増加にともなう変化が，心拍出量を増大させたと考えられる．また，心拍出量に対する膝窩動脈血流量の割合をみると（Fig. III.7.1-1），その割合は安静時に対して40％MVC以上で有意（p ＜

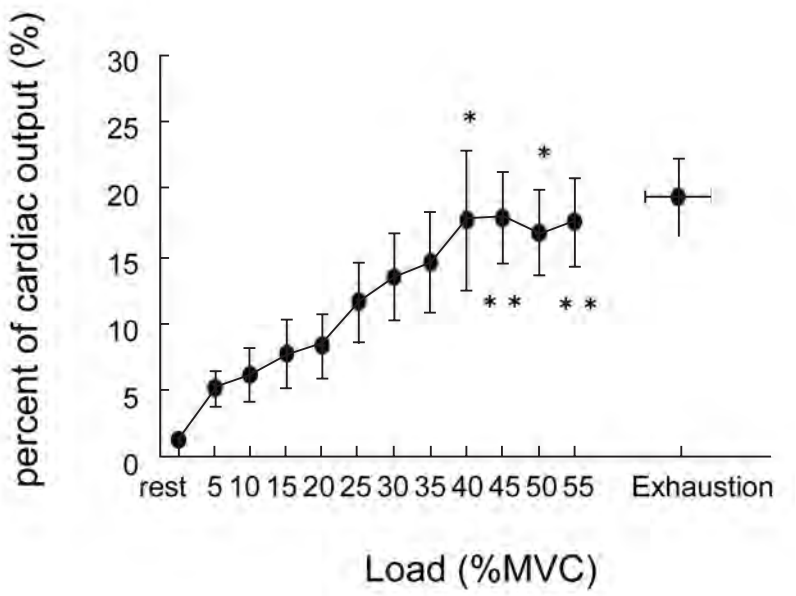

Fig. III.7.1-1　Popliteal arterial blood flow of cardiac output during incremental plantar flexion exercise to exhaustion.
At 40, 45, 50 and 55 %MVC increased significantly from baseline value.
*, **: $p < 0.05$, $p < 0.01$ compared to baseline value.

0.05）に高値（16.6～17.7％）を示した．これらの結果をまとめると，多段階静的足底屈運動時の活動筋への血流量と心拍出量は，負荷増加に対して必ずしも一致した変化を示さなかった．すなわち，低強度では心拍出量の増加なしに活動肢への血流増加が起こり，強度が高くなると両パラメータが増加を示した．そして，心拍出量が増加するにもかかわらず，高い負荷では心拍出量に占める活動体肢への血流の割合が高くなり，活動体肢への血流分配が高くなっていることが示された．すなわち，負荷増加に伴う活動筋における血流需要増加に対して，50％MVCまでは心拍出量の増加なしに運動が行われ，それ以上の強度においては心拍出量が上昇することにより，活動体肢の血流需要に対応していることが明らかになった．

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7.2　筋活動期および活動休止期における大動脈血流速度と活動体肢血流速度の対応

奥山（清水）静代，大森芙美子，岩館　雅子，佐藤　耕平，加賀谷淳子

The influence of aorta and femoral arterial blood flow valocity during contraction and relaxation phases

Abstract

The purpose of this study was to observe the changes in the blood velocity in aorta and femoral artery during muscle contraction and relaxation phases of knee extension exercise. Seven female subjects (aged 22.4 ± 1.9 years) participated in this study. They performed one-legged knee extension exercise (KE) in upright position at 10% and 50% of maximal voluntary contraction (MVC) until exhaustion. Blood velocity was measured using the Doppler ultrasound method for aorta artery and femoral artery. Blood pressure was monitored from the finger of the left hand at the heart level. During the muscle contraction phase of KE, the blood velocity in femoral artery was significantly ($p < 0.01$) lower than in aorta artery. In contrast, the blood velocity in femoral artery higher than the aorta during the relaxation phase. The femoral/aorta rations were -67.4 ± 9.2% (10%MVC), and -80.6 ± 4.9% (50%MVC) during the contraction phase. However, during the relaxation phase, they were 30.0 ± 11.6% (10%MVC), 50.7 ± 22.3% (50%MVC). Mean blood pressure was not different significantly between the contraction and relaxation phase. These results suggest that the effect of muscle contraction and relaxation on blood velocity differs between aorta artery and femoral artery. The femoral artery blood flow velocity was more accelerated compared to aorta during the relaxation phases.

● 目　的

本研究は，筋の活動期および活動休止期の大腿動脈血流速度が，心臓から拍出される血流速度とどのような関係にあるかを明らかにすること，さらに異なる強度で両者の関係に相違があるか否かを明らかにすることを目的とした．

● 方　法

健康な成人女性７名（年齢22.4 ± 1.9歳）を被験者とし，股関節角度110°とした椅座位姿勢で右脚による動的膝伸展運動（30°伸展，１秒収縮１秒弛緩）を行わせた．負荷は最大筋力の10および50％に相当する負荷とし，10％MVCは３分間，50％MVCは疲労困憊に至るまで行わせた．安静時および運動中の大動脈血流速度，活動肢大腿動脈血流速度（超音波ドップラー法）を測定した．

● 結果および考察

大腿動脈血流速度において筋活動期では，10，50％MVCともに時間経過にともなう変化がみられなかったのに対して，活動休止期では安静値と比較し有意に増加し，10％MVCでは8.8倍，50％MVCでは13.7倍増加した．大動脈血流速度は50％MVCのみ有意に増加したが，その増加は1.3倍であった．大動脈および大腿動脈血流速度を筋の活動期と休止期で比較した場合，低強度および高強度どちらにおいても，筋活動期では大腿動脈血流速度は大動脈血流速度より低く，筋活動休止期では大動脈血流速度より高値を示した．また，大動脈速度に対する大腿動脈速度の相対的な割合は，筋活動時には抑制され，筋活動休止期には亢進された．さらに，低強度よりも高強度の方が両血管における血流速度の差が大きかった（Fig. III.7.2-1）．筋活動期および活動休止期の平均血圧には差はみられず，どちらの時相においても50％MVCの方が10％MVCよりも高い値を示

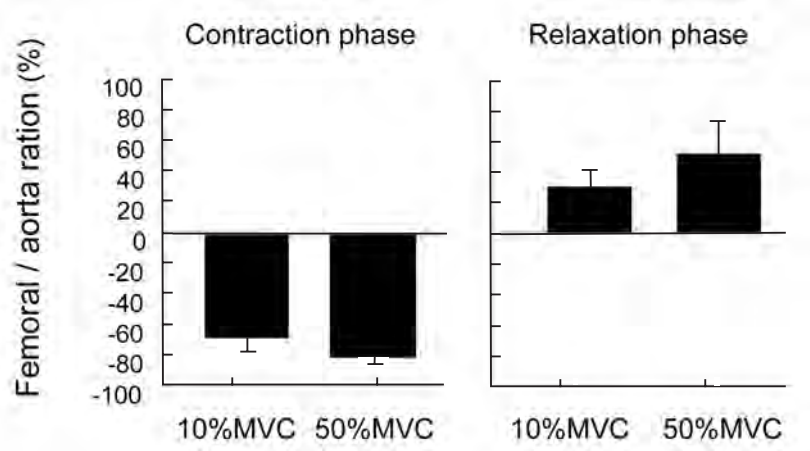

Fig. III.7.2-1　The femoral/aorta rations during the contraction and relaxation phases at 10, 50%MVC.
The femoral/aorta rations were -67.4 ± 9.2% (10% MVC), and -80.6 ± 4.9% (50% MVC) during the contraction phase. However, during the relaxation phase, they were 30.0 ± 11.6% (10% MVC), 50.7 ± 22.3% (50% MVC).

したが，有意には至らなかった．以上のことをまとめると，活動筋近位の末梢動脈における血流速度は筋の活動期に低く休止期には高いというように，筋活動による大きな変動が起きるが，中心動脈の血流速度は筋の活動期と休止期により大きな影響を受けないことが示された．すなわち，筋活動は，中心循環ではなく末梢循環の変動を起こすことが示された．その結果，中心動脈および末梢動脈の血流速度の関係は筋の活動期と休止期で異なり，活動期では中心動脈血流速度が活動筋へ血液を供給する末梢動脈血流速度を上回り，休止期では逆に末梢動脈血流速度が中心動脈速度より早くなるという関係にあることが示された．

7.3　高齢者における左室重量と骨格筋量との関係

奥山（清水）靜代，村岡　慈歩，大森芙美子，加賀谷淳子

The relationship between cardiac muscle and skeletal muscle mass in elderly women

Abstract

The purpose of this study was to clarify the relationship between left ventricular muscle mass [LVmass] and skeletal muscle volume in elderly women. We measured the thigh muscle thickness (Vastus intermedius and Rectus femoris) using B-mode ultrasound method. Posterior wall thickness, interventricular septal thickness and left ventricular end-diastolic internal diameter were measured by B-mode echocardiography. A significant correlation coefficients were obtained between vastus intermedius and interventricular septal thickness ($r = 0.221$, $p < 0.05$), rectus femoris and posterior wall thickness ($r = 0.240$, $p < 0.05$). In addition, significant correlation coefficients were also obtained between the estimated skeletal muscle volume and left ventricular mass in elderly women ($r = 0.561$, $p < 0.05$). These results indicate that the left ventricular muscle is closely related to the skeletal muscle volume in ordinary elderly women.

● 目　的

心臓は活動筋の酸素需要に応えるために，心拍出量を増加あるいは血流配分を増減させ，運動に必要な酸素の需要を満たそうとする．一方，骨格筋では筋収縮時に筋ポンプ作用が静脈還流量を高め，心臓の前負荷を増加させる（Froelicher *et al*. 2000）．すなわち，加齢による骨格筋量の低下（Kanehisa *et al*. 2004）は心筋や血管動態に対する刺激を低下させると考えられる．そこで，本研究は高齢者における心形態と骨格筋量の関連を明らかにし，その関連から高齢者における運動の重要性を明らかにすることを目的とした．

● 方　法

測定の対象者は女性61名（年齢：75.6±5.2歳）であった．被験者には事前に目的と内容，測定にともなう危険性と実験参加の任意性を説明した上で，実験参加への同意を書面によって得た．

1．心形態の測定

心形態の測定には循環器用超音波診断装置（SYSTEM V，GE）を用い，Bモード法で測定した．胸骨左縁3-5肋間に2.5 MHzの探触子をあて，仰臥位安静時の左室長軸画像を記録した．後日，得られた記録から大動脈径（AO），左室後壁厚（LVPWT），心室中隔厚（IVST），左室拡張（LVIDd）および収縮末期内径（LVIDs）の計測を行った．またDevereux ら（1977）の式を用いて左室重量を算出した．

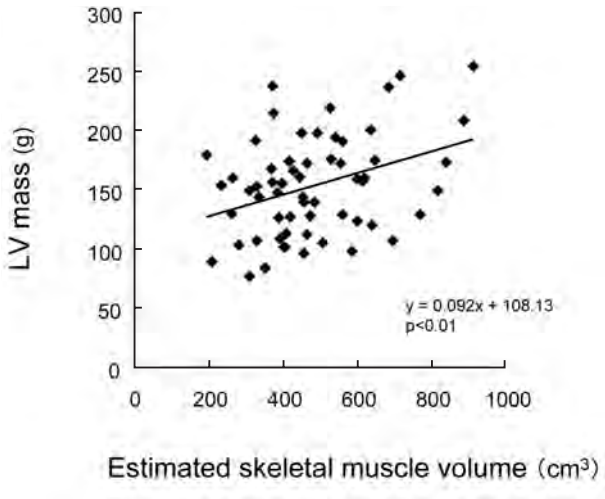

Fig. III.7.3-1　Relationship between estimated skeletal muscle volume and left ventricular muscle mass [LVmass] in elderly women.
Significant correlation coefficients were obtained between the estimated skeletal muscle volume and LVmass in elderly ($r = 0.543$, $p < 0.01$).

2. 筋形態の測定

大腿部筋厚の測定は超音波Bモード法（ALOKA SSD1000, 7.5 MHz）を用いて行った．測定部位は大腿長の50％部位とし，後日，得られた記録より大腿直筋（VI）の浅部腱膜から，中間広筋（RF）を含み大腿骨までを大腿前部の筋厚として計測した．また，大腿前面筋厚を二乗しその値に大腿長を乗じることにより，大腿部筋体積を算出した．

● 結果および考察

大腿直筋と心室中隔厚（$r = 0.221$, $p < 0.05$）および中間広筋と左室後壁厚（$r = 0.240$, $p < 0.05$）との間に有意な関係がみられた．また，心筋および大腿部筋厚を体表面積で正規化した値においても，大腿直筋と心室中隔厚との間には有意（$r = 0.610$, $p < 0.05$）な関係がみられた．Fig. III.7.3-1 に大腿部筋厚から推定した大腿部筋体積と心形態より算出した左室重量との関係を示した．その結果，大腿部筋体積が高値を示すほうが，左室重量も高い値を示し，両者の間には有意（$r = 0.561$, $p < 0.05$）な正の相関関係がみられ，左室重量は大腿部筋体積と密接に相関することが示された．以上のことから，心形態から求めた高齢者の心臓の重量は大腿部筋体積と密接に相関し，心臓の形態を大きく保つためには，高齢者も身体運動による筋量の維持が必要と示唆された．

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8　有疾患者における運動および筋虚血に対する血流調節プロファイル
－下肢閉塞性動脈硬化保有者における運動下肢血行動態の検討－

長田　卓也[1)]

Blood flow profile in relation to exercise-induced muscle ischemia in the patients with peripheral arterial disease

Takuya Osada

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8.1　有疾患者における運動および筋虚血に対する血流調節プロファイル
－下肢閉塞性動脈硬化保有者における運動下肢血行動態の検討－

長田　卓也，勝村　俊仁，村瀬　訓生，木目良太郎，下村　浩祐

Blood flow profile in relation to exercise-induced muscle ischemia in the patients with peripheral arterial disease

Abstract

The present study examined the femoral arterial blood flow response in each leg during intermittent isometric knee extension at incremental exercise intensities in patients with peripheral arterial disease. Changes in blood flow during exercise tend to be higher in the more-affected leg (PAD side) than the control healthy leg. Hyperemic response in the working skeletal muscle may be different in both legs. It is speculated that peripheral vascular disease may influence the blood flow response in muscle contractions during a state of exercise. The peripheral blood flow regulation may be altered due to the severity in the vascular disease during limb exercise as well as resting state.

● 目　的

末梢循環障害（Fontaine分類第Ⅱ度）をきたす下肢閉塞性動脈硬化症保有者を対象に，運動時における血行動態について検討を行うこととした．

● 方　法

末梢循環障害（血管造影にて確認されている）をきたす５名の男性閉塞性動脈硬化症保有者（平均年齢71 ± ２歳）を対象に，座位姿勢での多段階負荷等尺性片側膝伸展運動を行った．運動開始前の安静時に

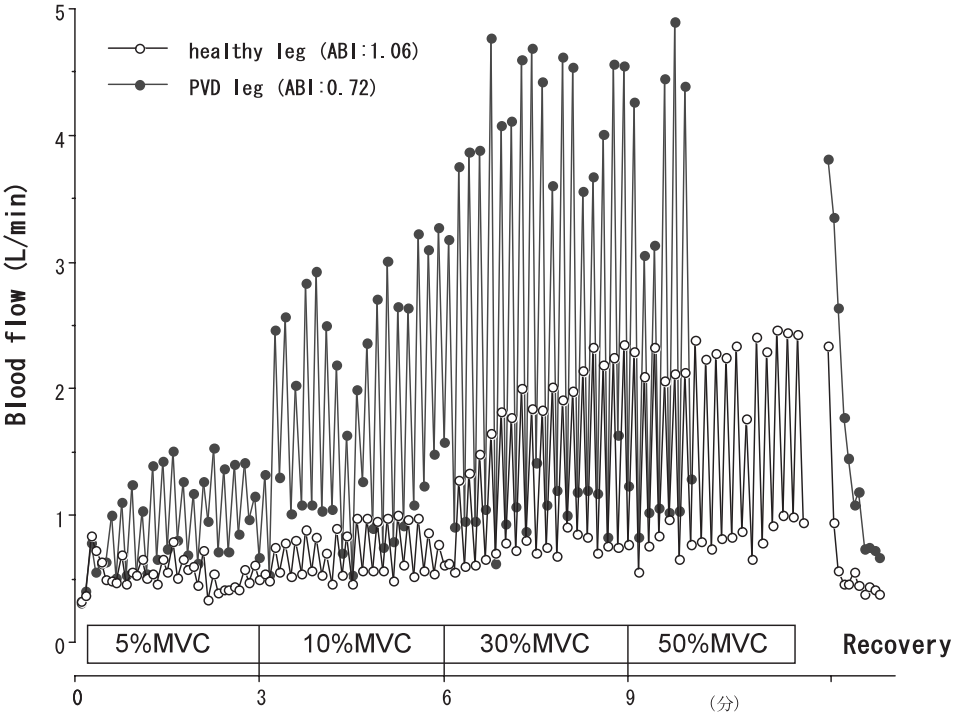

Fig. III.8.1-1　Limb blood flow response during incremental intermittent isometric knee extensor exercise. Changes in blood flow during exercise tend to be higher in the more-affected leg (PVD side) than the control healthy leg.

足関節上腕血圧比（ankle-brachial index：ABI）を測定し，運動は一足ごとに両側について行った．両下肢でABIが低い下肢を患側とし，反対側の下肢を健側（対照肢）とした．運動強度は，最大随意収縮力の５％，10％，30％そして50％とそれぞれの強度で３分間とし，多段階的漸増負荷とした．下肢運動の頻度は，５秒間の等尺性膝伸展運動にひき続き，５秒間の休止期を１サイクルとした．下肢血流の評価は，超音波ドプラー法にて大腿動脈部位において行い，血管径と血流速度により算出した．血流速度は，５秒間の等尺性膝伸展運動及び５秒間の休止期のそれぞれに得られた３～４拍動の波形を計測し，血流量評価に使用した．運動中の血流反応は，筋弛緩期である休止期血流量から筋収縮期のそれを差し引いた血流増加量を指標とした．

● 結　果

安静時において患側下肢のABI値は，健側に比べ低い値を示した．安静時下肢血流量は，患側が健側より低い傾向を示したが，運動中の下肢血流増加量は，患側において大きい傾向を示した．

● 考　察

動脈硬化が強い下肢動脈血管（ABI値が低い下肢側）における，運動時の血流増加反応が高い事が明かとなった．この事は，より運動強度の上昇に伴う骨格筋酸素消費量を代償するための血流増加調節，虚血に伴う血管拡張代謝産物なの影響が強い事が示唆される（Green 2002; Stewart *et al*. 2002）．本研究では，運動に伴う患側下肢血流反応は，健側と比べて異なることが明らかとなり，今後は末梢循環障害が安静時のみならず運動中の骨格筋循環に与える影響を検討する必要があると思われる．特に，基本的身体活動である下肢運動・歩行と骨格筋循環動態の検討は，疾病保有者の運動耐容能向上やトレーニング効果等，将来的に運動処方やQOL向上への糸口としての参考データになりうる事が考えられる．

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9　運動時の呼吸循環系変化に対する中枢性・末梢性の神経調節

佐藤　耕平[1)]

Central and peripheral neural control of respiration and circulation during exercise

Kohei Sato

■本課題の共同研究者
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9.1 Cerebral blood flow response at the beginning of voluntary exercise and passive movement

Kohei Sato, Mayumi Moriyama, Tomoko Sadamoto

Abstract

In this study, we try to reinvestigate the role of central command in regulating the cerebral blood flow at the onset of exercise under a non-invasive condition. Eleven young women performed voluntary elbow flexion-extension exercise with no-load (VOL), activating both the central command and the muscle mechanoreflex, and passive elbow flexion-extension (PAS), selectively activating the muscle mechanoreflex. We continuously monitored the cardiorespiratory and cerebrovascular responses at rest and during VOL and PAS over a 2-min duration. The V_{MCA} and $\dot{Q}_{CCA}$ began to increase before the onset of VOL and peaked immediately after the onset of exercise. VOL simultaneously produced a significant increase in the heart rate (HR) and cardiac output (CO) and a decrease in the mean arterial blood pressure (MAP), thereby inducing a significant decrease in the cerebrovascular resistance at the onset of VOL. There were no significant changes in these parameters at the onset of PAS. These results suggested that the increases in cerebral blood flow at the beginning of no-load voluntary exercise were most likely mediated by feedforward control of central command. To the contrary, the muscle mechanoreflex appeared to have little effect on the adjustments in cerebral blood flow responses at the onset of no-load voluntary exercise.

Purpose

We aimed to investigate the role of central command in regulating the cerebral blood flow at the onset of exercise. The comparison of the cerebrovascular adjustments between voluntary exercise and passive movement would provide the contribution of central command (Nóbrega *et al*. 1994; Williamson *et al*. 1997). In the present study, we studied the time course of the responses in cerebral blood flow at the onset of voluntary exercise with no-load and passive movement accomplished by dynamic elbow flexion and extension of a single arm.

Methods

Eleven young women (age, 23.5 ± 0.7 years) participated in this study. In this study, the single arm elbow flexor-extensor exercise and passive movement were performed using a computer-based multifunctional dynamometer device. For the voluntary dynamic exercise, the subjects were instructed to move their forearm between elbow angles of 50° and 90° (0° equaling full extension) at an angular velocity of 90 deg・sec^{-1} in time to a rhythmic sound from a cassette being played in a tape-recorder. Voluntary exercise was continued for 2-min. Passive movement was achieved by a motor-driven lever arm that rotated around an axis at a constant velocity. All the subjects were requested to relax and not to resist the arm movement. Passive movement was performed with the same range of movement, angular velocity, and frequency as the voluntary exercise. Common carotid artery blood flow ($\dot{Q}_{CCA}$) and mean middle cerebral blood flow velocity (V_{MCA}) examination was performed using a high-resolution ultrasound system (LOGIQ5; GE Medical Systems, Japan). The cardiovascular responses were measured noninvasively by photoelectric plethysmography using a Finometer (Finapres Medical Systems BV, Arnhem, Netherlands) and the respiratory parameters were determined using an online system for

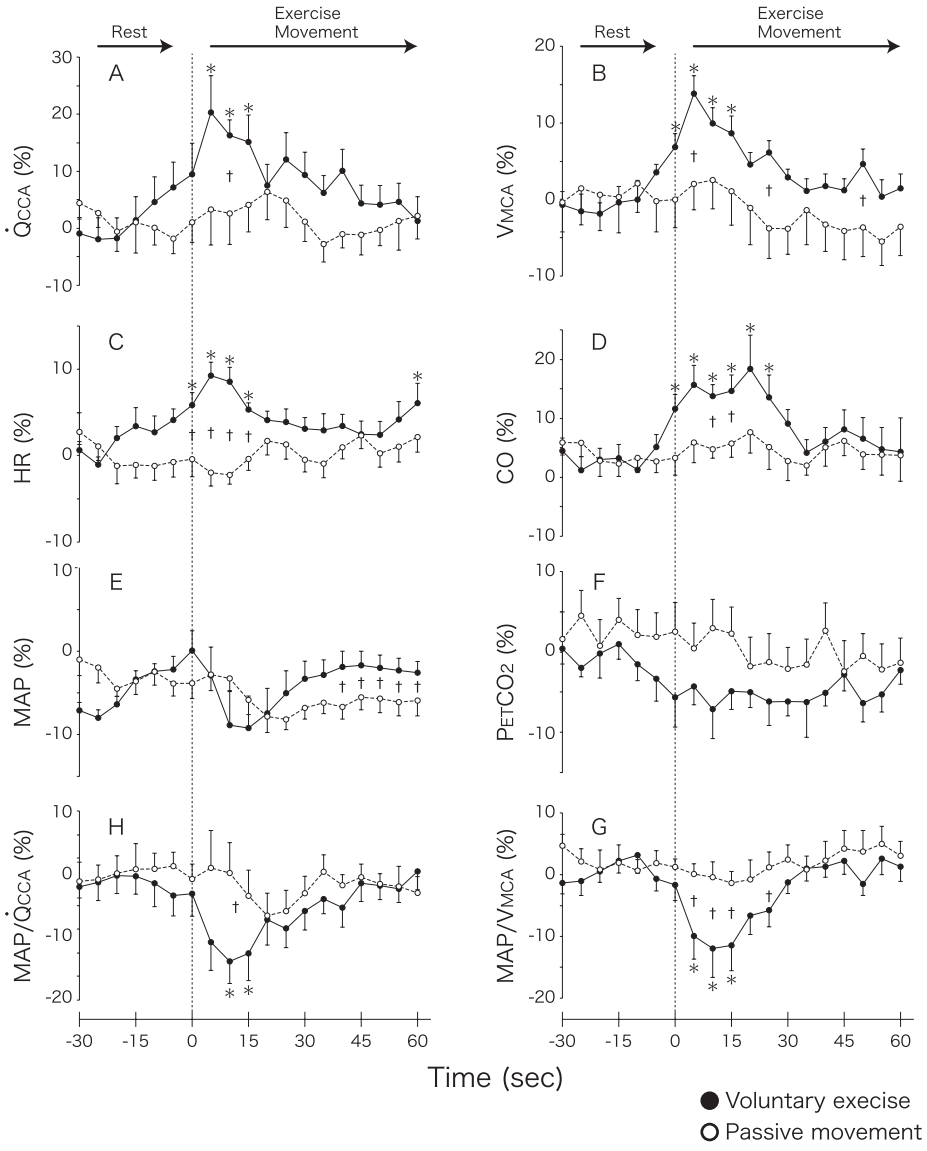

Fig. III.9.1-1 Changes in the cardiorespiratory and cerebral blood flow responses at the onset of voluntary exercise and passive movement. Relative changes were obtained by normalizing to the resting values. The time courses of the variables are shown from 30 s before to 60 s after the onset of exercise and movement. (A) V_{MCA}, middle cerebral artery mean blood velocity; (B) $\dot{Q}_{CCA}$, common carotid artery mean blood flow; (C) HR, heart rate; (D) CO, cardiac output; (E) MAP, mean arterial blood pressure; (F) $P_{ET}CO_2$, end-tidal CO_2; (G) MAP/V_{MCA}, index of the cerebrovascular resistance; (H) $MAP/\dot{Q}_{CCA}$, common carotid artery resistance. Values are expressed as the mean (SE).
* Different from the resting value ($P < 0.05$). †Difference between the voluntary exercise and passive movement at each time point ($P < 0.05$).

the breath-by-breath method.

● Results and Discussion

The major findings of this study were as follows. V_{MCA}, $\dot{Q}_{CCA}$, HR, and CO began to increase significantly immediately before and at the onset of voluntary exercise in parallel with a transient decrease in the cerebrovascular resistance. There were no significant changes in these parameters during passive movement, and thus, significant differences were observed in these parameters between voluntary exercise and passive movement immediately after their onset. These results indicate that the rapid adjustment in the cerebrovascular responses at the beginning of voluntary exercise with no-load was probably attributa-

ble to the feedforward control of central command descending from the higher brain centers.

The mechanism concerning the central command-related increase in the cerebral blood flow may be mainly explained by based on the following two possibilities. Studies investigating the functional anatomy of the central command-induced changes in the regional cerebral blood flow have shown a network of cortical structures involved (Williamson *et al*. 2006). Therefore, the first possibility is neural activation in these regions, which may serve as a central command network, is responsible for observed increases in brain blood flow (Williamson *et al*. 2002; Williamson *et al*. 2006). Second, the central command is generally thought to have a greater effect on HR and, thus on CO, than blood pressure. Thus, it is possible that an abrupt increase in HR and CO at the onset of exercise may contribute to the rapid change in V_{MCA} and $\dot{Q}_{CCA}$ because in this study, V_{MCA} and $\dot{Q}_{CCA}$ changed during voluntary exercise in parallel with the HR and CO responses. Recent studies have suggested that CO is an important factor involved in the change in V_{MCA} during exercise (Ide *et al*. 1998; Ogoh *et al*. 2005). Accordingly, it is suggested that the central command-mediated brain activity in several regions and/or the increase in circulatory variables, particularly the CO response, may significantly contribute to the rapid adjustment of the cerebral blood flow responses at the beginning of exercise.

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9.2 Effect of mode of ventilation on cerebral blood flow response during static arm exercise

Kohei Sato, Ai Hirasawa, Tomoko Sadamoto

Abstract

Heavy resistance exercise may be associated with a small risk of cerebral aneurysm rupture, subarachnoid hemorrhage, and symptoms of dizziness or outright weight-lifters' blackout, which may be induced by a rapid change in the cerebral blood flow. We hypothesized that these changes during heavy exercise could be associated with the mode of ventilation. The purpose of the present study was to elucidate the effect of the mode of ventilation on cerebral blood flow response during heavy upper body exercise. Subjects performed 15-s static exercises at 80% maximum voluntary contraction (MVC) under different modes of ventilation. In this study, we observed that heavy exercise with breath holding induced marked and rapid changes in the cerebral blood flow velocity in the middle cerebral artery during and after exercise as compared with that with continued normal ventilation. We also observed that hyperventilation before exercise could largely contribute to a lower cerebral blood flow velocity during exercise and extending to the recovery phase. Our data suggested that even during heavy upper body exercise, the mode of ventilation is very important for maintaining cerebral circulation.

Purpose

Change in the cerebral blood flow during heavy exercise could be associated with the mode of ventilation, including the forced expiration against a closed glottis (breath holding induced a Valsalva-like maneuver) and hypocapnia induced by hyperventilation before and during exercise. A previous study reported marked change in the mean cerebral blood flow velocity in the middle cerebral artery (MCA V_{mean}) during heavy two legged extension with concomitant Valsalva-like maneuver (Pott *et al*. 2002). Romero and Cooke (2006) demonstrated that hyperventilation before exercise exacerbates the reduction in MCA V_{mean} during leg-press resistance exercise. These studies suggested that during heavy exercise the associated mode of ventilation may be of deterministic importance for cerebral circulation. However, these investigations focus on cerebral blood flow regulation during lower-body exercise involving a large muscle mass. To date, there is no information regarding the effect of the mode of ventilation on the cerebral blood flow response during upper body heavy exercise involving a small muscle mass. Therefore, the purpose of the present study was to elucidate the effect of the mode of ventilation on cerebral blood flow response during heavy upper body exercise.

Methods

A total of 10 male field athletes (7 shot putters and 3 hammer throwers; mean age ± SD: 21.2 ± 1.2 years) volunteered to participate in this study after providing informed consent to the protocol, as approved by the ethics committee of Japan Women's College of Physical Education. In this study, single arm elbow flexion exercise was performed with the use of a multifunctional dynamometer device. The exercise load selected was 80% of the maximal voluntary contraction (MVC) force. After a 3-min resting period, the subjects performed 15-s static exercises at 80% MVC with the following 3 different modes of ventilation (in random order): 1) continued normal

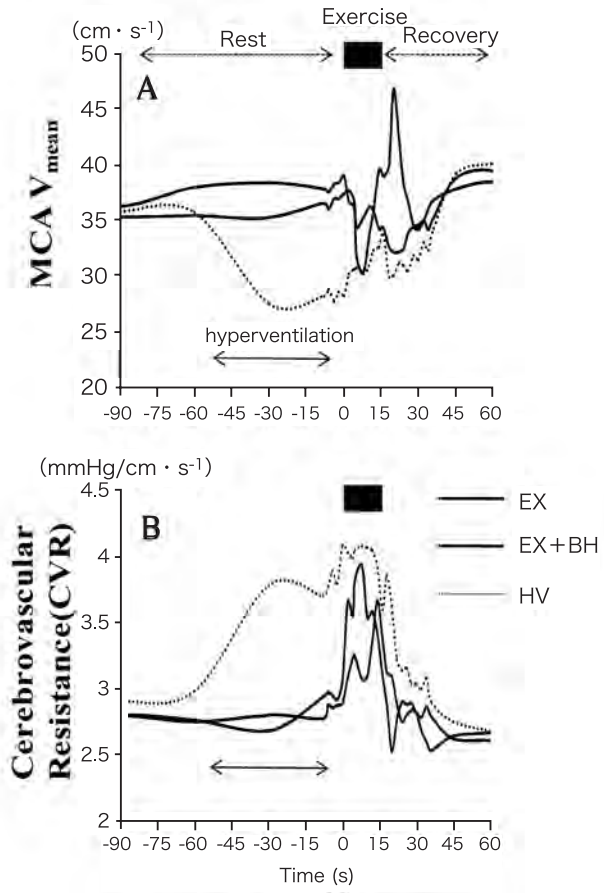

Fig. III.9.2-1 Cerebrovascular responses at rest, during, and after heavy exercise. (A) MCA V_{mean}, Mean middle cerebral artery mean blood velocity and (B) CVR, Cerebrovascular resistance index.

ventilation (EX), 2) exercise with concomitant breath holding (EX+BH), and 3) pre-exercise hyperventilation till an end tidal partial pressure of CO_2 ($P_{ET}CO_2$) of 3.5% was achieved (HV). In HV, after a 2-min rest, the subjects were instructed to perform voluntary hyperventilation for 1-min in order to achieve a $P_{ET}CO_2$ of ～3.5%. After the 1-min hyperventilation, the subjects performed 15-s static exercises with continued normal ventilation. MCA V_{mean} measurement was performed with an ultrasound system (Vivid 7pro; GE Yokogawa Medical Systems) equipped with a 2.0 MHz sector transducer. The MCA V_{mean} was defined as the time-averaged mean velocity obtained in automatic calculation mode. Mean arterial pressure (MAP) was measured non-invasively by photoelectric plethysmography with Finometer (Finapres Medical Systems BV). Furthermore, we determined the stroke volume (SV), and cardiac output (CO), from the blood pressure wave form by using the Modelflow method. Respiratory parameters were determined with an online system for the breath-by-breath method. The ratio of MAP/ MCA V_{mean} was calculated as an index of cerebrovascular resistance (CVR).

● Results and Discussion

The expiratory strain during a Valsalva-like maneuver might reduce blood flow to the brain. Forced expiration against a closed glottis increases intrathoracic pressure and central venous pressures and marked reduces in SV and thus CO. Previous studies indicated that CO is an important determinant of cerebral blood flow during exercise (Ogoh *et al*. 2005). However, our data suggested relationship between CO and MCA V_{mean} was not simply under this situation. Furthermore, the

rapid increase in the CVR at the onset of exercise may also contribute to the change in MCA V_{mean} and the increase in the CVR may be induced by sympathoexcitation due to heavy exercise and/or the reduction in CO and P_aCO_2. The increase in the CVR during EX+BH suggested vasoconstriction of the peripheral branches of the MCA. On the other hand, over shooting of the MCA V_{mean} immediately after the end of exercise may be induced by rapid decrease in CVR, with rapid recovery of CO and P_aCO_2.

In the HV trials, reduced MCA V_{mean} occurred in conjunction with increased CVR. This reduction in MCA V_{mean} before, during, and after exercise was attributable to the reduction in P_aCO_2. These results indicate that the increase in CVR was probably associated with vasoconstriction of the cerebral blood vessels. In summary, our data suggested that even during upper body heavy exercise involving small muscle mass, the mode of ventilation was very important for maintaining cerebral circulation. We think that the combination of hyperventilation before heavy exercise and breath holding during exercise is the worst scenario from the perspective of cerebral circulation. It may be that continued normal ventilation during heavy upper body exercise may be safer, in that it helps to avoid rapid changes in the cerebral blood flow and CVR that may in turn cause symptoms of dizziness or outright weight lifter's "black out" and intracranial hemorrhage.

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10　運動準備期のセントラルコマンドの働き

岩館　雅子[1, 2)]

Central command during the preparatory period before voluntary exercise

Masako Iwadate

■本課題の共同研究者

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10.1　運動準備期の大脳皮質運動野酸素動態と循環応答の対応

岩館　雅子，定本　朋子

Relationship between cortical oxygenation in the motor area and cardiovascular responses during the resting preparatory period before voluntary exercise

Abstract

We studied the cortical oxygenation in motor area (MA) and the concomitant cardiovascular responses during resting preparatory period either with sustaining handgrip exercise (Ex) or without handgrip exercise (Con) in 13 healthy subjects. The oxygenated hemoglobin (oxyHb), deoxygenated hemoglobin (deoxyHb) and total hemoglobin (totalHb) in the left motor cortex were measured by near-infrared spectroscopy. Heart rate (HR), cardiac output (CO), mean arterial blood pressure, and the oxygenation in the right forearm flexors muscles were simultaneously recorded in both Ex and Con experiments. During the resting preparatory period in Ex, the oxyHb and totalHb in motor cortex were significantly higher than those in Con while deoxyHb was similar to that in Con. These changes in Ex indicated the increase in regional cerebral blood flow resulting from the increases in the regional cerebral oxygen metabolic rate in MA. In accord with these changes, HR, CO, and the muscle oxyHb were elevated significantly in Ex but not in Con. However, the muscle totalHb was not higher significantly in Ex than that in Con. These results suggested that the increases in HR and muscle flow rate in Ex were coupled with the increase in cortical activation resulting from a preparation for exercise.

● 目　的

本研究の目的は，運動準備・想起により発現するセントラルコマンドが，大脳皮質運動野周辺領野の活動へ及ぼす影響を明らかにすることである．

● 方　法

被験者は13名の健康な女子大学生とした．被験者は，掌握運動を行う運動条件と行わない対照条件の2条件に参加した．運動条件では，1 Hzの音の回数を検者の合図に合わせて数え，50回まで数えた後には右腕による掌握運動（運動負荷：30％MVC）を10秒間実施した．対照条件では，音の計数の後の掌握運動は行わず，音の計数のみを続けて行った．

脳活動の指標として，左右運動野手領域脳酸素動態を近赤外分光法により記録した．循環応答の指標としては，心拍数，平均動脈血圧，心拍出量，前腕屈筋の筋酸素動態を記録した．本研究では被験者が音の回数を数え始めてから運動開始直前までの50秒間を運動準備期とし，解析対象とした．

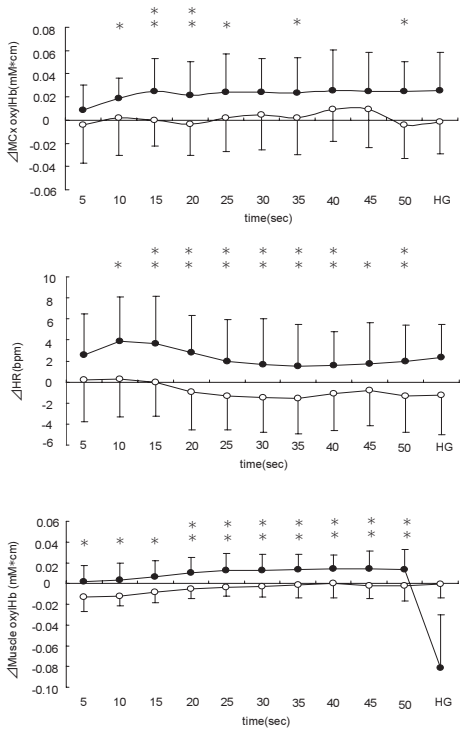

Fig. III.10.1-1　Changes in oxygenated hemoglobin obtained left motor cortex (MCx oxyHb), Heart Rate (HR), oxygenated hemoglobin obtained right forearm flexors muscles (muscle oxyHb) during preparatory period before handgrip exercise (HG). Values are means ± SD in 13 subjects. ○, control condition; ●, exercise condition; *, $p < 0.05$; **, $p < 0.01$.

● 結果および考察

運動準備や想起に伴い，循環応答としては，心拍上昇および心拍出量増加および筋血流速度上昇という応答がみられた．これに対し，大脳皮質運動野酸素動態においても，oxyHbおよびtotalHbの上昇，deoxyHbの低下傾向という，神経活動賦活に伴う血流増加を反映する脳酸素動態変化がみられた．

このことから，運動開始前において運動準備や想起により（Williamson *et al*. 2002），心拍数の上昇，心拍出量増加および活動肢の筋血流速度上昇が生じるとき，大脳運動野周辺の脳活動も同時に亢進することが示された．

● 文　献

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10.2　運動準備期と運動時の大脳皮質運動野酸素動態の関係

岩館　雅子，澁谷　顕一，定本　朋子

Cortical oxygenation in the motor area during the resting preparatory period and the following voluntary exercise

Abstract

We have compared the oxygenation changes in the motor cortex (MCx) during the maximal heart rate (HR) change session and minimum HR change session during the resting preparatory period with the sustaining handgrip exercise in 6 healthy subjects. During the resting preparatory period with the exercise, the oxygenation changes were larger during maximal HR change session than that of minimum HR change sessions. On the other hand, no significant differences in the oxygenation change during the sustaining handgrip exercise were observed between the maximal and minimum HR change sessions. These results indicate that the oxygenation changes in the MCx during the exercise are independent from that of the resting preparatory period with the exercise.

● 目　的

前課題において，運動準備・想起により心拍上昇と運動野酸素化動態上昇が同時にみられるという対応が示された（岩館と定本 2008）．本研究では，運動準備期と運動時の運動野酸素化動態の関係を明らかにすることとした．

● 方　法

被験者は6名の健康な女子大学生とした．被験者は15秒間の運動準備期（検者の合図5秒＋カウントダウン10秒）の後，掌握運動（60％MVC）を10秒間行う課題を10セット行った．

脳活動の指標として，左右運動野手領域脳酸素動態を近赤外分光法により記録した（Hoshi and Tamura 1993）．循環応答の指標としては，心拍数を記録した．本研究では，心拍数と脳酸素動態の対応を確認するため，準備期の心拍変化が最大の試行と最小の試行を選び，両試行における運動野酸素化動態を比較した．

● 結果および考察

運動準備期の運動野酸素化動態は，酸素化Hbおよび総Hbにおいて試行間に差がみられ，心拍最大変化試行においては，ベースラインからの酸素化Hbの上昇および脱酸素化Hbの減少が有意であった．このことから，心拍最大変化試行では，運動野血流速度の

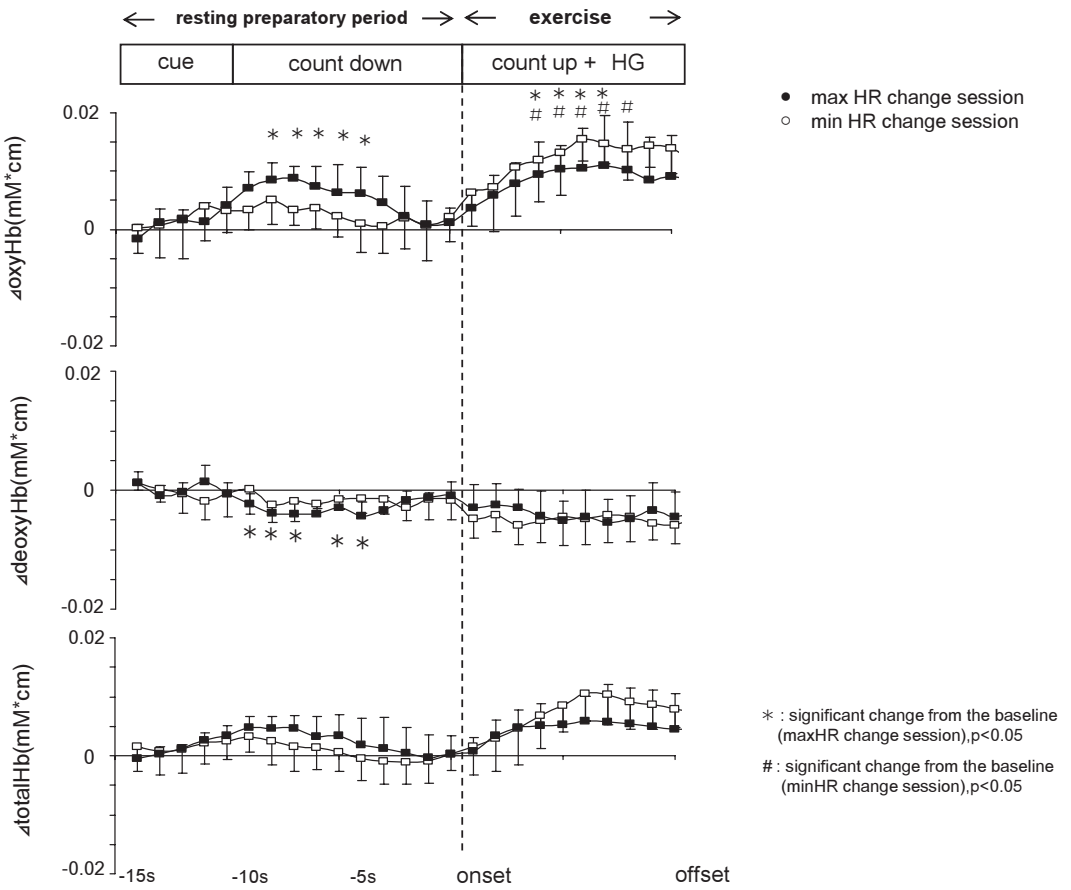

Fig. III.10.2-1　The oxygenation in the contralateral motor cortex during the resting preparatory period and the sustaining right hand grip exercise. Filled circles show that of maximal HR change session during the resting preparatory period and open circles show that of minimum HR change session during resting preparatory period.

上昇が生じていたことが確認された．一方，運動時については，準備期でみられたような，両試行間の差がみられなかった．このことから，運動準備期における運動野の活性化は，運動時に生じる活性化には関連しないことが示唆された．

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11　筋の酸素代謝特性と運動時循環応答との連関

笹原（上田）千穂子[1, 2)]

Associated changes in muscle oxygenation with circulatory responses during exercise

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11.1　異なる強度での静的膝伸展運動後における筋の浅部と深部の再酸素化

笹原（上田）千穂子，加賀谷淳子

11.1　異なる強度での静的膝伸展運動後における筋の浅部と深部の再酸素化

笹原（上田）千穂子，加賀谷淳子

Reoxygenation of muscles at the superficial and in the deep regions during static knee extension exercise at varying intensities

Abstract

The purpose of this study was to investigate a hypothesis that circulatory responses to various exercise intensities closely relate to muscle fiber type dominantly recruited during the exercise. We examined that muscle oxygenation in the vastus lateralis (VL) and circulatory responses to static knee extension exercise at various intensities. Method: Ten healthy female subjects performed static knee extension exercise at 10%, 20%, 30%, 40%, 50%, 60% and 70% maximal voluntary contraction (MVC) for 1-min at each level in sitting position. Muscle oxygenation in the VL was monitored using multi channel near-infrared spectroscopy and arterial mean blood pressure (MBP) was measured by photoelectric plethysmography. Result: Half time reoxygenation, the time taken to reach a value of half-maximal recovery after exercise, for all channels was significantly delayed in exercise at 70% MVC compared with the other intensities. However there were no significant differences between the channels. MBP also increased with respect to exercise intensity. Conclusion: This study shows that reoxygenation time in the VL after static knee extension was prolonged in accordance with increasing circulatory responses to ascending exercise intensities. However, reoxygenation was more delayed at higher exercise intensity than those expected from lower intensities, whereas circulatory parameters increased linearly.

● 目　的

本研究は，運動強度の増加に伴う循環指標の変化は動員される運動単位の代謝特性に密接に関与しているのではないかという仮説を検証することを目的とした．具体的には，①運動後の筋再酸素化時間（$T_{1/2}$ reoxy time，筋の有酸素性代謝貢献度が低いと延長する）が運動強度の上昇に伴い顕著に延長し始める負荷強度が存在するか否か，②筋の浅い部位と深い部位で筋線維組成が異なることが知られているが，これが$T_{1/2}$ reoxy timeと運動強度の関係に影響を与えるが否かについて検討した．

● 方　法

被験者は健康な成人女性10名であり，座位姿勢で静的膝伸展運動を行った．運動強度は最大随意筋力（MVC）の10，20，30，40，50，60，70％とし，各強度の運動負荷後十分な休憩時間をとった後，次の強度の測定を行った．運動時の平均血圧（MBP）を連続指血圧測定装置（Finometer，Finapres Medical Systems BV）で測定した．筋酸素動態は近赤外分光法装置（OMM-3000，Shimadzu）により，骨格筋の酸素化ヘモグロビン，脱酸素化ヘモグロビン，総ヘモグロビンを測定し，$T_{1/2}$ reoxy timeは先行研究（Hamaoka *et al*. 1992; Ichimura *et al*. 2006）と同じ方法で酸素化ヘモグロビンより算出した．測定プローブの送受光間距離を2 cm，3 cm，4 cm，5 cmとして，同一筋内の深さの異なる部位でのT1／2 reoxy timeを求めた．

● 結果および考察

MBPは負荷強度の増加に伴い上昇し，10％MVCに対して30％MVC以上の強度で有意に高かった．一方，$T_{1/2}$ reoxy timeは負荷強度に対して指数関数的な上昇を示し，10％MVCに対して70％MVCにおいて有意に高い値を示した．$T_{1/2}$ reoxy timeの筋の浅い部位と深い部位とにおける比較では，どの強度においても有意差はなかった．以上の結果から，筋再酸素化時間が顕著に延長する運動強度が存在す

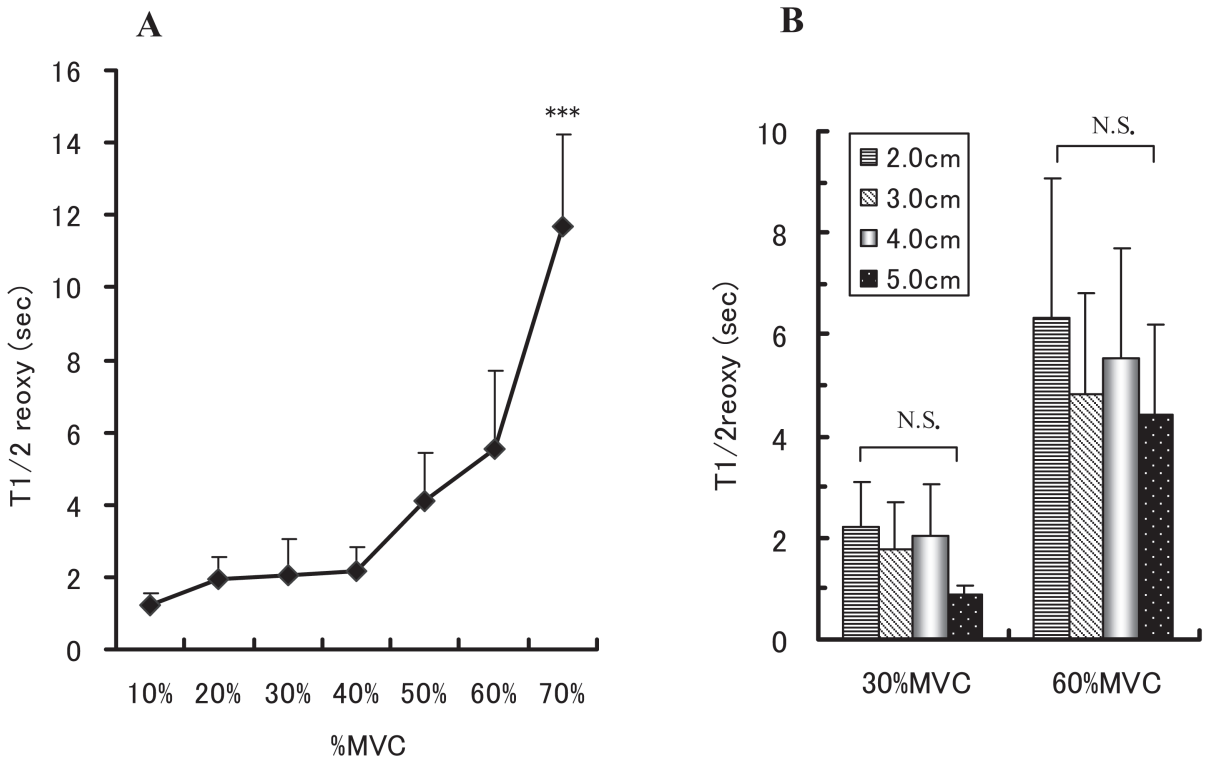

Fig. III.11.1-1 Half time reoxygenation (T1/2 reoxy time) after knee extension exercise. (A) The effects of exercise intensities. Light source and detector distance of NIRS prove was 4 cm. (B) The effects of light source and detector distance at the intensities of 30% and 60% MVC. Values are expressed as mean ± SE, n=10. *** Different from 10%MVC ($P < 0.001$).

ることが明らかになったが，筋の深さによる相異はみられなかった．筋再酸素化時間も血圧も，運動強度により変化しているが，筋再酸素化時間はより高強度の運動負荷で有意に延長することが明らかになった．

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12　運動時における一次運動野の酸素化動態

澁谷　顕一[1)]

Oxygenation kinetics in the primary motor cortex area during exercise

Kenichi Shibuya

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12.1. Quantification of delayed oxygenation in ipsilateral primary motor cortex compared with contralateral side during a unimanual dominant-hand motor task using near-infrared spectroscopy

Kenichi Shibuya, Tomoko Sadamoto, Kohei Sato,
Mayumi Moriyama, Masako Iwadate

Abstract

Using near infrared spectroscopy (NIRS) techniques, it is possible to examine bilateral motor cortex oxygenation during a static motor task. Cortical activation was assumed to be reflected by increased oxygenation. The purpose of the present study was to examine the time course of oxygenation in the bilateral motor cortex during a low-intensity handgrip task. Six healthy, right-handed subjects participated in the study. The near-infrared spectroscopy probes positioned over the bilateral motor cortex were used to measure the cortical activation throughout a handgrip task carried out. The subjects performed a 3-min handgrip task with increasing intensity in a ramp-like manner [10-30% of the maximal voluntary contraction (MVC) at 6.67% MVC.min^{-1}]. Contralateral motor cortex oxygenation increased significantly from 100 to 180 s after the start of the motor task compared with the baseline value ($p < 0.05$). Ipsilateral motor cortex oxygenation also increased significantly from 130 to 180 s after the start of the motor task ($p < 0.05$). The onset of increase in oxyhemoglobin ([HbO_2]) and decrease in deoxyhemoglobin ([Hb]) in contralateral motor cortex area (M1) were significantly earlier than in ipsilateral M1 (respectively, $p < 0.05$). These results show that there is a delayed oxygenation in ipsilateral primary motor cortex area compared with contralateral side during a unimanual dominant-hand motor task.

● Purpose

Muscle fatigue is characterized by an exercise-induced loss of power- and force-generating ability of the muscle during the course of or after exercise (Bigland-Ritchie and Woods, 1984; Booth and Thomason, 1991; Nybo and Nielsen, 2001; Gandevia, 2001). The purpose of the present study was to examine bilateral M1 oxygenation during a low-intensity unimanual handgrip task.

● Methods

Six right-handed, healthy volunteers (age: 21.4 ± 0.2 y, height: 159.1 ± 1.3 cm, weight: 56.3 ± 1.9 kg, MVC: 315.6 ± 11.8 N) participated in the present study.

Near-infrared spectroscopy (NIRS) techniques have been described elsewhere (Elwell *et al*. 1994). We used a three-wavelength NIRS apparatus (780, 805, and 830 nm; NIRStation, OMM3000, Shimadzu Co., Kyoto, Japan) for measuring motor cortex oxygenation. The optical probe consisted of one emitter and one detector (comprising three separate sensors). These probes were guided on the subjects' heads using glass fiber bundles and positioned over the bilateral motor cortex areas. The distance between the transmitting and the receiving probes was 3.0 cm. The probes were positioned over bilateral motor cortex areas for hand enclosing C3 and C4, according to the modified international EEG 10-20 system (American Electroencephalo graphic Society, 1994).

Before the start of the study, the subjects were familiarized with the protocol. They performed a static 3-min right-handgrip task with a ramp-like increase in intensity from 10% MVC to 30% MVC

Table III.12.1-1 The time for oxygenation after the start of motor task. Astarisks shows significant differences between the response on hemispheres ($p < 0.05$).

	Contralateral	Ipsilateral
HbO_2	50.8 ± 35.4	60.0 ± 31.3 *
Hb	32.5 ± 15.7	94.2 ± 38.1 *
tHb	45.0 ± 17.3	64.2 ± 9.2 *

(6.67%· min^{-1}). The subjects were seated and were given a handgrip meter.

● Results and Discussion

Changes in cerebral oxygenation reflect cerebral functional activation (Colier *et al*. 1997, 1999; Kleinschmidt *et al*. 1996; Obrig *et al*. 1996). In the present study, we observed a bilateral increase in M1 oxygenation during the course of a low-intensity static motor task. The increase in ipsilateral M1 oxygenation was delayed compared with the increase in contralateral M1 oxygenation. To the best of our knowledge, this is the first report showing that ipsilateral M1 oxygenation is delayed compared with contralateral M1 oxygenation during the course of a motor task.

In conclusion, the results of the present study show a delayed oxygenation in the ipsilateral primary motor cortex during the course of a unimanual low-intensity motor task. The increasing oxygenation in the ipsilateral motor cortex suggests a real-time interaction between bilateral hemispheres during a motor task.

12.2 Reduced activity of the ipsilateral primary motor cortex during repetitive handgrip exercise

Kenichi Shibuya, Masako Iwadate, Tomoko Sadamoto

Abstract

The brain function controlling muscle force modulation during exercise has remained unclear. The purpose of the present study was to examine the bilateral primary motor cortex (M1) oxygenation during static and repetitive handgrip exercise performed with the right hand (60% maximal voluntary contraction; 10 s exercise/75 s rest; 5 sets). Seven healthy, right-handed subjects participated in the present study. Near-infrared spectroscopy (NIRS) probes were positioned over the bilateral M1 area to measure cortical oxygenation during handgrip exercises. The oxygenation levels of the bilateral M1 significantly changed compared with their resting values in all trials ($p < 0.0001$). The oxygenation levels of the contralateral M1 did not change significantly across the trials (oxyhemoglobin (HbO_2): $p = 0.8050$; deoxyhemoglobin (Hb): $p = 0.8036$), while those of the ipsilateral M1 significantly decreased across the trials (HbO_2: $p = 0.0371$; Hb: $p = 0.0317$). The present results suggest an intracortical inhibition from the contralateral M1 to the ipsilateral M1 during the repetitive exercise.

● Purpose

The purpose of the present study was to investigate the effect of exercise task repetition on the ipsilateral M1 activity. The most noteworthy results of the present study were the constancy of oxygenation in the contralateral M1 and the significant decrease of oxygenation in the ipsilateral M1 with the increase in repetition.

● Methods

Seven healthy, right-handed volunteers participated in the present study. Informed consent was obtained from each subject after the subject received a complete explanation of the nature of

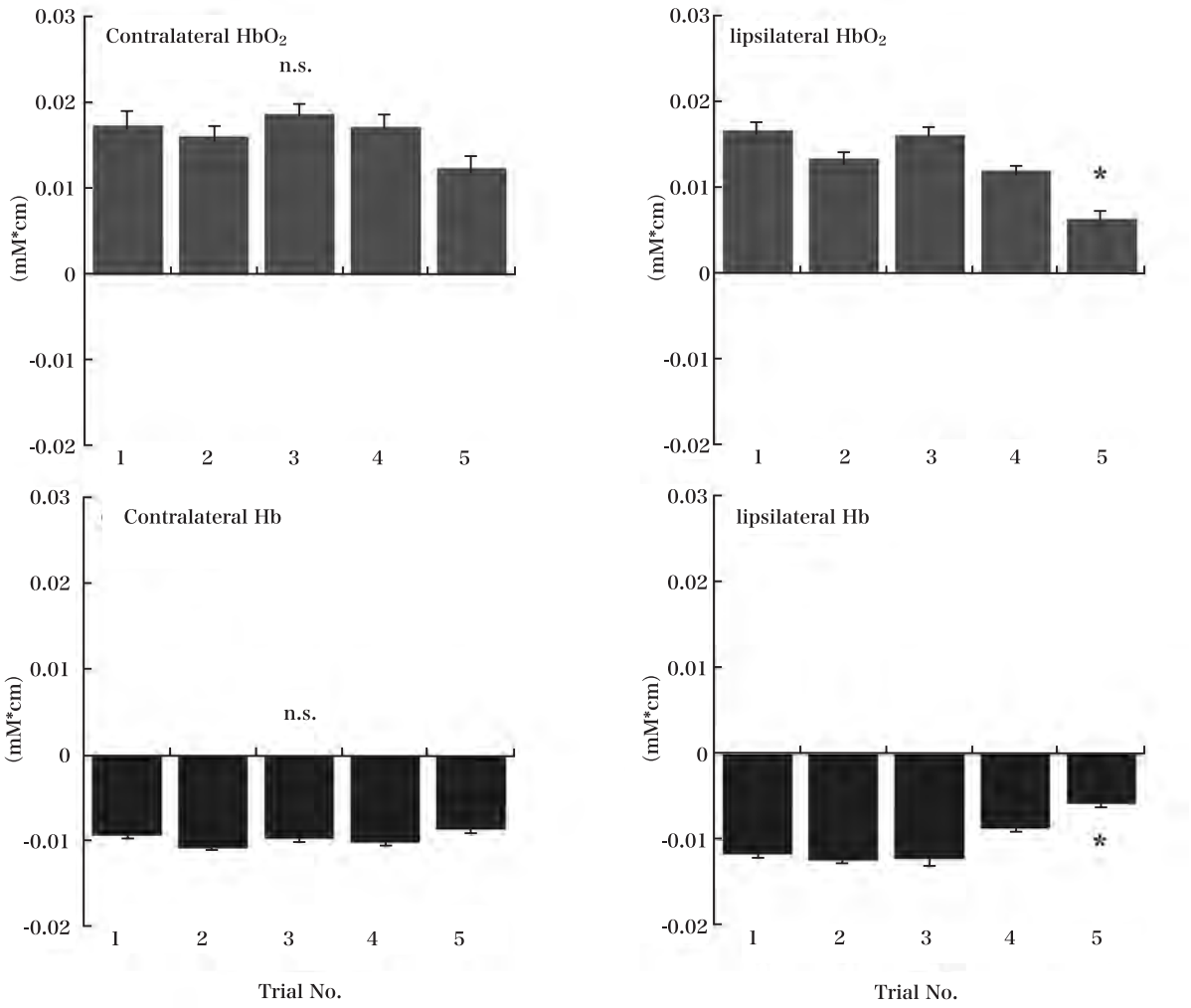

Fig. III.12.2-1 The peak value changes in oxygenation from resting levels. Upper panels represent the results of oxyhemoglobin (HbO_2) changes. Lower panels represent the results of deoxyhemoglobin (Hb) changes. Right panels represent the results of ipsilateral primary motor cortex oxygenation changes, and left panels represent the results of contralateral primary motor cortex oxygenation changes. The asterisks show significant differences from the first trial ($p < 0.05$). Error bars indicate s.e.m.

the study procedure and its noninvasiveness.

The Near-infrared spectroscopy (NIRS) technique has been described elsewhere (Elwell *et al.* 1994). We used a three-wavelength NIRS apparatus (780, 805, and 830 nm; NIRStation, OMM3000, Shimadzu Co., Kyoto, Japan) to measure motor cortex oxygenation. The distance between the transmitting and the receiving probes was 3.0 cm. The probes were positioned over the bilateral C3 and C4 hand motor areas according to the modified international EEG 10-20 system (American Electroencephalographic Society, 1994).

Subjects performed five to 10-s duration handgrip exercises. The subjects took a rest over 30 min after the detection of an optimal position for the probe. The subjects performed a static right-handgrip task [exercise: 10 s, rest: 75 s; the tasks were performed five times at 60% of MVC, taking a rest between sessions].

● Results and Discussion

In the present study, we found the early significant changes in HbO_2 and Hb after the start of exercises. The previous studies found the gradual changes in HbO_2 and Hb after the start of tasks with the exception of exercise (ef: Taga *et al.* 2003). We excluded the data just before the start of exercise to calculate the baseline values in HbO_2 and Hb for avoiding the inclusion of the

effects of the preparation and/or attention for the exercise on the oxygenation changes in the analyses. The early changes in HbO_2 and Hb after the start of exercises might be influenced by the way of analysis we used. Another possible explanation for the early changes in HbO_2 and Hb in the present study was the effect of blood flow changes after the start of exercise. It is generally believed that the cerebral blood flow does not change during static exercise (Rogers *et al*. 1990). The possibility of the influence of cerebral blood flow changes on the oxygenation in the bilateral M1 must be low. The early changes during exercise in the present study might be the effects of attention and/or preparation for the start of exercise.

The lack of oxygenation in the ipsilateral M1 during exercise at the fifth trial compared with the first trail might be affected by the inhibition from the contralateral M1 to the ipsilateral M1 due to the voluntary fatigue as reported by the previous studies (Shibuya *et al*. 2006; Shibuya e*et al*. 2007). On the other hand, the results of the present study might reflect that the ipsilateral M1 partially contributes to the force modulation. Muscle power output during exercise is fundamentally controlled by the contralateral M1.

The present results suggest an intracortical inhibition from the contralateral M1 to the ipsilateral M1 during the repetitive exercise and the possibility a collateral contribution of the ipsilateral M1 to force production, and that this contribution declines with the habituation for exercise. Further studies should focus on elucidating the contribution of the ipsilateral M1 to force production.

12.3 A comparison between sedentary subjects and athletes of oxygenation kinetics in the contralateral primary motor cortex area during exercise leading to voluntary exhaustion

Kenichi Shibuya

Abstract

Motor signals are commanded fundamentally from the primary motor cortex contralateral to the exercising limb ($M1_{contralateral}$). The signals from the $M1_{contralateral}$ reach the contracting muscle through the corticospinal and spinal motoneurons. When muscle fibers are repeatedly contracted, energy supplies are depleted, and the muscles become fatigued. Physiological fatigue is characterized by exercise-induced loss of the power- and force-generating ability of the muscle during the course of or after exercise. It remains unclear whether the activation kinetics in the motor cortex area could be different between athletes and sedentary subjects during exercise leading to voluntary exhaustion. We examined this in 7 athletes and 7 sedentary subjects. We performed near-infrared spectroscopy over the positioned motor cortex area to measure oxygenation throughout a handgrip exercise leading to voluntary exhaustion. The subjects performed a sustained 50%-60% maximal voluntary contraction handgrip exercise until voluntary exhaustion. In athletes, oxygenation in the $M1_{contralateral}$ decreased significantly at voluntary exhaustion compared with the resting values ($p < 0.05$). On the other hand, in sedentary subjects, oxygenation in the $M1_{contralateral}$ increased throughout the exercise ($p < 0.05$). These results suggest that the motor signals from the motor cortex area may be different between athletes and sedentary subjects, especially in a fatiguing exercise.

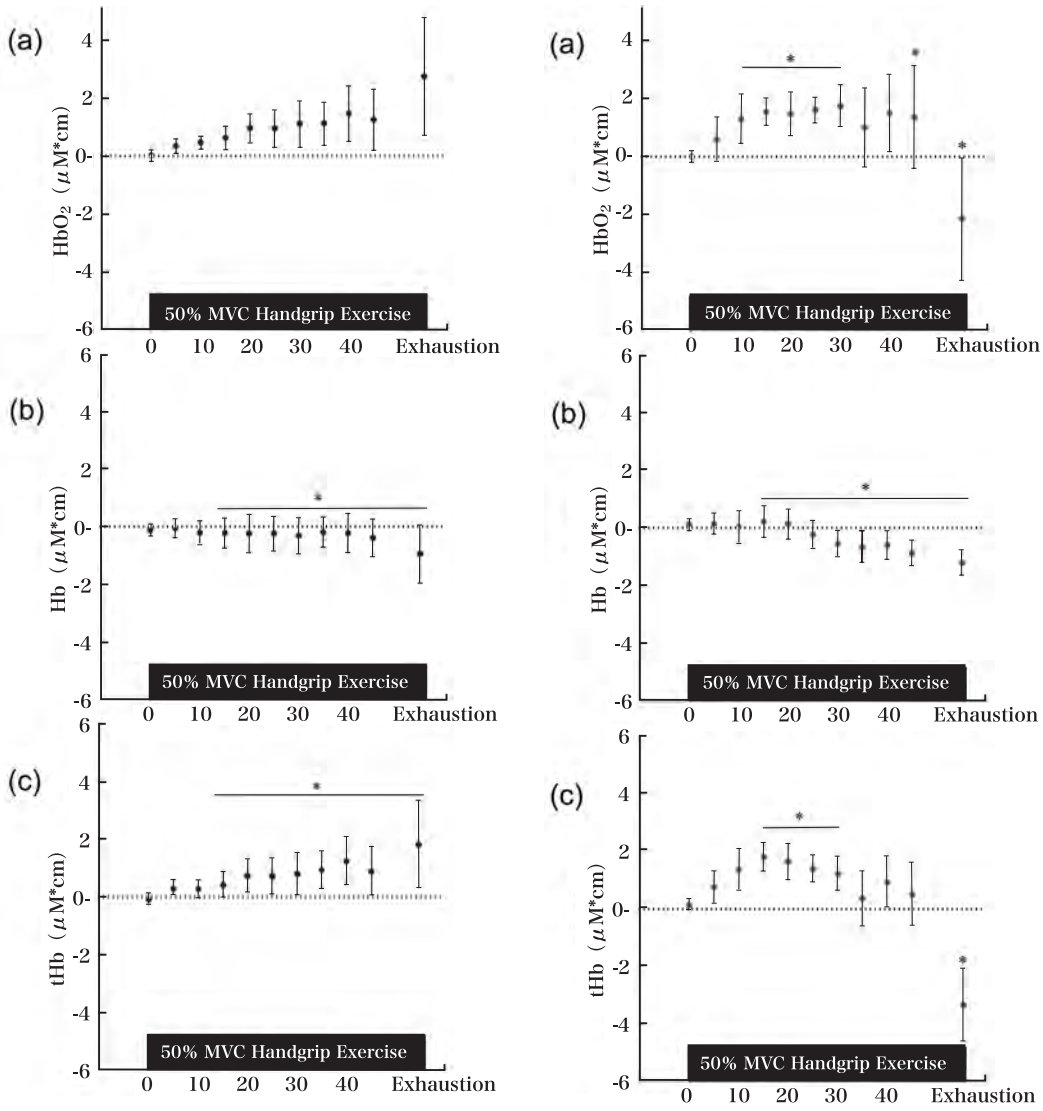

Fig. III.12.3-1 The values of changes in the sedentary subjects in the contralateral motor cortex from resting values in (a) oxyhemoglobin concentration (HbO_2), (b) deoxyhemoglobin concentration (Hb), and (c) total-hemoglobin concentration (tHb) during the handgrip exercise in left panels, and in the athletes in the right panels. Values are represented as means ± SD. Asterisks show significant differences, $p < 0.05$.

● Purpose

Using near-infrared spectroscopy to determine whether adaptation for exercise changes cortical activation dynamics during exhaustive exercise, in the present study, we compared the $M1_{contralateral}$ oxygenation kinetics between athletes and sedentary subjects during exercise reaching to voluntary exhaustion.

● Methods

Male, right-handed sedentary subjects and athletes (n = 7 each) participated in the present study. The sedentary subjects were individuals with little experience who did not exercise habitually.

Four wavelengths (775, 810, 850, and 905 nm) of near infrared spectroscopy (NIRS) were used (NIRO-300L, Hamamatsu Photonics, Japan) for motor cortex oxygenation. The optical probe consisted of an emitter and a detector (comprising 3 separate sensors). The system was guided on the subjects' heads through glass fiber bundles. The probes were positioned over the $M1_{contralateral}$ areas enclosing C3 according to the modified international EEG 10-20 system (American Electroencephalographic Society, 1994).

They performed a static right-hand handgrip task at 50%-60% MVC until they could sustain 50% MVC. While resting in an inclining position, they were asked to pinch the hydraulic handgrip meter, a nylon tube connecting the handgrip device and transducer that was held at heart level. The exercise trials were repeated 3 times for each subject. A static right-hand handgrip task at 50%-60% MVC until they could sustain 50% MVC. While resting in an inclining position, they were asked to pinch the hydraulic handgrip meter, a nylon tube connecting the handgrip device and transducer that was held at heart level. The exercise trials were repeated 3 times for each subject.

Results and Discussion

The notable findings in the present study were the different oxygenation kinetics between the sedentary subjects and athletes during exercise reaching to exhaustion. In the sedentary subjects, the oxygenation in the $M1_{contralateral}$ continued to increase even at voluntary exhaustion. By contrast, in the athletes, the oxygenation in the $M1_{contralateral}$ decreased at exhaustion as compared with the resting values. In conclusion, the noteworthy findings in the present study were that the oxygenation kinetics in the M1contralateral were different between elite athletes and sedentary subjects during the handgrip exercise leading to voluntary exhaustion.

IV. プロジェクトの共同研究における成果

共同研究 1

Redistribution of blood flow during exercise; Critical exercise intensity for circulatory and metabolic changes in response to knee extension exercise and its relationship to blood flow to exercising limb

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[1)] Japan Women's College of Physical Education, [2)] Toyota Technological Institute, [3)] University of L'Aquila, [4)] Tokyo Medical University, [5)] Keio University, [6)] Nihon University, [7)] National Institute of Fitness and Sports in Kanoya

1.1 General introduction and methods for the present study

A. Kagaya, M. Saito, T. Sadamoto, M. Ferrari, V. Quaresima, M. Kamo, T. Osada, S. Shimizu-Okuyama, K. Sato, M. Iwadate, F. Ohmori, and V. Cettolo

General introduction

Muscle contraction force is one of the most important factors in controlling blood flow to exercising muscles. Mechanically, it determines arterial inflow and venous outflow in exercising muscles by changing intramuscular pressure. As to muscle metabolism, a muscle action at different force changes muscle fiber type recruitment, thereby changing muscle metabolism, which will directly influence the blood vessels of exercising muscles. In addition, it affects various tissues of different organs such as the spleen, inactive muscles, skin, etc.

In response to the increasing demand of blood (oxygen) supply to the active muscles, the cardiovascular system adjusts itself either by increasing cardiac output or by attenuating blood flow to the other tissues. In previous literature, the regulation of cardiovascular system was discussed from several aspects of the system but was not discussed in an integrative manner.

In this study, we hypothesized that increasing muscle force requires recruiting type II fibers and switching metabolism from aerobic to anaerobic dependency, which will evoke metabo-receptor mediated sympathetic activation. Therefore, a critical intensity at which the physiological response to exercise should exist for limiting further increases in blood flow, despite an increase in exercise intensity.

The purpose of this study, therefore, was to test this hypothesis by studying blood flow redistribution to exercising muscles, in relation to cardiac output, muscle oxygenation, subjective muscle fatigue sensation, etc.

General Methods

● Subjects

Eight female physical education major students with no medical problems participated in this study after giving their written informed consent. Their mean (± SD) age, height, body mass, the femoral fat layer thickness, the thickness in the lateral vastus muscle (VL) and VL +the rectus femoris muscle (RF) were 22.1 ± 1.9 (SD) years old, 159.7 ± 4.7 cm, 55.1 ± 9.9 kg, 7.5 ± 2.1 mm, 22.4 ± 2.6 mm (VL), and 36.6 ± 3.2 mm (VL + RF), respectively.

● Experimental design

The subjects performed dynamic knee extension exercise with right leg using specially devised ergometer (Vine Co). They sat on a high chair with their back fixed to a support, and their ankles were connected to the pedal of cycle by a strap. Starting position of the knee was 90° from the horizontal, where the participants moved the weight through a range of 20°. We used six work loads (5-60 % MVC) for dynamic knee extension. Exercise frequency and exercise time were 60 times/min and three minutes or until exhaustion for all work loads, respectively.

● Measurements and analysis

Local Fatigue Sensation (LFS) and RPE

During dynamic knee extension, the rate of subjective fatigue sensation from the working right femoral muscles was reported by having the subjects point to a number with their blinking every 30s using a category scale by Saito (1989) for LFS

and Borg(1982) for RPE.

Femoral artery blood flow velocity and vessel diameter

Blood velocity and vessel diameter of common femoral artery were measured using a Doppler and B-mode ultrasound apparatus (Vivid7pro). A 7.5 MHz liner array transducer was placed over femoral artery, approximately 1 cm above the bifurcation into the superficial and profunda femoral branch. The probe position was stable and the sample volume was precisely placed in the center of the vessel, and then adjusted to cover the width of the diameter. A Doppler spectrum signal was recorded continuously.

Cardiac output and stroke volume

During exercise, stroke volume (SV) was measured using a Doppler ultrasound method with a 2.5 MHz transducer (SYSTEM V, ALOKA). Two-dimensional echo-cardiographic images were recorded in the parasternal long-axis view, the place where the aortic annulus diameter was measured, and in the apical 3 chamber view, immediately proximal to the aortic valve. The blood flow velocity was recorded on aorta continuously by the Doppler method throughout the experiment. Before each Doppler ultrasound recording, the transducer direction was adjusted in the 2D mode according to the Doppler signal sound and the aorta image. All the signals were stored on video tape recorder (VTR) for later analysis.

Cardiorespiratory responses

Respiratory parameters were determined with an on-line system for the breath-by-breath method. Respiratory gas was sampled continuously from a face mask. The gas fractions were analyzed by a mass spectrometer (ARCO-1000, Arco system, Chiba, Japan) that was calibrated and confirmed before each test. The expired gas volume was measured by a Fleisch pneumotachometer (WLSU-5201, Westron, Chiba, Japan). Breath-by-breath data were analyzed using customized software on a computer (PC-9821, NEC, Tokyo, Japan).

Systolic and diastolic arterial blood pressure (SBP and DBP) were measured no-invasively by photo-electric plethysmography with a Finometer (Finapres Medical Systems BV, Arnhem, Netherlands). Furthermore, the heart rate (HR), stroke volume (SV), and thus cardiac output (CO) were determined from the blood pressure wave form using the Model flow software program, incorporating gender, age, height, and weight (Beat Scope1.1, Finapres Medical Systems BV, Arnhem, Netherlands). CO was calculated as SV $\times$ HR.

EMG recording

EMGs were recorded using Ag-AgCL electrodes placed on 4 sites, the right medial vastus muscle (VM) , right lateral vastus muscle (VL), right rectus femoris muscle (RF), left lateral vastus muscle (VL) using bipolar lead, the details of which have been described elsewhere (Ebenbichler *et al*. 1998; Kamo, 2002) except for the sites of RVL. The electrodes for RVL were placed at the proximal area and distal area close to the sites of optical probe of NIRS.

NIRS measurements

The near infrared spectroscopy (NIRS) data were acquired with a sampling time of 0.19 s over the exercising vastus lateralis muscle by using a 54-channel imager (NIRStation OMM3000, Shimadzu, Japan). The optical probe covered an area of 4×6 cm^2 and it consisted of 12 transmitters and 12 receivers positioned in a rectangular matrix of 4 rows, 6 columns with a 1 cm separation. The center of the matrix corresponded to the center of the selected thigh muscle body verified by ultrasonography. Each channel resulted by a given association of a transmitter and a receiver placed at different distances parallel to the axis of the thigh muscle (from 1 cm to 5 cm) or oblique (from 1.41 cm to 5.1 cm).

1.2 Exercise intensity-dependent changes in femoral blood flow, electrical muscle activity and muscle oxygenation during dynamic knee extension exercise

A. Kagaya, M. Kamo, F. Ohmori, M. Iwadate, K. Sato, S. Shimizu-Okuyama, T. Osada, T. Sadamoto, M. Saito, M. Ferrari, V. Quaresima, and V. Cettolo

● Purpose

Blood flow to exercising muscles increased with exercise intensity, and reached its peak during regional exercise using small muscle mass (Kagaya 1994), under the conditions when the cardiac pumping capacity was not a limiting factor. Additional findings were that the peak blood flow during exercise did not reach maximal value obtained during maximal metabolic vasodilatation (Sinoway *et al*. 1999). These findings lead us to hypothesize that an inhibiting mechanism will work during exercise to overwhelm further vasodilatation. The purpose of this study was to clarify the physiological mechanism for regulating regional blood flow, in order to prevent increase to its maximal vasodilatation capacity. For this purpose, the exercise intensity to induce critical changes in the femoral arterial blood flow, electrical muscle activities, and muscle oxygenation of different depths of muscle layer were studied.

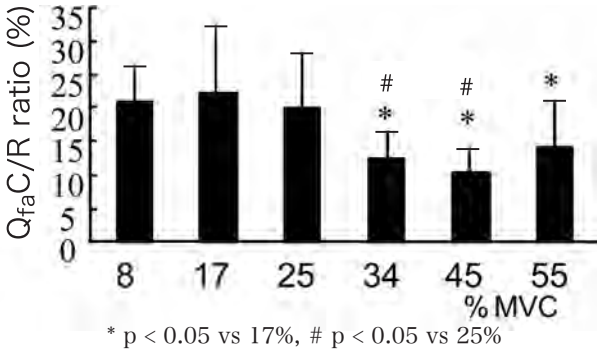
● Methods

Seven healthy females (22 ± 2 yrs) participated in the study as subjects. They performed dynamic knee extension exercise in upright position at 6 different intensities (5-60% MVC). Femoral arterial blood flow (Qfa) and muscle oxygenation (NIRS), were measured and EMG was recorded from thigh muscles (VL). The optical probes of NIRS were laced over VL at the distances of 1, 3, and 5 cm.

● Results and Discussion

The Qfa during the relaxation phases of 25-30s in exercise increased with exercise intensity and leveled off around 40% MVC, whereas it decreased during contraction phases at higher intensities.

The ratio of Qfa during the contraction phase to that during the relaxation phase, used as an indicator of blood flow impairment, significantly decreased when exercise intensity exceeded 30% MVC (Fig. IV.1.2-1). Increasing rate of iEMG with exercise duration was examined in relation to exercise intensity. Steeper elevation of iEMG was observed at the exercise intensities above 30% MVC. The de-oxygenation in the muscle was significantly accelerated at the higher intensities above 30% MVC. These results suggested that the exercise intensity approximately at 30% MVC will be a critical point to augment vasoconstriction effect via muscle metabo-reflex and mechanical compression of the vessel. Greater recruitment of type II fibers, elevated intramuscular pressure, and accumulation



* p < 0.05 vs 17%, # p < 0.05 vs 25%

Fig. IV.1.2-1 Qfa during muscle contraction (C) relative to that during the relaxation (R) phase.

of muscle metabolites (Grassi *et al*. 1999) accelerates vasoconstriction and prevents the vessels in exercising muscle from maximally dilating.

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Sinoway L, Prophet S : Skeletal muscle metaboreceptor stimulation opposes peak metabolic vasodilatation in humans. Circ Res, 66: 1576-1584, 1990.

1.3 The effect of the exercise intensity on the blood pressure response at the onset of dynamic exercise

K. Sato, F. Ohmori, M. Iwadate, T. Sadamoto, and A. Kagaya

Purpose

The purpose of the present study was to determine the effect of the exercise intensity on the relative change of the total systemic peripheral resistance (TPR) and cardiac output (CO) in establishing mean arterial blood pressure (MAP) response to immediately after the start of dynamic exercise in humans, and to elucidate whether the decrease in TPR at the onset of dynamic exercise was simply reflected change in peripheral vascular response in exercising muscle.

Methods

Cardiavasular [MAP, CO, TPR, heart rate (HR),

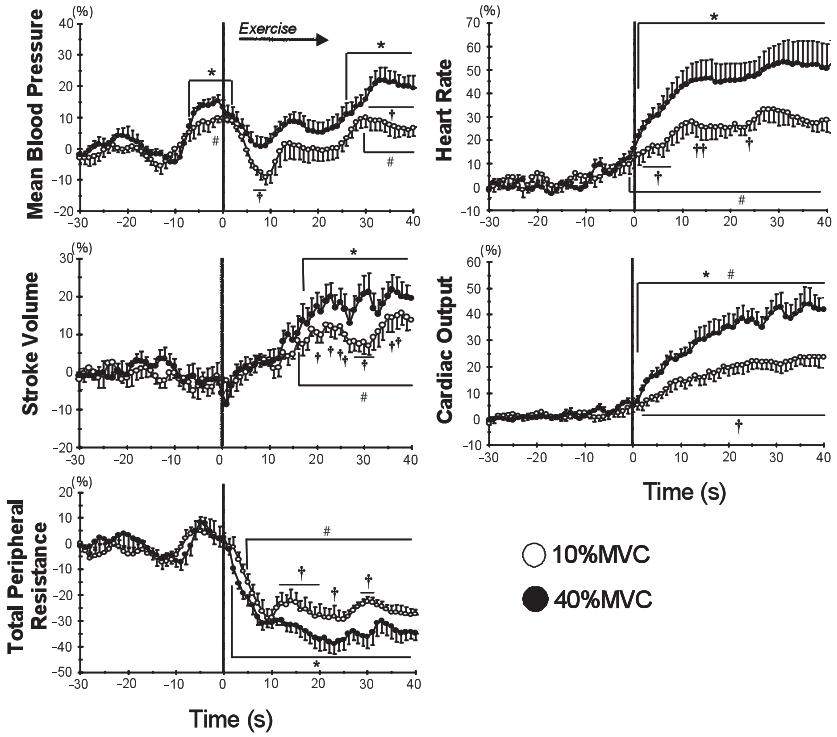

Fig. IV.1.3-1 The time course of averaged relative changes in the cardiovascular responses from 30-s before the onset of exercise to 40-s after the onset of exercise for 10% and 40% MVC. * # Different from Rest ($P < 0.05$). † Difference between 10% and 40% MVC at each time point ($P < 0.05$).

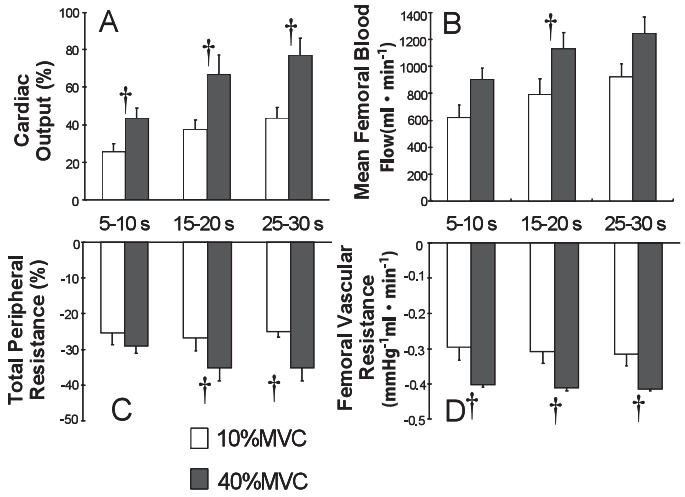

Fig. IV.1.3-2 Averaged relative change in CO (A) and TPR (B), and absolute change in MFBF (C) and FVR (D), calculated as difference between Rest and the average value for 5-s at 5-10-s, 15-20-s, and 25-30-s each time points after the start of exercise. † Difference between 10% and 40% MVC at each time point ($P < 0.05$)

and stroke volume (SV)], mean femoral vascular blood flow (MFBF), and then femoral vascular resistance (FVR) were measured in 7 healthy females at the onset of knee extension dynamic exercise at 10% and 40% maximal voluntary contraction (MVC).

● Results

In the present study, the following results were obtained (Fig. IV.1.3-1 and 2): 1) An initial fall in MAP at ～10-s after the start of exercise was reduced by an increase in the exercise intensity at 10% MVC to 40% MVC, combined with same level of decrease in TPR for 10% and 40% MVC, and enhanced CO response that accompanies an increase in exercise intensity; 2) The magnitude of decrease in FVR at the onset of 40% MVC was significantly larger than that of 10% MVC.

● Discussion

These results indicated that MBP responses at the onset of dynamic exercise is the variable being regulated with increasing exercise intensity. Therefore, combination mechanisms of TPR and CO responses due to baroreflex and central command mediated autonomic activity would produce an appropriate MBP response at the onset of dynamic exercise. Furthermore, change in TPR at the onset of dynamic exercise would not simply and necessarily reflect a change in peripheral vascular response.

1.4 Peak blood flow in the femoral artery during the contraction and relaxation phase of knee extension exercises

F. Ohmori, M. Kamo, M. Iwadate, S. Shimizu-Okuyama, and A. Kagaya

● Purpose

Blood flow to exercising limbs increases during exercise, and the increase was linearly related to exercise intensity at lower intensity (Lind and

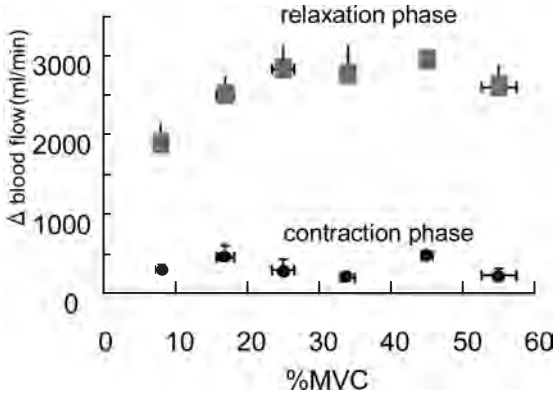

Fig. IV.1.4-1 Femoral arterial blood flow in relation to exercise loads during contraction (lower) and relaxation phases of dynamic knee extension exercise.

McNicol, 1967; Lind and Williams, 1979; Kagaya, 1996). However, it is still a matter of issue whether it continues to increase linearly up to maximal intensity (Radegran and Saltin, 1998), or it levels off at higher intensity (Lind and Williams, 1979; Kagaya *et al*. 1996). One possible reason for the opposing results may include whether the studies included intensive exercise with high contraction force that induced exhaustion within one minute. The purpose of this study, therefore, was to test the hypothesis that the regional blood flow to exercising limb levels off at higher intensity and reaches peak blood flow during dynamic exercise at high contraction force. For this purpose the femoral artery blood flow for the respective contraction and relaxation phase was studied during knee extension exercise at various intensities including exhausting high-intensity exercise with short duration.

● Methods

Seven physically active women participated in the study after giving their informed consents. Blood velocity and vessel diameter of femoral artery were measured using a Doppler and B-mode ultrasound apparatus (Vivid7) with a 7.5 MHz transducer. Blood pressure was measured using Finapres. Blood velocity signal, vessel diameter of systolic and diastolic phase of cardiac cycle and blood pressure were measured during muscle contraction and relaxation phase.

● Results and Discussion

The diameter of vessels became larger with the increase of exercise intensity, and was significantly ($p < 0.05$) larger at 25-55% MVC than that at 8% MVC during the muscle relaxation phase. Adjustment for systolic blood pressure during the muscle relaxation phase was significantly ($p < 0.05$) higher in exercise at 55% MVC than those at 8-34% MVC. Femoral arterial blood flow during the contraction phase was unchanged with increasing contraction force. In contrast, it increased during the relaxation phase with an increase in exercise intensity up to 25% MVC, and leveled off when exceeding 25% MVC (Fig. IV.1.4-1). The highest blood flow during exercise was obtained within a significantly ($p < 0.05$) shorter time at 55% MVC compared with at 25% MVC. In conclusion, the femoral arterial blood flow during knee extension exercise reaches its peak at 25-55% MVC, and the time reaching peak blood flow was shorter during exercise at higher intensity. The increase in blood flow velocity and enlargement of vessel diameter during the systolic phase contributed to the increase of the blood flow.

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1.5 Aorta and femoral arterial blood flow velocity during the contraction and relaxation phases of dynamic knee extension exercise

S. Shimizu-Okuyama, F. Ohmori, M. Iwadate, K. Sato, and A. Kagaya

Purpose

The purpose of this study was to observe the changes in the blood flow velocity in the aorta and femoral artery during the muscle contraction and the relaxation phases of dynamic knee extension exercise (KE).

Methods

Seven female subjects (aged 22.4 ± 1.9 years) participated in this study. All subjects gave informed consent prior to their participation after receiving a full written explanation of the experiment. They performed one-legged knee extension exercise in the upright position at 10% and 50% of maximal voluntary contraction (MVC) until exhaustion. Blood velocity was measured using the Doppler ultrasound method for aorta artery [ao] and femoral artery [fa] (SYSTEM V, GE). Blood Pressure was monitored from the finger of the left hand (Finapres, Ohmeda, USA) at the heart level.

Results and Discussion

During the muscle contraction phase of KE, the blood velocity in femoral artery was significantly ($p < 0.01$) lower than that in the aortic artery (fa: 10% 15.8 ± 4.9, 50% 10.7 ± 3.1, ao: 47.6 ± 2.6-53.8 ± 3.7 cm/s). In contrast, the blood velocity in the femoral artery was higher than the aorta during the relaxation phase (fa: 10% 61.6 ± 5.8, 50% 79.2 ± 11.9, Ao: 47.6 ± 2.6-53.8 ± 3.7 cm/s). The femoral/aorta ratios were − 67.4 ± 9.2% (10%), and − 80.6 ± 4.9% (50%) during the contraction phase (Fig.IV.1.5-1). However, during the relaxation phase, they were 30.0 ± 11.6% (10%), and 50.7 ± 22.3% (50%), respectively. Mean blood pressure was not significantly different between the contraction and relaxation phase.

These results suggest that the effect of muscle contraction and relaxation on blood flow velocity differs between the aorta artery and femoral artery. The femoral artery blood flow was more accelerated compared to aorta during the relaxation phases.

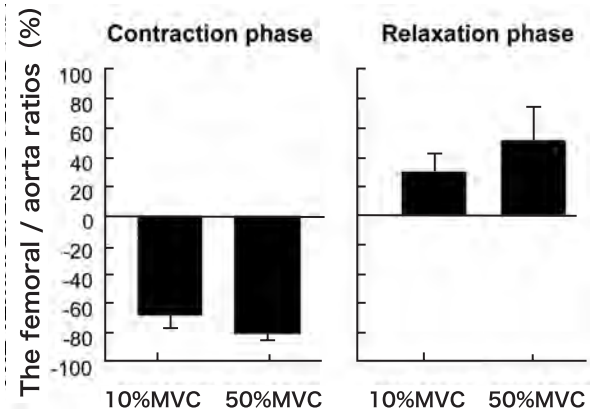


Fig. IV.1.5-1 The femoral/aorta blood velocity ratios

1.6 The quadriceps oxygenation heterogeneity during dynamic knee extension exercise

V. Cettolo, V. Quaresima and M. Ferrari

● Purpose

The heterogeneity muscle oxygenation during exercise has been reported for distal and proximal or lateral or medial, but not for vertical into muscle layer. The purpose of this study was to clarify the vertical heterogeneity of quadriceps oxygenation during dynamic knee extension exercise.

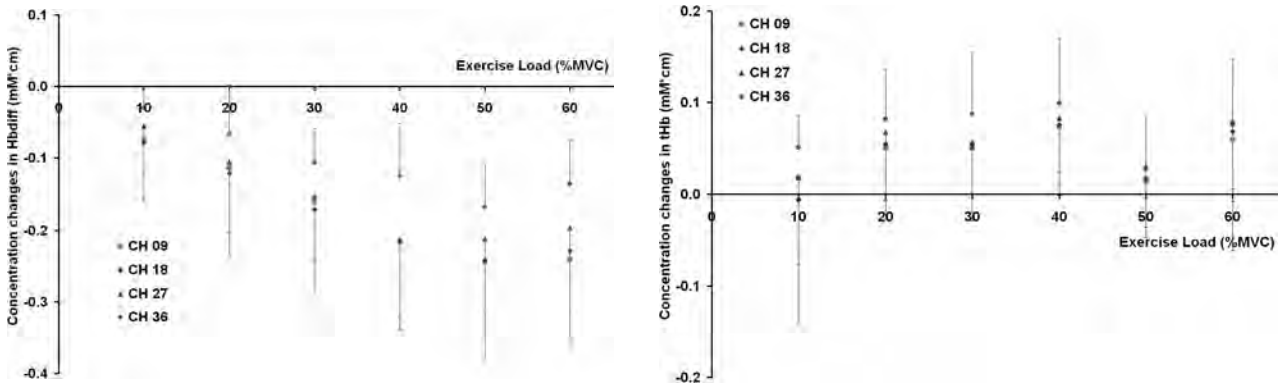
1) Quadriceps oxygenation heterogeneity during dynamic knee extension exercise measured by multi-channel near infrared spectroscopy

● Methods

The near infrared spectroscopy (NIRS) data were acquired with a sampling time of 0.19 s over the exercising vastus lateralis muscle by using a 54-channel imager (NirStation, Shimadzu, Japan). The optical probe covered an area of 4×6 cm^2 and it consisted of 12 transmitters and 12 receivers. NIRS measurements were performed while the 8 subjects were performing maximal voluntary contraction (MVC) or dynamic knee extension exercises at 10, 20, 30, 40, 50 and 60% MVC. For each channel, maximal oxyhemoglobin (O_2Hb), deoxyhemoglobin (HHb) and total hemoglobin (tHb=O_2Hb+HHb) changes observed during the post MVC phase were calculated as the average, over the time interval 3-6 s after the end of the MVC exercise. Only the 4 channels (9/18, and 27/36) corresponding to the medial and lateral portions, respectively, of the investigated muscle area with the longest receiver-transmitter distance were considered. Changes in Hbdiff (O_2Hb-HHb) and in tHb were calculated. To explore the possible heterogeneity of muscle metabolic and hemodynamic response within each exercise intensity, and the effect of the exercise intensity on muscle response, the mean changes in Hbdiff and tHb were calculated over the last 5 s of exercise for each data-set.

● Results and Discussion

As expected, the duration of the exercise was variable and it depended on the exercise intensity. The changes in Hbdiff in response to each exercise intensity were clearly evident. In the most medial muscle portion, the rate of Hbdiff decrease raised with the increase of the exercise intensity. At the end of the exercise, Hbdiff reached the plateau in all the intensities (20-60% MVC) except for the 80% MVC. A similar kinetics was found also in the most lateral portion of the thigh muscle. A not statistically significant difference for the Hbdiff changes was found when the exercise was performed at the lowest intensity (i.e. 10% MVC, channel effect, F=2.80, P=n.s). For the other exercise intensities, the most lateral portion (i.e. channel #36) showed Hbdiff decrease significantly lower than that observed in the medial portion (channel effect, $F = 4.40$, $P < 0.02$, 20% MVC; $F=4.24$, $P < 0.02$, 30% MVC; $F = 9.69$, $P < 0.0005$, 40% MVC; $F = 3.87$, $P < 0.05$, 50% MVC; $F = 4.34$, $P < 0.02$, 60% MVC). The tHb changes were not statistically different between the medial and lateral portions for all exercise intensities (channel effect, $F < 2.45$, P = n.s.). However, the amplitude of Hbdiff decrease was lower in the most lateral than in the most medial portion of thigh muscle. This suggests that the most medial portion, having a higher oxidative metabolic



A B

Fig. IV.1.6-1 Concentration changes in Hbdiff (panel A) and tHb (panel B) as function of the exercise intensity (expressed in % MVC). Each data point represents the average over the 8 subjects. For each subject the mean value was calculated over the last 5 s of the exercise for each considered channel.

activity, is more involved than the most lateral portion in the dynamic knee extension performed at any intensity. As expected, after a transient decrease at the onset of the exercise, the tHb increased during the exercise but only in the medial muscle portion and for lower intensity load (i.e. 20 and 30% MVC) the tHb reached the plateau. Therefore, only in these cases it is possible to consider the changes in Hbdiff as an index of muscle oxygenation. Unlike the Hbdiff changes, the amplitude of tHb changes were almost similar in both portions of the investigated thigh muscle. The concentration changes in Hbdiff and in tHb during the last 5 s exercise as function of the exercise intensity are depicted in the figure. It is evident that at low-moderate intensity exercise (10-30% MVC) the Hbdiff and the tHb changes decreased and increased, respectively; whilst when the exercise was stopped for exhaustion of the subjects (i.e. prevalently at 40, 50 and 60% MVC) the Hbdiff intensity reached a minimum stable value, whilst the tHb changes did not increase.

In conclusion, these results suggest that the hemodynamic response (expressed as tHb) was almost uniform over the investigated muscle thigh area for all exercise intensities, whilst the muscle oxidative metabolic response (expressed as Hbdiff) was heterogeneous. In particular, the medial portion of the thigh muscle was more involved than the lateral one, especially for moderate-high intensity exercises. Furthermore, the decrease in Hbdiff and the increase in tHb were dependent on the exercise intensity until the intensity did not induce exhaustion in most of the subjects.

2) Quadriceps oxygenation during dynamic knee extension exercise on non-exercising leg measured by two-channel near infrared spectroscopy.

● Methods

The NIRS measurements over the nonworking left leg were performed by the NIRO-200 oximeter (Hamamatsu Photonics K.K., Japan). The two optical probes (consisting of one emitter and one detector 4.0 cm apart) were attached to the skin of the vastus Lateralis (VL) and rectus Femoralis (RF) main body muscles. The NIRS data were collected with a sampling rate of 6 Hz. The measured NIRS data were: 1) tissue oxygenation index (TOI, expressed in %), 2) concentration changes in O_2Hb and HHb (expressed in (M (cm), and 3) the derived changes in tHb. TOI reflects the local balance between O_2 supply and O_2 consumption. The tHb volume changes, being strictly related to blood volume changes, can be considered an indirect measure of local blood flow changes. NIRS measure-

ments were performed while the 8 subjects were performing dynamic knee extension exercises at 10, 20, 30, 40, 50 and 60% of MVC with the right leg. The maximal duration of each exercise was of 3 min or until the exhaustion of the subject.

To explore the muscle metabolic and hemodynamic response within each exercise intensity, and the effect of the exercise intensity on muscle response, the mean changes in TOI and tHb were calculated over the last 5 s of rest and of exercise. For each trial we calculated the mean tHb and TOI changes during exercise ((tHb and (TOI, respectively) as the exercise minus the relative rest values.

● Results and Discussion

During contralateral exercise the TOI increased similarly in both muscles; instead tHb decreased more in the RF muscle. The tHb and TOI of left leg changed significantly during exercise with respect to the rest condition (Exercise effect: $F = 12.47$, $P < 0.0001$ and $F = 14.13$, $P < 0.0001$ for tHb and TOI, respectively). The amplitude of these changes was similar in both muscles for TOI (Muscle effect: $F = 1.38$, $P = 0.42$; Muscle x Exercise effect: $F = 1.17$, $P = 0.32$), instead the tHb changes were larger in RF respect to VL muscle (Muscle effect: $F = 6.39$, $P < 0.001$; Muscle x Exercise effect: $F = 6.67$, $P < 0.005$). Analyzing the tHb and TOI as function of the exercise intensity, only the tHb of RF muscle decreased as the exercise levels increased ($F = 7.40$, $P< 0.01$).

1.7 The relationship between the oxygenation in active muscle and local fatigue sensation during dynamic knee extension exercise

M. Iwadate, M. Saito, M. Kamo, K. Sato, F. Omori and A. Kagaya

● Purpose

We have examined whether local fatigue sensation (LFS) was related to the oxygenation of exercising muscles during dynamic knee exercise.

● Methods

Six female subjects participated in three exercise experiments (low intensity 10% MVC, middle intensity 30% MVC, high intensity 50% MVC). The changes of fatigue sensation in working muscles [levels of fatigue sensation (LFS); scale 0-10] and the oxygenation in the lateral vastus muscle (VL) and the mean arterial blood pressure (MAP) were analyzed. In this study, we used three distances between the light source and an optical detector in the NIRS probe; 5.0 cm, 3.0 cm and 1.0 cm. Thus, the depth of penetration was suposed to be ～2.5 cm, 1.5 cm and 0.5 cm, respectively . In this manner, we examined the difference in the metabolic changes in the superficial and deeper layers of the VL, and investigated the most relative area to LFS changes. These data were analyzed at 2 time points of 30 s after the onset of exercise and the end of exercise in three kinds of exercise.

● Results and Discussion

LFS increased significantly from 30 s after the onset of exercise to the end of exercise during three intensity exercises.

The oxygenation changes were shown in the low-intensity exercise, and ΔO_2Hb increased at

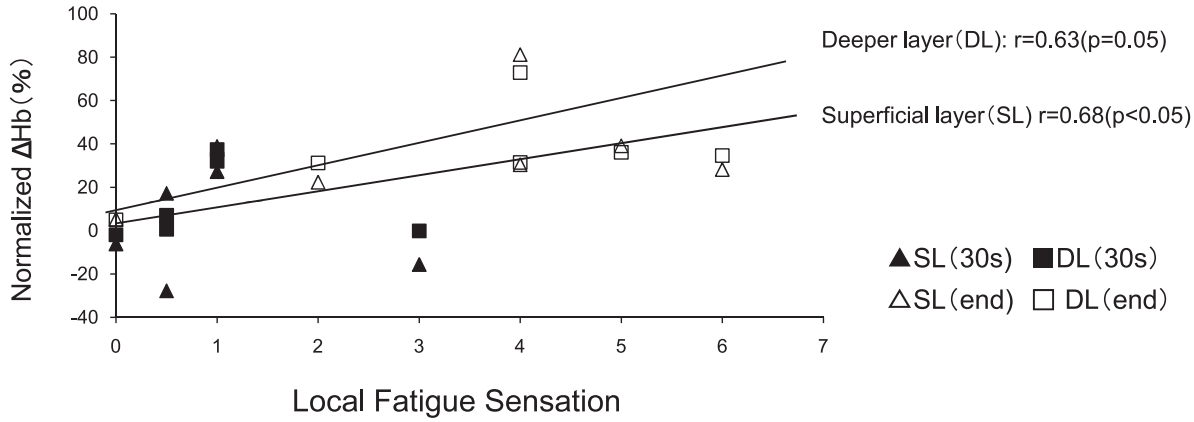


Fig. IV.1.7-1 Relationship between local fatigue sensation and Δ Hb in active muscle in low-intensity exercise. SL : superficial layer of VL, DL : deeper layer of VL.

the medial and lateral superficial layers from 30 s after the onset of exercise and the end of exercise. ΔHHb also increased significantly at the lateral deeper layer and medial superficial layers of the lateral vastus muscle. However, ΔHbT did not change significantly from 30 s after the onset of exercise and at the end of exercise. In the middle-intensity exercise, ΔHHb increased in the medial superficial layer of the muscle. However, ΔO_2Hb did not change significantly from 30 s after the onset of exercise and at the end of exercise. In the high-intensity exercise, ΔHHb increased in the medial deeper layer of the muscle.

The MAP increased significantly in the middle- and high intensity exercise from 30 s after the onset of exercise and the end of exercise; however the significant changes were not observed in the low-intensity exercise.

The correlation between LFS and muscle oxygenation was statistically significant in ΔHHb of the low-intensity exercise but not in that of exercise of other intensities. The correlation between LFS and ΔMAP was also significant in the middle- and high-intensity exercise.

These results indicate that LFS changes were related to the muscle oxygenation of active muscle in the low-intensity exercise. In the middle- and high-intensity exercises which MAP changed prominently, LFS changes were independent from the muscle oxygenation changes during exercise.

共同研究２

Role of central command in the cerebral and renal blood flow responses during static exercise

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2.1 Effect of tendon vibration during submaximal static elbow flexion exercise on muscle oxygenation

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● Purpose

Previous studies reported that muscle vibration stimulus effect on motor units recruitment (Bongiovanni & Hangbarth 1990; Shinohara 2005). Whole limb vibration stimulus induces a lower tissue oxygenation during submaximal dynamic exercise because of a greater recruitment of fast twich motor units (Mileva *et al*. 2006). However it remains unclear whether static exercise with direct vibration on the contracting muscles also produces the lower oxygenation. The purpose of this study was to investigate the influence of tendon vibration during submaximal static exercise on muscle oxygenation.

● Methods

Nine healthy females (mean ± SD: 23.8 ± 4.1 years, 162.6 ± 4.4 cm, 56.6 ± 4.2 kg) completed two trials, non-vibrated exercise (Ex) and vibrated exercise trials (Vib+Ex). In both trials, an elbow flexion exercise at 30% of their maximum voluntary contraction (MVC) was statically sustained for

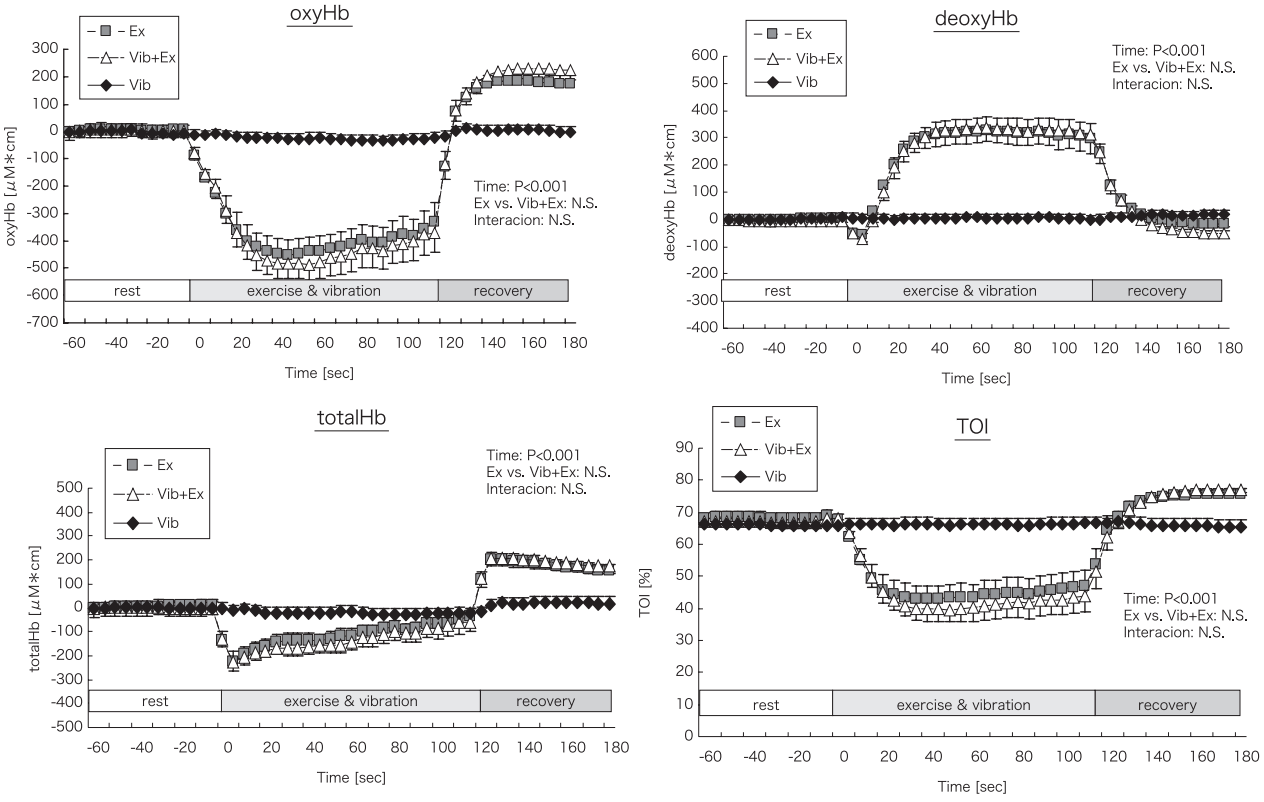

Fig. IV.2.1-1 The changes in oxygenated hemoglobin (oxyHb), deoxygenated hemoglobin (deoxyHb), total hemoglobin (totalHb) and the Tissue Oxygenation Index (TOI). Values are Mean ± SE, n = 9. Significant differences between Ex and Vib+Ex; ∗: $P < 0.05$.

2-minutes by a visual feedback system. In Vib+Ex, an oscillating stimulation by a vibrator (frequency 100 Hz, amplitude 0.8 mm) was applied to the distal tendon of the biceps brachii during exercise. The changes in oxygenated hemoglobin (oxyHb), deoxygenated hemoglobin (deoxyHb) and total hemoglobin (totalHb) in the biceps brachii were recorded by near-infrared spectroscopy (NIRS, NIRO-200, Hamamatsu Photonics, Japan). The tissue oxygenation index (TOI) was measured by the technique utilizing near-infrared spatially resolved spectroscopy (Matcher *et al*. 1994).

● Result and Discussion

The torque output of elbow flexion was identical between Ex and Vib+Ex. The decrease in oxyHb during exercise was greater in Vib+Ex than that in Ex whereas there were similar increases in deoxyHb and totalHb in both trials. The decrease in TOI during exercise was greater in Vib+Ex than that in Ex.

Since muscle oxygenation measured by NIRS reflects the balance between muscle oxygen consumption and supply, there are two possible reasons for the greater deoxygenation in Vib+Ex in the present study. One is a greater recruitment of fast twitch motor unit caused to increase muscle oxygen consumption. The other is decrease in oxygen supply due to limitation of blood flow into the working muscle.

In conclusion, this study suggested that the submaximal static exercise with tendon vibration reduces muscle oxygenation as similarly observed during dynamic exercise.

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2.2 Perceived exertion is not necessarily associated with altered brain activity during exercise

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● Purpose

The vibration technique gives the changes in the perceived exertion at the same internal- and external-workloads (Goodwin *et al*. 1972), and it helps in understanding the effects of the changes in perceived exertion on prefrontal cortex activity. This technique has been commonly used in previous studies (e.g., Ogoh *et al*. 2002; Goodwin *et al*. 1972). The purpose of the present study was to determine whether perceived exertion was associated with prefrontal cortex activity by using the muscle-spindle stimulation technique during static exercise.

● Methods

Subjects and paradigm

Ten normal, right-handed females (age, 21.0 ±

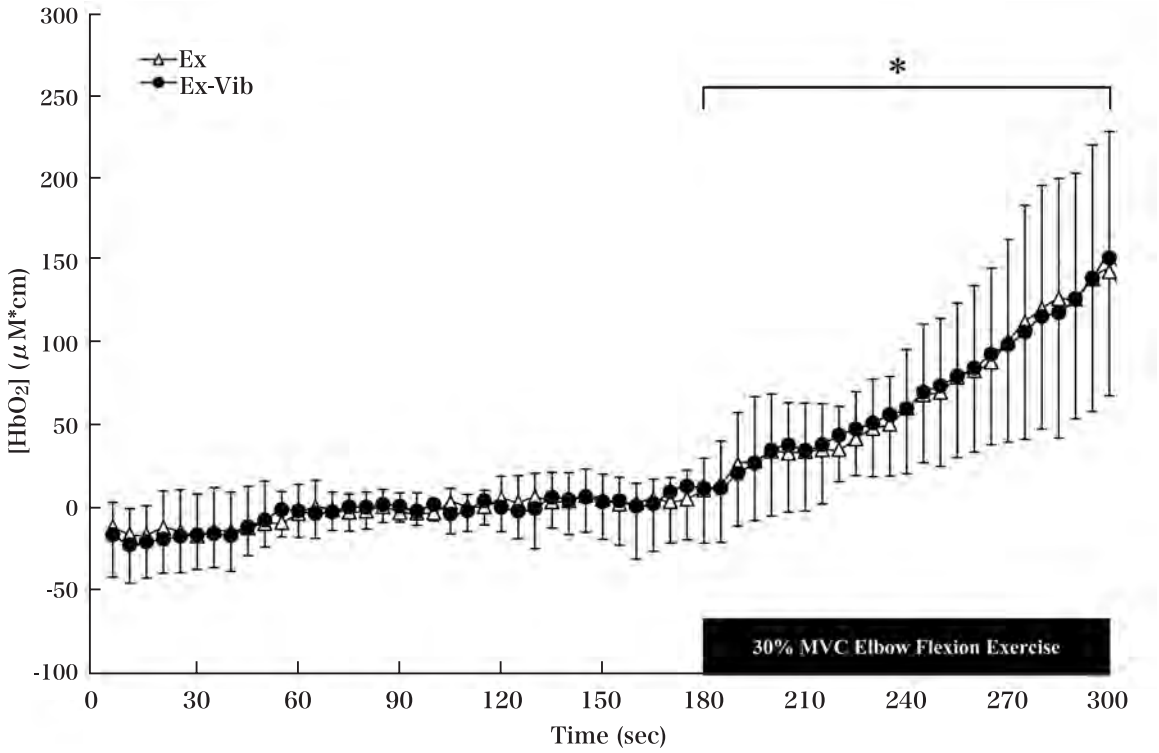

Fig. IV.2.2-1 Oxyhemoglobin ([HbO_2]) levels in the prefrontal cortex. Changes in the baseline values of [HbO_2] concentration in the prefrontal cortex during exercise without (Ex) or with muscle spindle stimulation (Ex-Vib). Values are represented as means ± SD. The asterisks show significant differences from the baseline values, $p < 0.05$.

0.7 years; height, 159.9 ± 4.8 cm; and weight, 55.6 ± 5.9 kg) participated in the present study. A vibrator was used to induce muscle contraction by the reflex stimulation of the distal tendon of the biceps brachii. In the present study, the oscillating vibration was applied to the distal tendon of the biceps brachii, while the subjects performed sustained isometric contractions of the biceps brachii. Each subject performed 2 sessions of elbow-flexion exercise with or without muscle-spindle stimulation (Ex-Vib and Ex respectively). The order of these sessions was randomized. The RPE [the subject rated her perceived effort on the Borg scale (Borg, 1975)] was recorded immediately after the exercise. Prefrontal tissue oxygenation levels were recorded from the muscle and brain by using an NIRS unit (Hamamatsu NIRO-200; Hamamatsu Photonics KK, Tokyo, Japan).

● Results and Discussion

With regard to [HbO_2], [Hb], and [tHb] levels, ANOVA revealed significant changes with time and no significant changes between the Ex and Ex-Vib conditions. The post-hoc test for changes in the [HbO_2], [Hb], and [tHb] levels under the Ex and Ex-Vib conditions revealed that the values from the start of exercise to the end of exercise were significantly higher than those at the baseline ($p < 0.05$).

The present study revealed no significant difference in the prefrontal cortex activity during exercise under the Ex and Ex-Vib conditions. Borg's RPEs have enabled the measurement of impending fatigue during exercise testing (Borg, 1982; Ekblom and Goldbarg, 1971). The RPE increases with increase in exercise intensity (Ceci and Hassman 1991; Ueda *et al*. 2006). Additionally, Nybo and Nielsen (2001) found a significant correlation between the RPEs and prefrontal cortex activity. The prefrontal cortex is most likely involved in the initiation of volitional movements (Nowak *et al*. 1999; Pedersen *et al*. 1998). The activity (oxygenation) of the prefrontal cortex increases with increase in exercise intensity (Ide *et*

al. 1999). As such, the prefrontal cortex activity described by Nybo and Nielsen (2001) is a reflection of 2 dimensions, i.e., exercise intensity and the RPE. Thus, in order to determine the relationship between the RPE and prefrontal cortex activity, the effect of the RPE should be separated from that of exercise intensity. In conclusion, the present study revealed that oxygenation of the prefrontal cortex did not significantly differ in the Ex and Ex-Vib conditions. The results of the present study suggest that perceived exertion is not necessarily associated with prefrontal cortex activity.

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2.3 Role of central command for the increase in middle cerebral artery mean blood flow velocity during static exercise in humans

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● Purpose

Cerebral blood flow (CBF) increases along with cardiovascular responses upon the transition from rest to exercise. The exercise-mediated increase in mean blood flow velocity in middle cerebral artery (V_{MCA}) is eliminated after the arm is blocked by regional anesthesia (Jørgensen *et al*. 1993), suggesting that CBF during exercise determined by neural integration of afferent input from the exercising muscle. Also evidence is provide by from that the increase in CBF is likely to be dependent on the muscle mechanoreflex (Jørgensen *et al*. 1992; Jørgensen *et al*. 1993). In contrast, Williamson *et al*. (2002) reported an increase in regional blood flow of the insular cortex during imagined exercise. Nowak *et al*. (2005) showed a significant increase in regional CBF during attempted movement in spinal cord-injured subjects. These observations argue in favor of a central command effect with regard to changes in CBF during exercise. Tendon vibration reflexly assist an exercising muscle while developing a

given force and thereby decrease the cardiovascular responses during static exercise (Goodwin *et al*. 1972; Ogoh *et al*. 2002). Using tendon vibration to the biceps brachii, we evaluate whether central command influence on V_{MCA} during static arm exercise. The purpose of the present study was to clarify the role of central command for the increase in CBF during static exercise.

● Methods

Eleven young women (mean ± SE: age, 21.2 ± 1.0 years) participated in this study. Written, informed consent was obtained according to the Ethics Committee of the Japan Women's College of Physical Education, and the study was conducted in accordance with the Declaration of Helsinki.

Maximal voluntary contraction trials

On the first day, subjects performed three maximal static 90° elbow angle flexions of the right arm to determine the maximal voluntary contraction strength (MVC). After the MVC trials, the subjects were familiarized with the exercise protocol.

Muscle spindle vibration

The custom-made vibrator was used to induce muscle contraction by the reflex stimulation of the distal tendon of the biceps brachii. In the present study, the oscillating vibration was applied to the distal tendon of the biceps brachii while the subjects performed sustained isometric contractions of the biceps brachii muscle (elbow flexion). The oscillating frequency of the vibrator was 100 Hz, and its amplitude was 0.8 mm. Vibration of the tendon of the biceps brachii during elbow flexion aided tension development in the biceps brachii muscle and thereby lessened the degree of the central command required.

Exercise protocol

On the second day, subjects performed static elbow flexion with and without vibrations. In this study, the elbow flexion exercise was performed using a computer-based multifunctional dynamometer (VINE, Japan). The subjects were seated in an exercise chair in which a constant body position could be maintained throughout the exercise. The right elbow was kept (90°) on a padded armrest and the wrist was attached to the arm lever by a Velcro strap.

After a 2-min resting period in the seated position, each subject performed the two-exercise protocol as follows: (1) elbow flexion (CONT) and (2) elbow flexion with biceps brachii tendon vibration (EX+VIB). The protocol consisted of a 3-min resting control period followed by 2 min of static contraction at 30% of the predetermined MVC ending with a 2-min recovery period. The subjects were shown the tension that was being achieved after which the subjects were asked to reach the line of required tension. In the resting condition, 7.9 ± 2.9% of the MVC was achieved by the application of vibration. Therefore, static elbow flexion was performed at ～22% MVC in this study. Before exercise, subjects were read standardized instructions on the use of the 6-20 Rating of Perceived Exertion (overall RPE) category scale developed by Borg (1973). These ratings were obtained immediately after the end of exercise. In addition, arm rating of muscle fatigue sensation (arm RPE) was taken after the end of the exercise by using a 1-10 category scale (Saito *et al*. 1989).

Measurement

Middle cerebral artery mean velocity

V_{MCA} measurement was performed with an ultrasound system (VIVID 7; GE Medical Systems, Japan) equipped with a 2.0-MHz sector transducer. We first used B-mode imaging to visualize the ipsilateral MCA, and then the real-time Doppler velocity spectrum was identified in PW-mode. Blood flow velocity measurements were taken with the sample volume set at 7-8 mm and with

the vector of the cursor positioned in the center of the blood stream, parallel to the vessel axis. Mean blood flow velocity of middle cerebral artery (V_{MCA}) was defined as the time-averaged mean velocity ($cm \cdot s^{-1}$) obtained in the automatic calculation mode.

Cardiorespiratory responses

The mean arterial blood pressure (MAP) was measured non-invasively by photoelectric plethysmography with a Finometer (Finapres Medical Systems BV, Arnhem, Netherlands). Furthermore, the heart rate (HR), stroke volume (SV), and thus cardiac output (CO), were determined from the blood pressure wave form using the Modelflow software program, incorporating gender, age, height, and weight (Beat Scope 1.1; Finapres Medical Systems BV, Netherlands). The CO was given by SV × HR. Respiratory parameters were determined with an online system for the breath-by-breath method. Respiratory gas was sampled continuously from a face mask. The gas fractions were analyzed by a mass spectrometer (ARCO-1000; Arco System, Japan) that was calibrated and confirmed before each test. Breath-by-breath data were analyzed using customized software on a computer (Dynabook; Toshiba, Japan), and the end-tidal partial pressures of CO_2 ($P_{ET}CO_2$) were calculated.

Data processing and statistics

In the present study, the ratio V_{MCA} / MAP was calculated as an index of averaged cerebrovascular conductance (CVCi). The beat-to-beat values for MAP, HR, SV, and CO and the breath-by-breath values for $P_{ET}CO_2$ were averaged over 30-sec intervals. Moreover, V_{MCA} and CVCi values for each subject were averaged over 30-sec intervals. To calculate the percentage change (relative change) from resting values, all resting parameters were obtained during the 2-min resting period 30 sec before the beginning of exercise. The percentage changes in cerebrovascular and cardiorespiratory parameters were obtained by calculating the ratio of the changes in the resting values (Rest). The cardiorespiratory (MAP, HR, CO, and $P_{ET}CO_2$) and cerebrovascular (V_{MCA} and CVCi) parameter values at rest were defined as the 0% control levels for each subject.

Differences in the cardiorespiratory and cerebrovascular responses between the two exercise conditions (CONT or EX+VIB) were tested by using two-way ANOVA with repeated measurement. If a significant F-value was present between the two conditions, the mean values at a given time were compared by a non-parametric Wilcoxon's signed rank test. These statistical analyses were computed by the SPSS 12.0 software (SPSS, Japan), and $P < 0.05$ was considered to indicate a significant difference. All data are expressed as mean ± SE.

● Results and Discussion

We observed that the increase in the V_{MCA} during exercise with tendon vibration (i.e., decreased central command) was significantly lower than that during control exercise without vibration (Fig. IV.2.3-1). The effect of vibrations on V_{MCA} response was similar to their effect on cardiovascular responses. Our results suggested that central command actively contributed to the CBF responses as well as the cardiovascular responses during static exercise.

Previous studies have suggested that the V_{MCA} responses during voluntary exercise are predominantly controlled by a peripheral neural reflex arising from exercising muscles and that the central command has a minor role in CBF regulation (Jørgensen *et al*. 1992; Jørgensen *et al*. 1993). However, our data supports the theory that a change in the V_{MCA} during static exercise may be mediated by central command, which is reflected by the individuals' RPE or "effort sense" during physical activity. With the decrease in V_{MCA} during

EX+VIB, the mechanism(s) that may drive the attenuated flow are of interest. Studies concerning the functional anatomy of central command-related changes in regional CBF have identified a network of structures activated in the human brain (Williamson *et al*. 2006). Their studies have suggested that the insular cortex, anterior cingulate cortex, the medial prefrontal region, and thalamic regions may be activated in response to an increased perception of effort during exercise when circulatory responses are elevated (Williamson *et al*. 2006). Therefore, it is possible to speculate that the attenuated activation of these regions in the brain, namely the central command network, may be related to the observed decrease in V_{MCA} during EX+VIB.

The other mechanisms that may contribute to the CBF regulation in exercise are MAP and CO. The V_{MCA} recorded at the end of the EX+VIB was lower (by ～11%) than that in CONT, and the effect of vibrations on the V_{MCA} response during exercise was similar to their effects on MAP and CO. Furthermore, despite the effect of vibration on V_{MCA}, the CVCi values did not differ significantly during exercises with and without vibration, indicating that the central command-mediated decrease in MAP and/or CO responses during EX+VIB may contribute to the reduction in the CBF responses. In this case, central command may have an indirect and secondary effect on the CBF during static exercise via the cerebral perfusion pressure and/or perfusion rate.

Recent studies have suggested that CO is an important factor involved in the change in V_{MCA} during dynamic exercise (Ide *et al*. 1998; 2000; Ogoh *et al*. 2005). When CO was reduced by using a β_1-blockade or atrial fibrillation, the increase in V_{MCA} during bicycling was reduced (Ide *et al*. 2000). These findings were confirmed in healthy subjects by changing the central blood volume and CO at rest and during dynamic exercise; this indicated a linear relationship between CO and

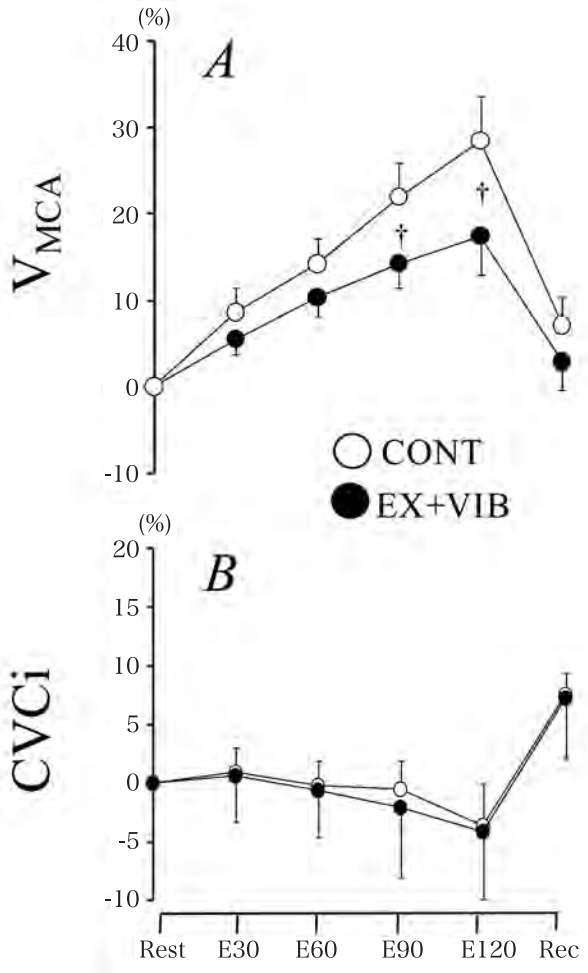

Fig. IV.2.3-1 The relative changes in middle cerebral artery mean blood flow velocity (V_{MCA}) and index of cerebrovascular conductance (CVCi) during and after static exercise. Baseline cardiorespiratory values before exercise were defined as the 0% control levels in each subject. Their relative percent changes for the control levels were sequentially calculated during static exercise. Values are expressed as mean ± S.E.M. † Significant difference between CONT and EX+VIB, $P < 0.05$.

V_{MCA} at rest and during exercise (Ogoh *et al*. 2005). These results demonstrated that any regulation of CO via the cardiac baroreflex would directly influence dynamic CBF regulation during exercise (Ogoh *et al*. 2005). Considering these observations and our results together, the CO response-induced decrease via the reduction in central command may have affected V_{MCA} during exercise.

In conclusion, the present investigation supports the hypothesis that central command actively contributes to CBF regulation during static exercise. The decrease in V_{MCA} when central com-

mand was reduced is caused by attenuated brain activation, probably representing neural activity in the central command network and/or by the reduction in CO.

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2.4 Role of central command in the renal arterial blood flow responses during static elbow flexion in humans

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Purpose

The role of central command in the renal flow regulation has remained elusive. A prior study reported that central command was not essential for producing the renal vasoconstriction during exercise because the renal vascular resistance was almost identical during voluntary and electrically induced (involuntary) contractions (Momen *et al*. 2003). However, the studies in conscious animals demonstrated a significant role of central command during voluntary static and dynamic exercises (Matsukawa K *et al*. 1991; O'Hagan *et al*. 1993). One reason for the discrepant data was due to the lack of non-invasively studies during exercise in humans. The magnitude of involvement of the central command during exercise can be "non-invasively" decreased or increased in the previous studies. By using tendon vibration to assist or to oppose an exercising muscle group while developing a given force one can decrease (agonist activation) or increase (antagonist inhibition) the influence of central command without inducing nociceptor afferent input or augmenting normal exercise pressor reflex activation (Goodwin *et al*. 1972; Ogoh *et al*. 2002). Using this manipulation of agonist activation, we examined whether a decreased influence of central command would produce a concomitant decrease in renal flow responses during voluntary static exercise.

Methods

Ten healthy female volunteers whose mean age

Table IV.2.4-1 Resting values in vibration (VIB), vibration plus static elbow flexion exercise (VIB+Ex), and static elbow flexion exercise (Ex) conditions.

		Condition		
		VIB	VIB + EX	EX
HR	(bpm)	70.91 ± 4.31	71.65 ± 5.31	71.31 ± 5.83
MAP	(mmHg)	75.49 ± 9.90	80.54 ± 9.59	83.86 ± 9.53
CO	(L/min)	4.57 ± 0.54	4.56 ± 0.65	4.83 ± 0.61
SV	(mL)	64.60 ± 7.34	63.68 ± 8.58	67.65 ± 5.67
MBV	(cm/sec)	21.27 ± 3.75	22.41 ± 3.63	23.06 ± 3.32
RVR	(a.u.)	3.58 ± 0.78	3.68 ± 0.87	3.76 ± 0.65

HR, heart rate; MAP, mean arerial blood pressure; CO, cardiac output; SV, stroke volume, MBV, mean blood velocity; RVR, renal vascular resistance . Values are mean ± SD in 10 subjects.

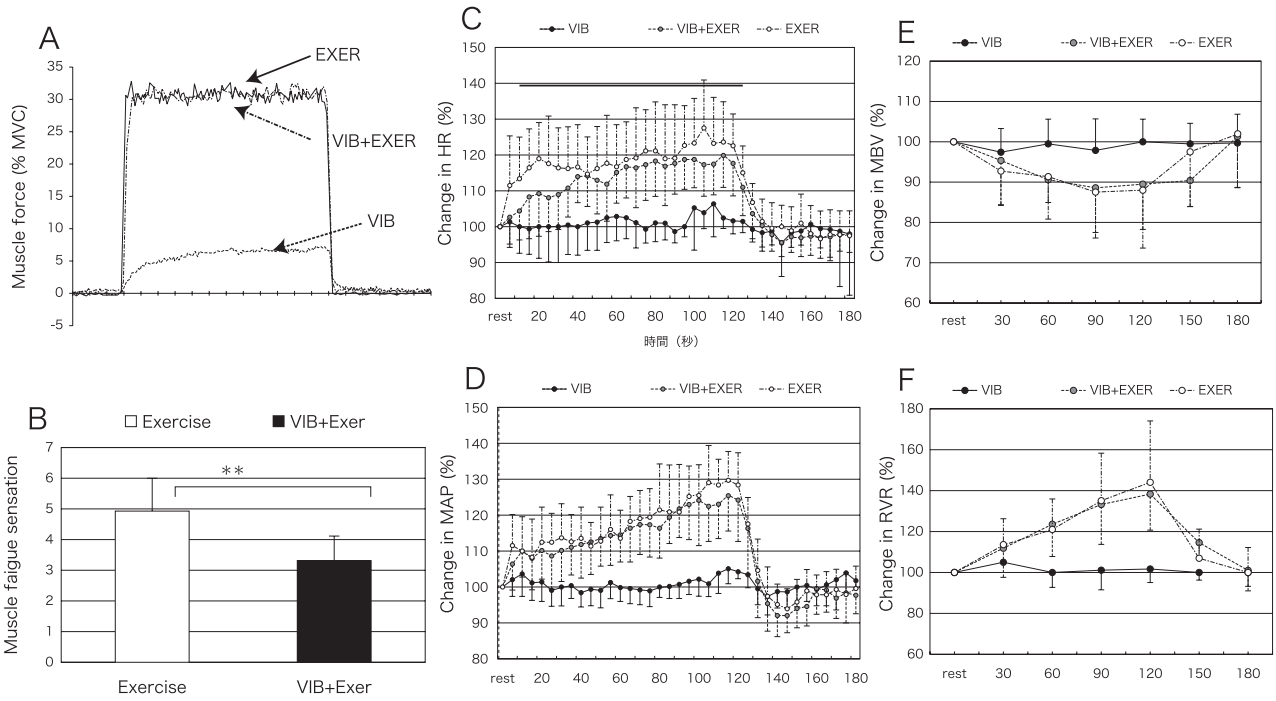

Fig. IV.2.4-1 Percent changes in heart rate (HR), mean arterial blood pressure (MAP), mean blood velocity in renal artery (MBV) and renal vascular resistance (RVR) at rest and during 2 min exercise and recovery. Vibration in the resting arm during rest indicates VIB. Values are mean (SD in 10 subjects. Time from 0 to 120 sec indicates the static voluntary exercise. Changes in HR and muscle fatigue sensation were significantly lower in Vibration + Exercise (VIB+EXER) than those in Exercise (EXER).

was 22 ± 3.3 (SD) yr participated in the present study. After 10-min resting, the subject performed a 2-min static elbow flexion at a constant load of 30% of maximum voluntary contraction (MVC) with vibration (EX+VIB) and without vibration (EX). In the experiments of EX+VIB and EX, the vibration (frequency, 100 Hz; amplitude, 0.8 mm) was applied to the distal tendon of the biceps brachii in the exercising arm. The same vibration was only applied in the resting arm (VIB) as control experiment to test what to degree the vibration itself induce muscle force and cardiovascular responses. Time-averaged mean blood flow velocity (MBV) in the renal artery (RA) was measured by using Doppler method (Logic 5, GE Medical systems). Muscle fatigue sensation of the subject, as an index of the magnitude of central command (Saito *et al.*), was monitored. Heart rate (HR: ECG) and arterial

mean blood pressure (MAP: Fino- meter, Finapres Medical Systems BV) were continuously measured. Cardiac output (CO) was estimated from a arterial pressure curve by Model Flow method (Finapres Medical Systems BV). The index of resistance in RA (RVR) was calculated as MAP/MBF.

Results and Discussion

Table IV.2.4-1 shows the resting levels in HR, MAP, CO, SV, MBV and RVR in three conditions of VIB, VIB+EX, and EX. The muscle force, muscle fatigue sensation, HR, MAP, MBV and RVR are shown in Fig. IV.2.4-1. The vibration itself reflexly induced the tension corresponding to 7-8% of MVC but had no significant effects on the cardiovascular responses. The increase in HR during exercise and the muscle fatigue sensation in the exercising arm were significantly lower during EX+VIB than those during EX. These results indicated that the vibration technique of agonist activation substantially decreased the influence of central command during EX+VIB because the muscle fatigue sensation (Gandevia 1987; Saito *et al*. 1989; Williamson *et al*. 2001) and HR (Victor *et al*. 1989) responses have been considered to dictate the magnitude of central command. The MAP responses during EX+VIB also tended to be lower than those during EX. In contrast, the MBF and RVR were identical during both EX+VIB and EX suggesting that the decreased influence of central command was not effective in the renal flow regulation. The present data verified the previous report in humans (Momen *et al*. 2003) examined under “non-invasive” condition that central command was not essential for regulating blood flow responses in RA but the actual work load of force production was an important determinant for renal flow adjustment during voluntary static exercise.

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Mapping of calf muscle oxygenation and haemoglobin content during dynamic plantar flexion exercise by multi-channel time-resolved near-infrared spectroscopy

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Abstract

A compact and fast multi-channel time-resolved near-infrared spectroscopy system for tissue oximetry was developed. It employs semiconductor laser and fibre optics for delivery of optical signals. Photons are collected by eight 1 mm fibres and detected by a multianode photomultiplier. A time-correlated single photon counting board is used for the parallel acquisition of time-resolved reflectance curves. Estimate of the reduced scattering coefficient is achieved by fitting with a standard model of diffusion theory, while the modified Lambert–Beer law is used to assess the absorption coefficient. *In vivo* measurements were performed on five healthy volunteers to monitor spatial changes in calf muscle (medial and lateral gastrocnemius; MG, LG) oxygen saturation (SmO_2) and total haemoglobin concentration (tHb) during dynamic plantar flexion exercise performed at 50% of the maximal voluntary contraction. At rest SmO_2 was 73.0 ± 0.9 and $70.5 \pm 1.7\%$ in MG and LG, respectively ($P = 0.045$). At the end of the exercise, SmO_2 decreased (69.1 ± 1.8 and $63.8 \pm 2.1\%$ in MG and LG, respectively; $P < 0.01$). The LG desaturation was greater than the MG desaturation ($P < 0.02$). These results strengthen the role of time-resolved near-infrared spectroscopy as a powerful tool for investigating the spatial and temporal features of muscle SmO_2 and tHb.

1. Introduction

The possibility of monitoring non-invasively the haemodynamics and the oxygenation status/kinetics (indirect measurement of oxidative metabolism) in the muscle or in the brain is a challenging task. In the muscle, this can not only help in studying the mechanisms related to exercise physiology, but also to pathology caused by myopathies and/or peripheral circulatory diseases. In the brain, it can lead to the monitoring of cerebral oxygenation and the reactivity in response to some stimuli (motor, visual, cognitive), and thus it can help in the study of cognitive processes, evaluation of mental diseases, assessment of brain injuries, etc. These studies were fostered by the capabilities offered by magnetic resonance imaging and positron emission tomography (Posner and Raichle 1998). In this framework light is a powerful diagnostic tool especially in the region between 650 and 1100 nm where penetration depth in biological tissues is relatively high, and also oxygenated haemoglobin (O_2Hb) and deoxygenated haemoglobin (HHb) exhibit distinct spectral features (see Delpy and Cope 1997 for a review). The widespread use of near-infrared spectroscopy (NIRS) for non-invasive investigation has been hampered by the high scattering coefficient typical of biological tissues that hinders spatial and spectral information contained in endogenous chromophores. Recently, deeper knowledge of the physics of photon migration and technical developments in optoelectronics components have made it possible to extract valuable optical information from the probed medium. Also, several instruments for optical tissue oximetry—either commercial systems or laboratory prototypes—have been constructed. A first approach to monitoring tissue oxygenation is to measure light attenuation at two wavelengths between a couple of optical fibres set normal to the tissue surface at a known relative distance. Assuming a fixed value of the scattering coefficient, and applying the Lambert–Beer law, relative changes in the HHb and O_2Hb concentrations can be tracked. This rather straightforward technique has grown in time and led to instruments working at more wavelengths, or with multiple source, multiple detector geometries[4]. In particular this latter feature offers the possibility of probing different regions in the tissue under study and thus of producing functional maps. Actually, using such advanced continuous wave (CW) systems the response of brain oxygenation and perfusion to finger tapping, mental calculations, light flashing and other stimuli was demonstrated (see Obrig and Villringer 2003 for a review). Yet, the key limitations of this technique are the coupling between the absorption and the scattering coefficients (μ_a, μ_s') causing the lack of quantitative assessment, sensitivity to artefacts and experimental conditions. A possible way to uncouple μ_a from μ_s' still using a CW source is to use a multi-distance approach, and to analyse the spatial decay of re-emitted light (Kienle *et al* 1996). Some commercial instruments are available exploiting this principle, yet the method relies on a strong correlation between different interfibre distances, and thus is based on the assumption of a homogeneous medium. Effects caused by the inherent multi-layer structure of the human body are still to be clarified (Farrell *et al* 1998). A possible extension of the CW approach towards the spectral domain can overcome some of these limitations since the use of a full spectral range (e.g., 700–1000 nm) provides more information and redundancy to get rid of scattering assumptions, interference from other absorbing chromophores or the heterogeneous tissue structure. Matcher *et al* (1994) described a simple method for measuring the differential pathlength of photons in a scattering medium utilizing the spectral absorption features of water. A completely different approach is based on the use of sinusoidally modulated laser sources, and on the measurement of signal phase and amplitude changes caused by propagation. The frequency-domain technique extracts both

[4] Instruments: NIRO-300 (Hamamatsu Photonics Co., Japan), OXYMON (Artinis Medical Systems, The Netherlands), INVOS 4100 (Somanetics Co., USA), OM-200 (Shimadzu Co., Japan), ETG-100 (Hitachi Co., Japan).

the mean μ_s' and μ_a of the probed medium provided that a non-trivial calibration of collection efficiencies is performed. This approach was successfully applied to the measurement of tissue oxygenation, and led to the first identification of a rapid change of μ_s' following a cerebral stimulus (Gratton *et al* 1997). The dual approach is the study of photon migration in the time domain first introduced *in vivo* by Chance *et al* (1988) and Delpy *et al* (1988). The temporal dispersion of a short laser pulse travelling through a diffusive medium can provide both the mean μ_s' and μ_a using a proper model of photon migration. By applying the Fourier transform, the time-domain measurement can be converted into a set of frequency-domain measurements distributed over a wide range of frequencies ultimately limited by the temporal resolution of the system in use, and by the strong attenuation of photon density waves at a high frequency. Thus, the temporal approach could provide even broader information than phase-resolved measurements. Yet, the real advantage of having a full time-resolved curve instead of a single frequency measurement is still to be investigated. In the past, the cost, size and complexity of the time-resolved instrumentation have prevented this technique from being effectively used in tissue oxygenation studies. Large laboratory systems have been developed for spectral (Andersson-Engels *et al* 1993, Cubeddu *et al* 1999a) or spatial (Cai *et al* 1999, Eda *et al* 1999, Schmidt *et al* 2000) characterization of turbid media, but are unsuitable for fast tissue oximetry. Recently, semiconductor lasers have made it possible to construct more compact time-resolved instruments (Benaron and Stevenson 1993, Miwa *et al* 1995, Cubeddu *et al* 1999b, Grosenick *et al* 1999, Ntziachristos *et al* 1999), yet none of them offers the required complexity of source/detector configuration needed to produce optical maps for functional monitoring and/or the short acquisition time essential to follow biological dynamics.

In this paper, we report on the development and characterization of a novel compact multi-channel optical system, based on the time-resolved reflectance spectroscopy technique with two sources, eight detectors and 6 Hz acquisition frequency. Moreover, we report the spatial changes in calf muscle (medial gastrocnemius (MG) and lateral gastrocnemius (LG)) oxygen (O_2) saturation (SmO_2) and total haemoglobin concentration (tHb) monitored on healthy volunteers during dynamic plantar flexion exercise executed at 50% of the maximum voluntary contraction (MVC).

2. Materials and methods

2.1. System set-up: eight-channel time-resolved tissue oximeter

The scheme of the system set-up is shown in figure 1. A couple of semiconductor pulsed lasers (PDL, Picoquant, Germany), working at 685 nm and 780 nm, with 80 MHz repetition rate and 1 mW average power, are used as light sources. Multimode graded index fibres (50/125 μm) of different lengths and a fibre optics integrated device (VIS/NIR 2 $\times$ 2 fused splitter, OZ Optics, Canada) are used to multiplex in time the output pulses of the two laser heads so as to create two independent injection points. A compact 16-anode photomultiplier (R5900-01-L16, Hamamatsu, Japan) and a PC board (SPC-630, Becker & Hickl, Germany) for time-correlated single photon counting (TCSPC) are used to detect and acquire time-resolved reflectance curves. Due to 20% optical cross talk among adjacent channels, only 8 out of 16 channels are used by placing the optical fibre only on odd channels (1, 3, 5, . . . , 15). In this configuration the cross talk is lower than 3% (see section 3.1.1). The typical measurement time for the parallel acquisition of time-resolved curves from the eight channels is 166 ms (6 Hz).

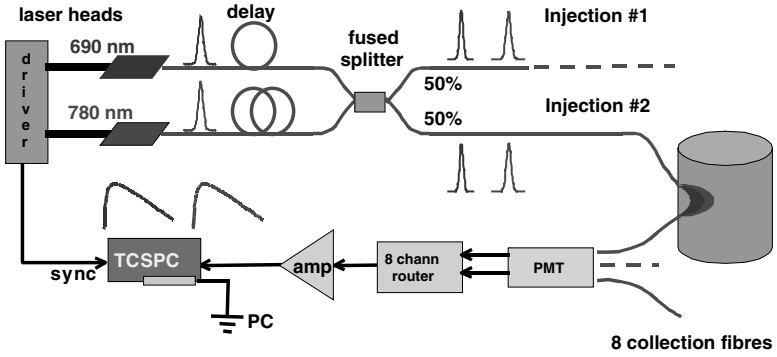

Figure 1. Scheme of the two-source eight-detector time-resolved tissue oximeter. (TCPSC: time-correlated single photon counting; PMT: photomultiplier tube.)

2.2. System characterization

The performances of the system were tested on tissue phantoms in terms of reproducibility among channels, stability and linearity in the determination of the optical properties (absorption and scattering coefficients).

A cylindrical glass box (10 cm diameter and 10 cm height) was filled with an aqueous solution of Intralipid (Kabi Vitrum, Italy), to mimic a scattering tissue and ink (Mod. R591-009 Blue, Rotring, Germany), to mimic tissue absorption. Throughout the paper, the concentration of Intralipid refers to the fraction of solids in the examined solution, while the concentration of ink pertains to the fraction of the original product, as obtained from the supplier, present in the solution under study. The scattering properties of Intralipid and the absorbing properties of the ink were characterized using time-resolved reflectance spectroscopy under optimal conditions for both the technique and the theoretical method (Cubeddu *et al* 1996). This allowed us to fix the absorbing and scattering properties of the phantom solutions to values typical for human tissues in the visible and near-infrared regions of the spectrum. The injection and collection fibres, were placed at a relative distance $\rho = 3.0$ cm, in contact with and at a right angle to the sample surface. A black, rigid plastic strip firmly held the fibres, and avoided possible direct (not re-emitted) stray light to be collected by the fibre.

2.3. Data analysis

During data analysis an integration time of 1 s is used to increase the signal-to-noise ratio. Summing six time-resolved reflectance curves, each of them acquired with a measurement time of 166 ms, performs this operation.

Simultaneous estimate of μ_s' and μ_a may be achieved by best fitting of time-resolved reflectance curves with a standard model of diffusion theory (Haskell *et al* 1994). Therefore, to reduce dispersion of the fitted absorption coefficient values, we use the methods described by Nomura *et al* (1997) and known as the modified Lambert–Beer law. First, for each wavelength a reference time-resolved reflectance curve $R_0(\rho, t, \lambda_i)$ is derived by averaging the curves corresponding to an initial resting period (typically 0.5 min). Fitting of $R_0(\rho, t, \lambda_i)$ yields the reference absorption value $\mu_{a0}(\lambda)$. Then $\Delta\mu_a$, the variation from the reference value, is derived according to the following equations:

$$\mu_a(\lambda) = \mu_{a0}(\lambda) + \Delta\mu_a(\lambda) \tag{1}$$

$$\Delta\mu_a(\lambda) = -\frac{1}{vt} \ln\left(\frac{R(\rho, t; \lambda_i)}{R_0(\rho, t; \lambda_i)}\right). \tag{2}$$

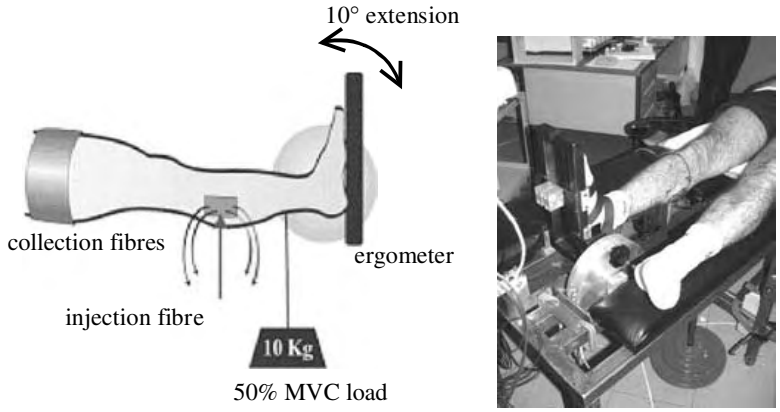

Figure 2. Scheme of the dynamic plantar flexion exercise (left) and a photograph of the foot ergometer (right). (MVC: maximal voluntary contraction.)

Improvement over the standard methods is more effective when the absorption is high. In this condition in fact standard fitting with the non-linear least-squares methods yields high dispersion in the fitted data (Cubeddu *et al* 1996). Taking the assumption that O_2Hb and HHb are the main chromophores contributing to absorption, their concentrations are easily derived by using the knowledge of the extinction coefficient (Prahl 2001). Water absorption in this spectral region is in fact much lower than haemoglobin absorption (Prahl 2001). A fixed amount (30%) of absorption was attributed to water and subtracted from μ_a before calculation of HHb and O_2Hb. Then, tHb (tHb = HHb + O_2Hb) and muscle O_2 saturation (SmO_2 = O_2Hb/tHb) are derived.

2.4. Protocols for in vivo measurements

In vivo measurements were performed on five healthy volunteers (male, age: 34–50 years) to monitor SmO_2 and tHb changes in the calf muscle during dynamic plantar flexion exercise. All subjects gave their written informed consent. Figure 2 (left) shows the ergometer designed and built at the Politecnico di Milano, Dipartimento di Fisica to perform the exercise (Kagaya 1992). The day before measurements all subjects received adequate training on the exercise, and their own MVC was measured (48, 50, 36, 34 and 42 kg). The protocol consisted of 1 min rest condition, followed by 1 min plantar flexion (1 Hz, 50% of MVC, 10° extension) and 3 min recovery. Time-resolved reflectance measurements were performed with 6 Hz acquisition frequency (166 ms acquisition time). A pair of custom-made fibre holders were designed so as to collect re-emitted photons from four points, equidistant (3 cm) from the injection (see figure 3). The holder is made of soft black rubber, and is kept in place by adhesive strips wrapped around the leg of the subject (not too tight to avoid blockage of blood flow). No downward sliding of the fibre holder was observed at the end of the measurements in any subject. Fibres are kept normal to the sample by black plastic hollow tubes. Measurement points were located in the MG and LG, in the distal (D1 and D2) and proximal (P1 and P2) regions. The typical distance between the light source located in the LG (MG) and detectors placed over the MG (LG) was 10 cm. This avoided cross talk between the optical signals detected simultaneously in the two areas.

Adipose tissue thickness underlying the monitored areas of the muscle groups was measured with a skinfold calliper. The mean value of the adipose tissue thickness was 3.3 ± 1.3 mm and 3.9 ± 1.0 mm over MG and LG, respectively. Considering that the thickness of the adipose tissue over all the investigated area of the right calf was less than 5 mm, it can be

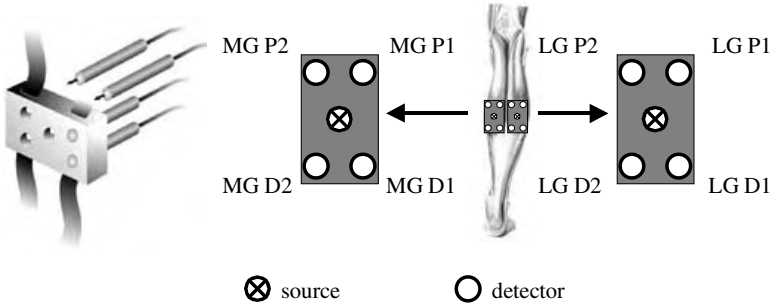

Figure 3. Scheme of the rubber pad probe designed to hold the fibres (left), and scheme of the positioning of the probes on the calf muscles (right). The source–detector distance is 3 cm. (LG: lateral gastrocnemius; MG: medial gastrocnemius; P: proximal; D: distal.)

assumed that SmO_2 variations reflect the metabolic changes occurring mainly in the muscle tissue (Matsushita *et al* 1998). In addition, the lack of difference in adipose tissue thickness between MG and LG allowed their comparison.

Maximal desaturation observed in the exercising muscle was calculated by calculating the difference of the absolute values of SmO_2 between the rest condition (mean value over the 1 min baseline) and the end of the exercise (mean value over the last 10 s). SmO_2 was calculated after 3 min recovery (mean value over the last 10 s). The same averaging procedure was utilized for tHb.

The mean and standard deviation of SmO_2 and tHb values within MG and LG were determined separately and compared using analysis of variance. Significant differences were identified using Tukey's honestly significant difference multiple comparison test. The paired *t* test was used to compare the SmO_2 and tHb values corresponding to MG and LG. The criterion for significance was $P < 0.05$.

3. Results

3.1. System characterization

3.1.1. Detector uniformity and cross talk. To test detector uniformity and cross talk among channels, channel 1 of the photomultiplier was illuminated and photons were simultaneously detected from channels 1 to 16. This test was then repeated also with illumination in channels 3, 5, 7, 9, 11, 13 and 15. All results are shown in figure 4. Detector uniformity (i.e. the dispersion of the peak intensity in the illuminated channel) is 13%. Cross talk between adjacent channels is 20% while it reduces to 2% if the first non-adjacent channels are considered.

These results are in agreement with the typical values for anode uniformity and cross talk reported in the detector datasheet (see Hamamatsu, multianode photomultiplier tube R5900U-L16 series, TPMH1146EO5, Sept. 1999, Japan). Anode uniformity is in fact 1:0.6 (relative output is in the range 100–80%) and electronic cross talk is 3%.

In a further experiment, a configuration with a double source and a single detector was used to study differences due to the use of multiple sources. Time-resolved reflectance curves from a tissue phantom were measured (interfibre distance 3 cm, acquisition time 1 s) and estimates of μ_a and μ_s' were derived. The coefficient of variation is 1.8% and 1.7% for μ_a and μ_s', respectively. Then, a configuration with eight detectors and a single source was employed with the same measurement protocol. The coefficient of variation is 1.9% and 2.2% for μ_a and μ_s', respectively.

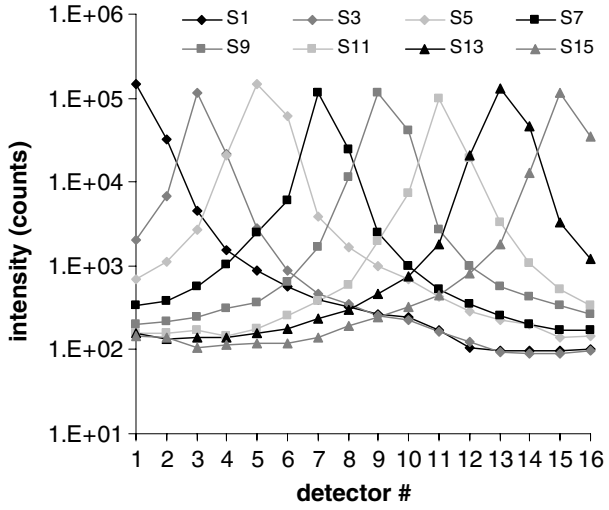

Figure 4. Photon counts in the 16 detectors as a function of the position of the illumination point. S1 indicates that the light source is located in front of channel 1.

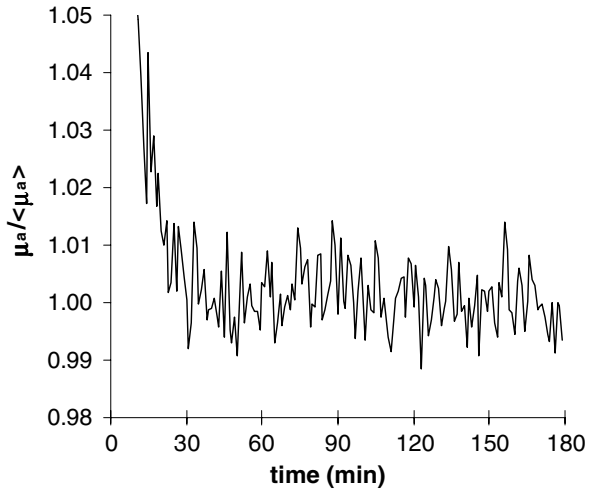

Figure 5. Stability test: the variation as a function of time of μ_a is reported after normalization to the average values estimated in the last 60 min of the test.

3.1.2. Stability. System stability was tested by performing a 3 h long measurement, starting from the turning on of the instrumentation. Figure 5 shows the variation of μ_a over the whole period. Values are plotted after normalization to the average value calculated in the last 60 min of the test. Similar results were found for μ_s' (data not shown). It is clear that the system needs about 30 min warm-up time. Drift of power and sync timing of semiconductor diode lasers mostly limit stability. After warm-up, the coefficient of variation (standard deviation/average) in the estimated absorption and reduced scattering coefficients is as low as 0.5% and 0.6%, respectively.

3.1.3. Absorption linearity. In the absorption linearity experiment the blue ink concentration was varied ranging from 0.3×10^{-5} to 2.1×10^{-5}, while the Intralipid concentration was 7.0×10^{-3}. Figures 6(a) and (b) show the absorption coefficient and the reduced scattering coefficient respectively, as a function of ink concentration. Points represent the average values while error bars are the dispersion among the eight channels. At both wavelengths, μ_a is found

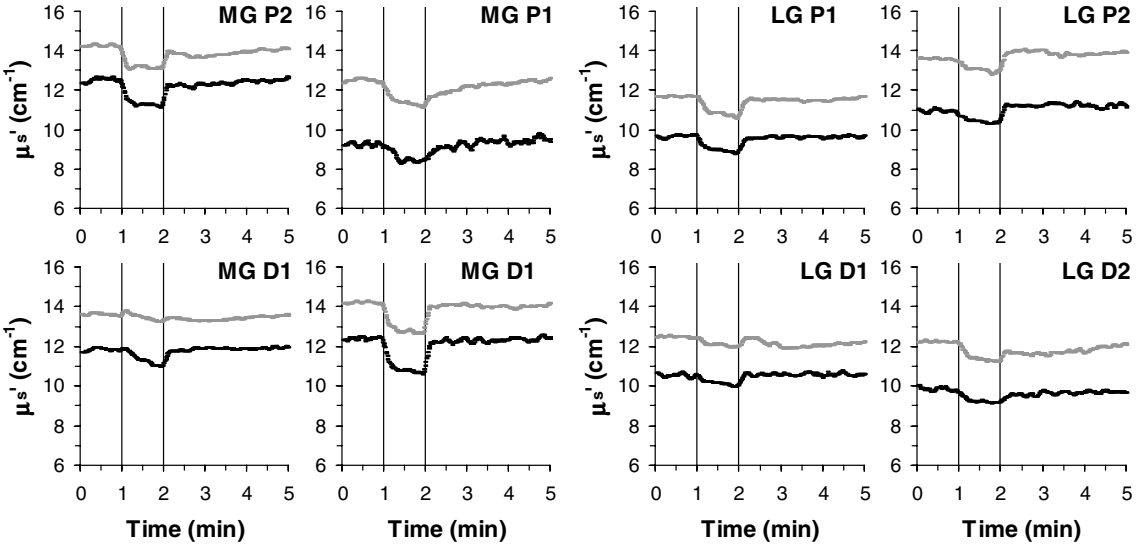

Figure 8. Typical time course of μ_s' at 690 nm (grey curve) and at 780 nm (black curve). Refer to figure 7 for abbreviations and details.

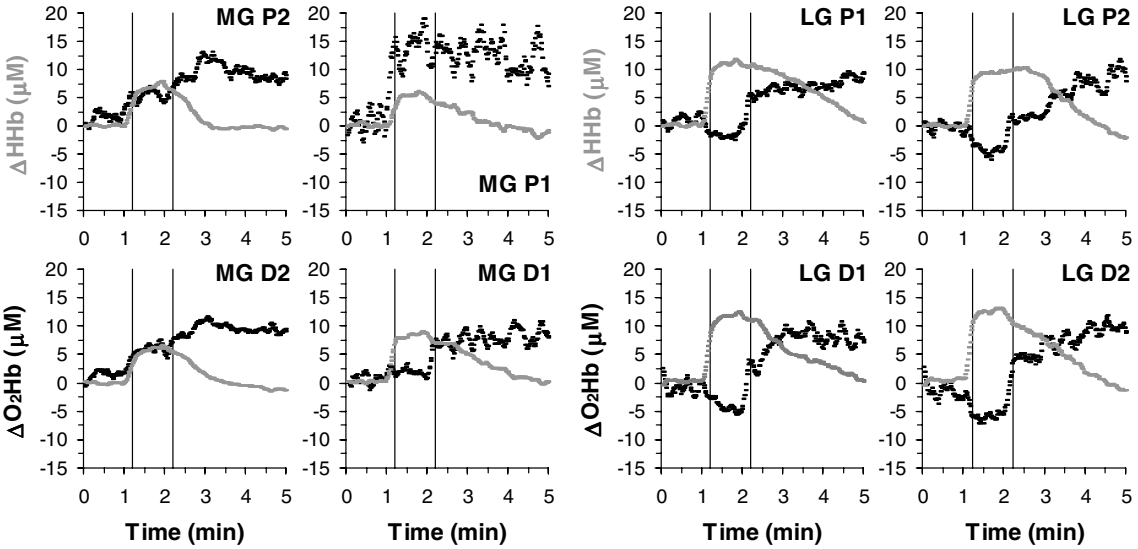

Figure 9. Typical time course of changes in HHb (grey curve) and O_2Hb (black curve). Refer to figure 7 for abbreviations and details.

typical plots of μ_a at 690 nm and at 780 nm over the protocol. During the initial resting period (0–1 min), μ_a is rather constant in all locations. The absorption coefficient is higher at 690 nm than at 780 nm for all locations except MG P1, which also presents a higher noise level, suggesting a non-optimal optical coupling, or an inadequate positioning, between the corresponding fibre and the muscle. Data from MG P1 were therefore not considered for the analysis. Then, during the dynamic plantar flexion exercise (1–2 min) there is at both wavelengths an abrupt increase of μ_a, with a saturation in the final part of the rise. After the end of the exercise, μ_a at 690 nm returns to the initial value with a slow recovery, while μ_a at 780 nm presents a further increase followed by a very slow recovery. As expected, μ_s' is lower at 780 nm than at 690 nm (figure 8). μ_s' is rather constant during the baseline, while it shows a 10% decrease during the plantar flexion exercise. At the end of the exercise μ_s' rapidly returns to values closer to the initial ones. SmO_2 rapidly decreases within the first 20 s after

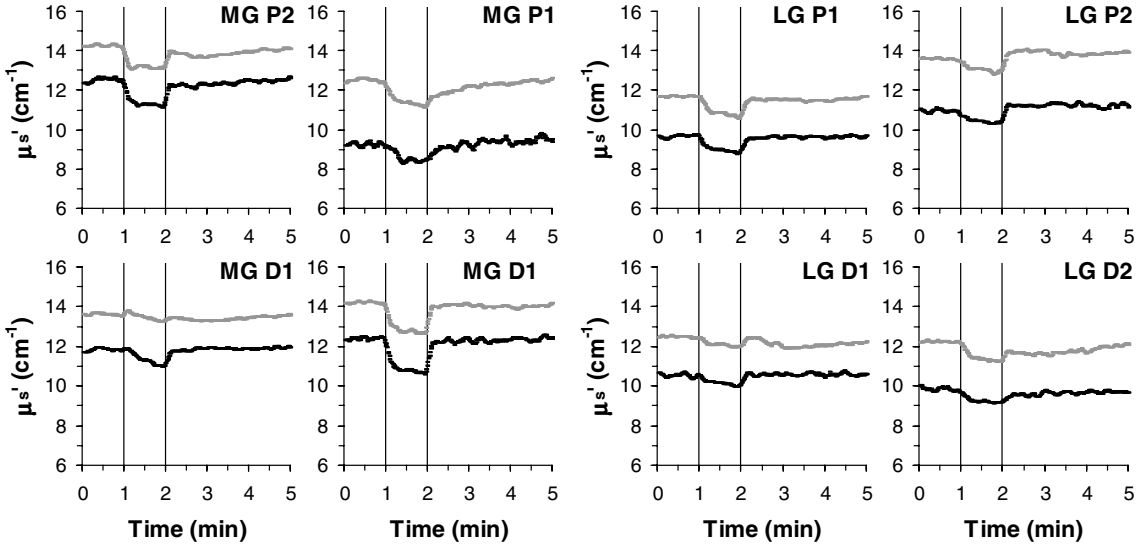

Figure 8. Typical time course of μ_s' at 690 nm (grey curve) and at 780 nm (black curve). Refer to figure 7 for abbreviations and details.

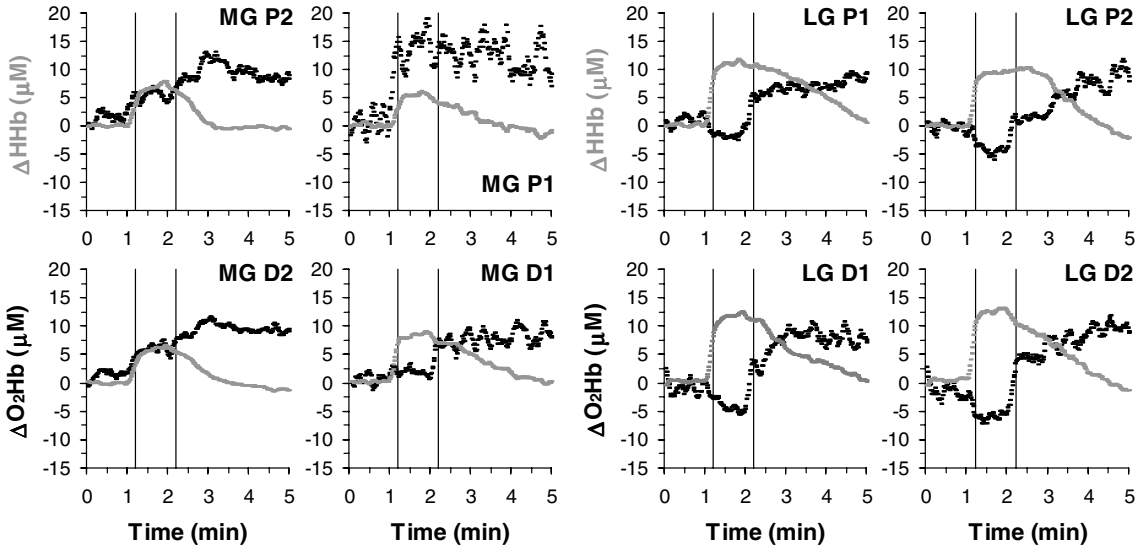

Figure 9. Typical time course of changes in HHb (grey curve) and O_2Hb (black curve). Refer to figure 7 for abbreviations and details.

typical plots of μ_a at 690 nm and at 780 nm over the protocol. During the initial resting period (0–1 min), μ_a is rather constant in all locations. The absorption coefficient is higher at 690 nm than at 780 nm for all locations except MG P1, which also presents a higher noise level, suggesting a non-optimal optical coupling, or an inadequate positioning, between the corresponding fibre and the muscle. Data from MG P1 were therefore not considered for the analysis. Then, during the dynamic plantar flexion exercise (1–2 min) there is at both wavelengths an abrupt increase of μ_a, with a saturation in the final part of the rise. After the end of the exercise, μ_a at 690 nm returns to the initial value with a slow recovery, while μ_a at 780 nm presents a further increase followed by a very slow recovery. As expected, μ_s' is lower at 780 nm than at 690 nm (figure 8). μ_s' is rather constant during the baseline, while it shows a 10% decrease during the plantar flexion exercise. At the end of the exercise μ_s' rapidly returns to values closer to the initial ones. SmO_2 rapidly decreases within the first 20 s after

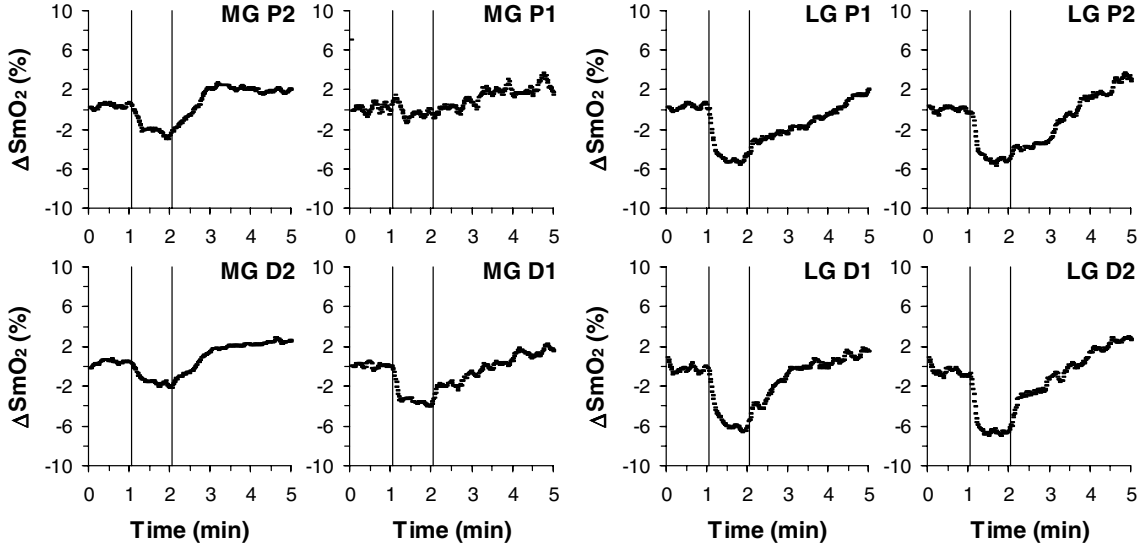

Figure 10. Typical time course of changes in SmO_2 (%). Refer to figure 7 for abbreviations and details.

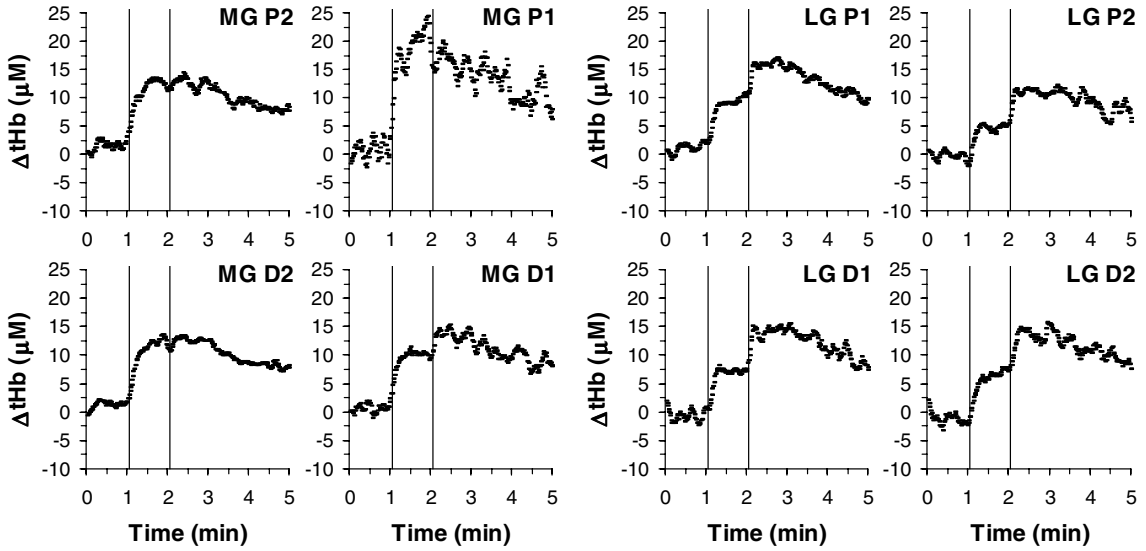

Figure 11. Typical time course of changes in tHb (μM). Refer to figure 7 for abbreviations and details.

the beginning of the exercise in all locations (figure 10), then it decreases more slowly up to the end of the exercise with different patterns in the MG and LG. In particular, SmO_2 of MG P2 and MG D1 progressively decreases, while in the remaining locations it reaches a constant value. At the end of the exercise, in all locations SmO_2 recovers with different patterns and reaches in 3 min values above the pre-exercise ones. Concomitantly tHb, after an abrupt rise occurring within the first 20 s of exercise, is constant until the end of the exercise (figure 11). Immediately after, tHb increases very rapidly in LG and MGD1; then it progressively decreases and maintains values above the pre-exercise ones 3 min after the end of the exercise (passive reactive hyperaemia).

Considering that no significant difference in SmO_2 and tHb was found amongst the four locations within each muscle group, SmO_2 and tHb were averaged within LG and MG.

Table 1. SmO_2 (%) and tHb (μM) in the medial (MG) and lateral (LG) gastrocnemius muscle groups of the right leg at rest (REST), at the end of the dynamic plantar flexion exercise (EXER), and 3 min after the end of exercise (REC). CHANN is the number of measurement points averaged in LG/MG, respectively. var: variable.

			MG			LG		
Subject	CHANN	Var	REST	EXER	REC	REST	EXER	REC
A	3/4	SmO_2	70.1 ± 1.1	63.4 ± 1.8	72.2 ± 0.9	69.2 ± 1.9	60.8 ± 1.4	71.6 ± 1.4
		tHb	147.8 ± 22.7	155.2 ± 24.1	154.7 ± 22.2	130.0 ± 3.9	128.8 ± 5.6	136.6 ± 4.3
B	4/3	SmO_2	69.5 ± 0.9	66.4 ± 1.7	71.0 ± 0.3	61.9 ± 1.5	56.0 ± 1.3	66.2 ± 0.8
		tHb	127.3 ± 3.5	138.3 ± 2.7	130.9 ± 3.7	133.4 ± 1.8	141.3 ± 3.0	137.8 ± 2.7
C	4/2	SmO_2	75.9 ± 0.9	71.0 ± 2.6	78.4 ± 0.4	74.9 ± 1.9	68.7 ± 3.5	75.8 ± 2.0
		tHb	162.7 ± 16.3	169.5 ± 21.5	171.8 ± 16.0	152.4 ± 8.6	159.8 ± 7.7	156.8 ± 9.6
D	4/3	SmO_2	73.6 ± 0.9	69.7 ± 1.4	76.0 ± 1.2	68.9 ± 1.6	60.9 ± 2.5	71.7 ± 2.0
		tHb	157.3 ± 7.4	161.2 ± 8.2	163.9 ± 7.7	151.9 ± 19.2	155.5 ± 20.1	155.0 ± 19.2
E	4/3	SmO_2	78.7 ± 0.5	75.4 ± 1.5	80.3 ± 0.7	77.8 ± 1.5	72.8 ± 1.8	79.8 ± 1.6
		tHb	112.0 ± 5.7	128.8 ± 5.7	119.3 ± 6.4	111.8 ± 7.4	116.3 ± 9.4	117.2 ± 7.2
Mean $\pm$		SmO_2	$73.6^{c} \pm 0.9$	$69.1^{a,c} \pm 1.8$	$75.6^{a,b,c} \pm 0.7$	70.5 ± 1.7	$63.8^{a} \pm 2.1$	$73.0^{a,b} \pm 1.6$
sd		tHb	141.4 ± 11.1	$150.6^{a,c} \pm 12.4$	$148.1^{a} \pm 11.2$	135.9 ± 8.2	$140.3^{a} \pm 9.1$	$140.7^{a} \pm 8.6$

[a] Significantly different from the corresponding value at REST.
[b] Significantly different from the corresponding value at the end of the exercise (EXER).
[c] Significantly different from the corresponding value in LG. Significance was set at $P < 0.05$.

Table 1 summarizes for each subject the absolute values of SmO_2 and tHb measured at rest, at the end of the dynamic plantar flexion exercise and 3 min after the end of the exercise. The baseline value of SmO_2 in LG is lower than in MG ($P = 0.0447$). Both in LG and MG, SmO_2 decreases at the end of the exercise ($P < 0.01$) with lower values found in LG than in MG ($P = 0.0199$). Both in LG and MG, SmO_2 at the end of the protocol reaches higher values than the pre-exercise ones ($P < 0.05$). Either in LG or MG, tHb increases at the end of the exercise ($P < 0.05$) with lower values found in LG than in MG ($P = 0.0499$). tHb at the end of the protocol reaches higher values than the pre-exercise ones ($P < 0.05$).

4. Discussion

In this study we report the development of a fast eight-channel portable instrument aiming at increasing the informative content of tissue oximetry data, as compared to existing devices. In the last five years, several groups have begun to use multi-channel CW imaging systems that allow the generation of images of a relatively large area of the subject's head/muscle with high temporal resolution (up to 100 ms) and, thereby, the production of maps of cortical/muscle oxygenation changes (see Miura *et al* 2001, 2003, Niwayama *et al* 2000, Obrig and Villringer 2003 for a review of brain studies; Quaresima *et al* 2001a, 2002). In particular, Miura *et al* (2003) using a multi-channel CW NIRS system found regional differences in the oxygenation of the gastrocnemius muscle during exercise and recovery performing the standing plantar flexion exercises for 2 min (one contraction/s) with the distal portion having greater deoxygenation and tHb changes. This is consistent with the distal portion having a greater impairment of muscle blood flow possibly because of the higher intramuscular pressure during the exercise. Quaresima *et al* (2001a) investigated vastus lateralis and rectus femoris O_2 consumption at rest and during MVC using a 12-channel CW NIRS system (100 ms acquisition time). O_2 consumption either at rest or during MVC was found to be non-uniform in the 12 measurement sites over a surface of 8×8 cm^2.

The results of the previous studies have strengthened the role of NIRS as a powerful tool for investigating the spatial and temporal features of muscle oxygenation changes as well as muscle O_2 consumption. Unfortunately few CW imagers are commercially available; they are quite expensive, and lack the US Food and Drug Administration approval. Although many interesting studies have been performed with multi-channel CW systems, the lack of pathlength determination limits the accuracy of the results (Ferrari *et al* 1992, Zhao *et al* 2002).

Imagent (ISS Inc., Urbana, IL, USA) is a new device allowing the measurement of O_2Hb and HHb concentration maps in muscle and brain by the phase modulation method. The instrument has been recently and successfully utilized in brain and muscle studies (Wolf *et al* 2002, 2003).

Absolute concentrations can also be measured by time-resolved spectroscopy. Few instruments working in the time domain are nowadays present at the research level. A two-wavelength and a three-wavelength instrument have been used in muscle studies, but they offer poor acquisition time and are limited by the use of a single detection channel (Hamaoka *et al* 2000, Oda *et al* 2000). Companies and academic institutions have been developing multi-channel time-resolved systems (Eda *et al* 1999, Schmidt *et al* 2000). The first multi-channel (64) time-resolved optical imaging system was developed by Japanese companies (Eda *et al* 1999) and it has been successfully tested in human brain functional studies (Hoshi *et al* 2000). However, the 64-channel system is characterized by an extremely poor time resolution (some minutes). A 16-source and 32-channel time-resolved optical imaging instrument has been developed principally to study functional parameters of the newborn brain by the University College of London. Images representing the internal scattering and absorbing properties of the arm, as well as images revealing physiological changes during a simple finger flexion exercise were presented (Hillman *et al* 2001). Three-dimensional images (tomographic approach) of the newborn infant brain with a cerebral haemorrhage predominantly located within the left ventricle have been recently generated (Hebden *et al* 2002). Unfortunately, this imager is inherently limited to the acquisition of quasi-static images by the time needed to multiplex the different sources. A recently developed compact system is characterized by a similar apparatus but it is limited by the reduced number of channels (Steinbrink *et al* 2001).

The developed instrument was designed as a trade-off between imaging capabilities (i.e. need for a high number of measurement points) and fast monitoring requirements (i.e. maintaining a high acquisition frequency).

A limitation of the developed instrument is related to the spectral sensitivity. It is worth noting that the higher noise level in the absorption coefficient at 780 nm as compared to 690 nm is due to the reduced sensitivity of the photomultiplier at longer wavelengths. This could also influence the estimate of O_2Hb and subsequently tHb.

Moreover, the multi-channel acquisition could be specifically a key element to face presently unsolved problems related to the presence of multi-layer structures in biological tissues (e.g., the undesired effects caused by the subcutaneous fat layer in muscle measurements and by the extra-cranial contribution in brain measurements). To this purpose there is the need to collect data at multiple source–detector distances and apply recently developed methods (Martelli *et al* 2003). In this paper we preferred to focus on the monitoring of spatial variation over a wide area, therefore positioning the eight collection fibres at a fixed equal distance from the source.

Work is in progress to replace the fused splitter with a fibre optics switch, so as to further increase the number of injection points from 2 to 9, still keeping acquisition times as low as 200 ms (data not shown). Also, by means of a newly developed photomultiplier tube it is foreseen to double the number of independent collection channels.

An intrinsic limitation of the NIRS applied to monitoring of biological tissues is the poor spatial resolution due to the effect of light diffusion. On the other hand, the problem of penetration depth is still a research topic. However, it is foreseen that the TRS system may have advantages over CW systems (Del Bianco *et al* 2002).

The NIRS technique is unable to differentiate between the amount of O_2 released by haemoglobin (Hb) and myoglobin (Mb). However, within a given volume of muscle there are differences in the concentration of both Hb and Mb (i.e. Hb is about 1.5 fold higher than Mb), and in their binding capacities (i.e. Hb has four times the oxygen binding sites) (Richardson *et al* 2002). Therefore, one can estimate the Mb mass as a confounding factor at about 20% of the whole NIRS signal.

For the first time a fast multi-channel time-resolved instrument was effectively used to monitor SmO_2 and tHb regional differences in human calf muscle during dynamic plantar flexion exercise. The possibility of mapping tHb, which is strictly related to the tissue blood volume/flow, appears extremely interesting to evaluate regional vasodilatation and/or capillary recruitment.

It has been previously demonstrated by the one-channel NIRS that MG is the muscle mostly involved in dynamic plantar flexion exercise (Quaresima *et al* 2001b). The SmO_2 values of MG measured at rest are comparable with those obtained by Boushel *et al* (2000) and Quaresima *et al* (2001b, 2002). The heterogeneous SmO_2 response to the dynamic plantar flexion exercise found between the MG and LG (table 1) might be explained by either one or a combination of the following points: (a) different local blood supply produced by differences in the intramuscular pressure (Sejersted *et al* 1984); (b) divergence of the mechanical activity within the triceps surae; (c) differences in oxidative metabolic activity; (d) variations in the vascularization, i.e. distribution of arterial, venous and capillary vessels; (e) the recruitment of different fibre types within the investigated muscle volume. Indeed, muscle blood flow heterogeneity was also found in the quadriceps during dynamic and isometric exercise by using positron emission tomography imaging (Laaksonen *et al* 2003). Moreover, also ^{31}P-magnetic resonance spectroscopy revealed pH heterogeneity in the tibial anterior muscle during isometric activity (Houtman *et al* 2001). This diverse pH distribution was attributed to intramuscular differences in blood supply.

5. Conclusion

An instrument for multi-channel time-resolved tissue oximetry was developed. The system operates with two wavelengths, two injection points and eight independent collection points, and the typical acquisition time is 166 ms. *In vivo* measurements were performed on five healthy volunteers to monitor spatial and temporal changes in calf muscle (medial and lateral gastrocnemius; MG, LG) oxygen saturation (SmO_2) and total haemoglobin concentration (tHb) during dynamic plantar flexion exercise performed at 50% of the maximal voluntary contraction. The results strengthen the role of time-resolved near-infrared spectroscopy as a powerful tool for investigating the spatial and temporal features of muscle SmO_2 and tHb. Considering that human cortical mapping is the most interesting challenge for multi-channel TRS, work is in progress to test the TRS system with multi-layer models of the human head, and to map the human cortical activation under different stimuli.

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Review : Physiology

Muscle Architecture and its Relationship to Muscle Circulation

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Muscle contraction mechanically changes vessel geometry and consequently muscle circulation. Lengthening of muscle fiber straightens capillary tortuosity and further increase in muscle fiber length reduces blood flow by extending the capillary while reducing its diameter. The direction of capillary to the fiber long axis will modify the extent of capillary lumen diameter change due to lengthening muscle fiber. During passive stretching in human subjects, the relationship between changes in blood volume (determined by near-infrared spectroscopy: NIRS) and fascicle length differed among the three heads of triceps surae muscles with different fascicle length and pennation angle. Muscle thickness, muscle curvature, and muscle fascicle angle are potential determinants of intramuscular pressure during muscle contraction. Muscle circulation is impeded more in short bulging muscles with great curvature of fibers than in long slender muscles with less curvature. The different response of circulatory parameters across the synergist muscles in the calf and heterogeneity of muscle circulation in the same muscle were observed, partly due to the difference in the pennation angle of the muscle fascicle. The muscle architecture will influence venous outflow by changing the muscle pumping action. This is possibly an indirect way of modifying vasodilation due to difference in muscle architecture.

Keywords: pennation angle, muscle fiber length, blood volume

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1. Introduction

Blood flow during rhythmic exercise dramatically changes concomitant with muscle contraction and relaxation (Barcroft and Dornhorst 1949, Barnes 1986, Kagaya and Ogita 1992, Walløe and Wesche 1988). This mechanical disturbance of muscle circulation originates from the anatomical arrangements of muscle fibers and vessels.

Figure 1 shows a schematic illustration of artery and capillary alignment in relation to muscle fiber. The conduit artery (brachial artery, femoral artery, etc.) branches into the feeding artery, whose daughter arteries run into the muscles as terminal arterioles and capillaries (**Figure 1A**). When the muscle fibers are extended, the capillaries running parallel to the fiber long axis will be lengthened (**Figure 1B**), whereas those running in a perpendicular direction will be shortened (**Figure 1A**) (Nakao and Segal 1995, Poole, et al., 1997). When the muscle fibers are shortened, the opposite occurs. In addition, the muscles develop tension during muscle contractions and thereby the elevated intramuscular pressure compresses the capillaries between the fibers (Sjø gaard, et al., 1986, Sejersted, et al., 1984) (**Figure 1B**). This causes blood flow restriction or occlusion to the contracting muscles on the arterial side and expels blood from the muscle on the venous side (muscle pump) (Barnes 1986, Bonde-Petersen, et al., 1975, Gaskell 1877, Kagaya and Ogita 1992, Lind and McNicol 1967, Sadamoto, et al., 1983, Sjø gaard, et al., 1986,). Accordingly, changes in vessel geometry due to muscle lengthening/shortening and vessel compression due to developed muscle tension are two major factors which mechanically modify muscle circulation.

On the other hand, muscle architecture differs from muscle to muscle, (Kawakami, et al., 1998,

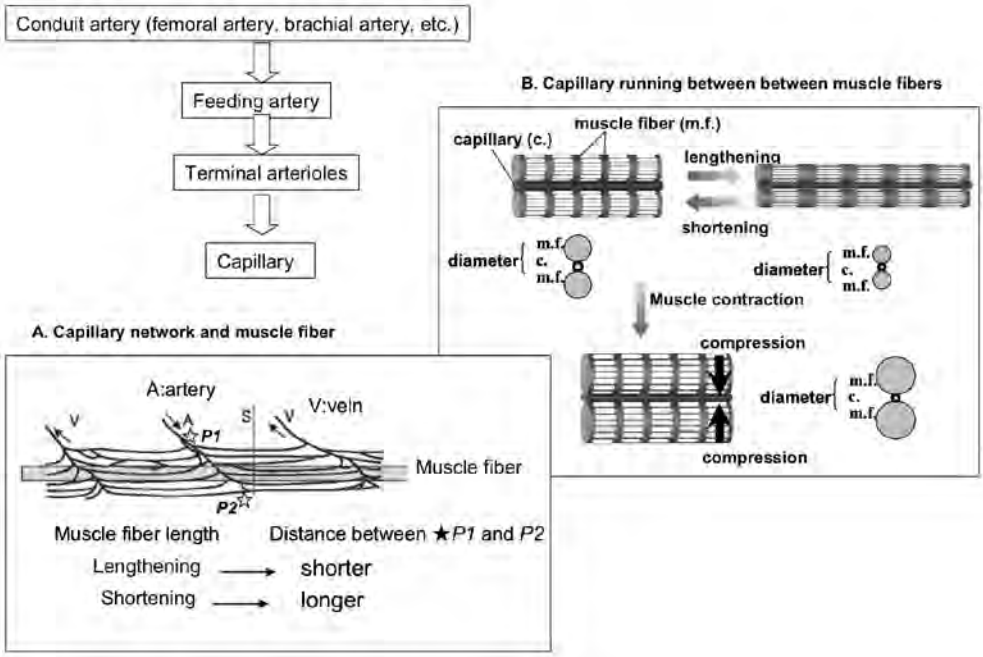

Figure 1 Schematic illustration of vessels and muscle fiber alignment.
Capillaries running away from (A) and running parallel to (B) the long axis of muscle fiber are differently influenced by muscle fiber lengthening. Compression of the capillary between the fibers is illustrated in (B).

Maganaris, et al., 1998, Kanehisa, et al., 2003, Muraoka and Kagaya, 2003) and even within the same muscle (Maganaris, et al., 1998, Muramatsu, et al., 2002a). Thus the question arises as to how the difference in muscle architecture, such as fascicle curvature, fascicle angle, fascicle length, muscle thickness, etc., alters muscle circulation via changes in intramuscular pressure or muscle fiber geometry.

This paper reviews the effects of muscle architecture on muscle circulation and attributes these effects to the changes in capillary geometry and intramuscular pressure. The topics of this review include 1) the effect of muscle fiber length on muscle circulation in resting muscle, 2) the effects of muscle architecture on muscle circulation via intramuscular pressure change, 3) the heterogeneity of muscle circulation depending on muscle architecture, and 4) the effect of muscle architecture on the relationship between venous outflow and vasodilation.

2. Effect of muscle fiber length on muscle circulation

Results from animal studies indicated that the lengthening of muscle fiber reduced muscle blood flow at rest (Supinski, et al., 1986; Poole, et al., 1997) and during exercise (Supinski, et al., 1986). The reduction of blood flow was caused not only by the reduced capillary diameter (Welsh and Segal 1996, Poole, et al., 1997), which resulted in the augmented vessel resistance, but by the enhanced sympathetic nerve activity initiated by muscle lengthening (Welsh and Segal 1996).

However, the capillary diameter and muscle blood flow did not change linearly with increasing muscle fiber length (Supinski, et al., 1986; Poole, et al., 1997). Instead, it changed in a biphasic way (**Figure 2**, Poole, et al.,1997). The capillary lumen diameter of spinotrapezius muscle in rats decreased moderately up to sarcomere lengths of ~2.9 μm and steeply declined as it became longer. The authors suggested that these results were attributable to capillary tortuosity. The moderate increase in sarcomere lengths (up to 2.9 μm) did not influence muscle circulation, because it may only straighten capillary tortuosity, but further increases in sarcomere lengths reduced the capillary diameter and consequently blood flow.

Another effect of change in muscle fiber length is on the geometry of the vascular network in the

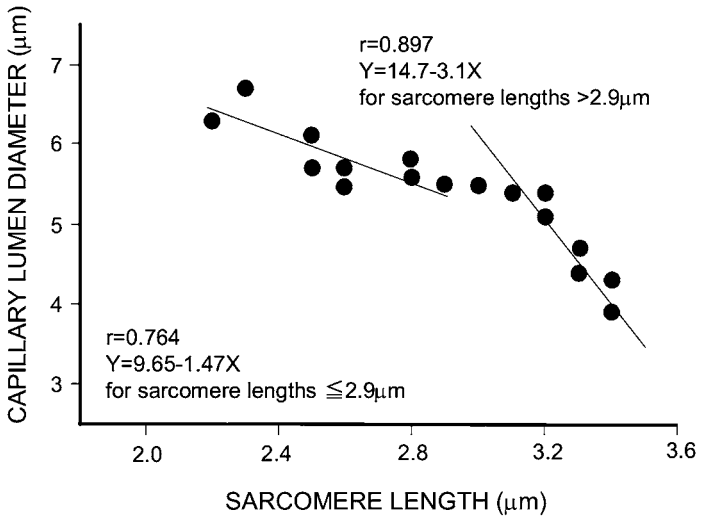

Figure 2 Relationship between sarcomere length and capillary lumen diameter in spinotrapezius sarcomere length in rat (Poole, et al., 1997).
The capillary lumen diameter decreased moderately up to sarcomere lengths of ~2.9 μm and steeply declined as it became longer than this.

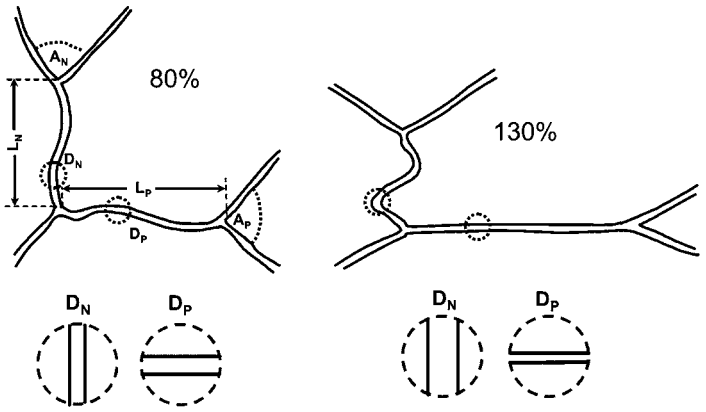

Figure3 Illustration of effect of muscle length on microvessel geometry. (Nakao and Segal 1995)
A schema of the effect of shortened (left, 80% of in vivo resting length) and lengthened (right, 130% of in vivo resting length) muscle fiber length on the vessel geometry and diameter (2 straight lines in the circles DN and DP) are presented. When muscle fiber is lengthened, the vessel oriented parallel to the muscle fiber long axis is lengthened and its diameter is reduced. In contrast, the vessel running in a perpendicular direction is shortened, or the tortuosity and bifurcation angle of the vessel become greater.
D: distance, L:length, A: angle, P:parallel to the muscle fiber, N: normal (perpendicular)

muscle. This effect will depend on the orientation of microvessels to the muscle fibers axis; whether the direction of the capillary long axis is identical or not to the long axis of muscle fiber. A sophisticated investigation by Nakao and Segal (1995) demonstrated how muscle length change would alter the geometry of arterioles and venules in the parallel-fibered retractor muscle of anesthetized male hamsters. When muscle fiber was lengthening, the capillary lumen changes differed between vessels running parallel to muscle fiber axis and those bifurcating away from the muscle fiber long axis (**Figure 3**, Nakao and Segal 1995). Accordingly if muscle fiber was lengthened, the former vessel (paralleled) lumens will become smaller, whereas the latter vessels could become larger. Therefore, the ratio of the number of capillaries running parallel to, and running away from the muscle fiber long axis

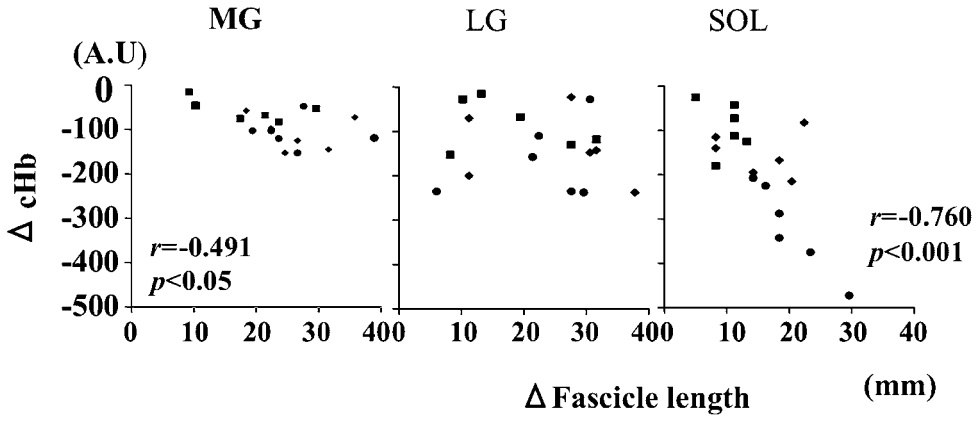

Figure 4 Effect of stretching on muscle blood volume (Yokozawa, et al., 2000)
Ankle joint angles were flexed by 30degrees (■), 60degrees (◆) and to peak range of motion (●).

will have some influence on the sum of the vessel diameters in the whole muscle.

On human subjects, the different relationships between fascicle length and muscle circulation were reported in three heads of calf muscles (Yokozawa, et al., 2002). During passive stretching, Yokozawa, et al. (2002) studied fascicle length and muscle blood volume (total hemoglobin/myoglobin) using NIRS. They found that the blood volume decreased in two (medial gastrocnemius; MG and soleus muscle; SOL) of the three heads of calf muscles (**Figure 4**). However, in the lateral gastrocnemius muscle (LG), no blood volume reduction was detected with increasing muscle fascicle fiber length. The reason speculated is that the stretching used in the study was not enough to lengthen the long fascicle fibers in LG, which had the longest fascicle length of the three heads of gastrocnemius muscles (Kawakami, et al., 1998). Another possibility is that the capillaries in LG may be more tortuous than in MG and SOL and they might be not straightened during stretching used in the study.

3. Effects of muscle architecture on muscle circulation via intramuscular pressure change

This section will firstly deal with how muscle architecture, such as muscle thickness, muscle curvature, etc., modulates intramuscular pressure during muscle contraction, and secondly the difference in muscle circulation due to muscle architecture in synergist muscles.

3.1. Effects of muscle architecture on intramuscular pressur

A study by Sejersted, et al. (1984) demonstrated that contraction force and muscle layer thickness were determinants for intramuscular pressure. They recorded intramuscular fluid pressure in human vastus lateral muscles and showed that the intramuscular pressure increased with the increasing muscle contraction force and with the intramuscular distance (approximately this means the depth of the muscle tissue) from the point where the catheters penetrated the muscle fascia (**Figure 5**). They proposed the following formula for muscles with curvature, which showed that the pressure increased linearly with depth;

$$P=P_0+n\cdot\Delta h\cdot s/r,$$

where P is the increment in tissue pressure, P_0 is the pressure just beneath the fascia, Δh is the thickness, s is stress and r is the radius curvature. The result suggests that the intramuscular fluid pressure increases more in short bulging muscles with great curvature of fibers than in long slender muscles with less curvature (Sejersted, et al., 1984, Van Leeuwen and Spoor 1992).

This suggestion was supported by a study by Naamani, et al. (1995) who showed that the inhibitory effect of muscle contraction on muscle circulation was greater in gastrocnemius muscles compared with diaphragm muscles. They explained this difference by different muscle structure; more cylindrical shaped muscle (gastrocnemius) and a muscle with a flat thin surface diaphragm.

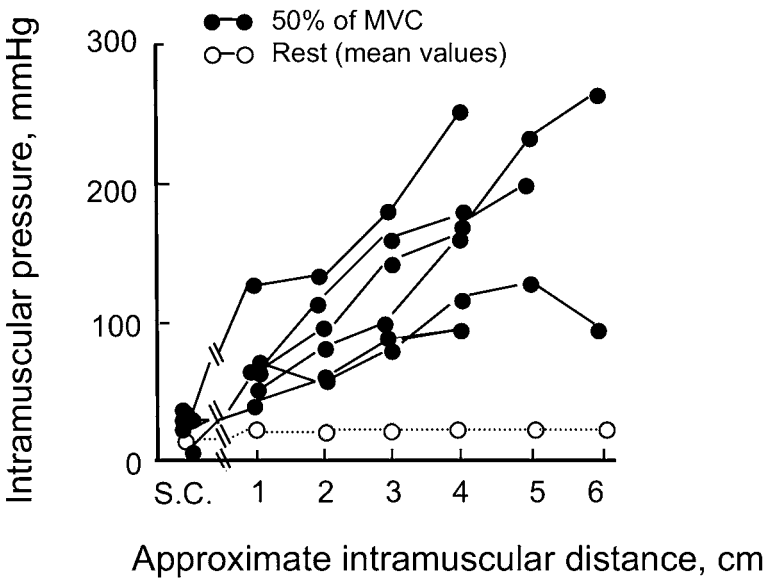

Figure 5 Relationship between intramuscular distance and intramuscular fluid pressure recorded in vastus medialis muscles at rest and during knee extension at 50%MVC (Segersted, et al., 1984).
S.C.; pressure measured in subcutaneous tissue.

Furthermore, in the study of human skeletal muscles using B-mode ultrasonography, the fascicle curvature of the medial gastrocnemius muscle was reported to be positively correlated to pennation angle and muscle thickness during isometric contraction (Muramatsu, et al.,2002b). Pennated muscle has another disadvantage in tension transfer from muscle fiber to the tendon. To induce a given tendon force at the site of the joint, muscle with a larger pennation angle is required to develop higher muscle tension (Gans, et al., 1987), leading to greater intramuscular pressure.

Accordingly, the shape of the muscle, indicated by the pennation angle of the fibers, muscle thickness, muscle fiber length etc., will be the important determinants of changes in intramuscular pressure due to muscle action and the consequent muscle circulatory alteration.

3.2. Muscle circulation difference due to muscle architecture in synergist muscles

Muscle architecture differs among the synergist muscles. Therefore, the effect of muscle action on muscle circulation was hypothesized to differ among muscles with different architecture.

In human skeletal muscles, Kawakami, et al., (1993) and Fukunaga, et al., (1997) developed muscle structure determination from the pennation angle of the muscle-tendon complex. Geometrical difference of the pennated muscle was demonstrated between synergists of calf muscles (Kawakami, et al., 1998).

To assess the effect of inhomogeneous muscle architecture on muscle circulation across synergistic muscles, the total hemoglobin was measured as an indicator of blood volume using near-infrared spectroscopy (NIRS) during static plantar flexion exercise in triceps surae muscles (Muraoka and Kagaya 2003). Blood volume decreased during static action in medial gastrocnemius (MG) and soleus (SOL) muscle and the reduction became greater with increasing force generation (%MVC) (**Figure 6**). However, in lateral gastrocnemius (LG), it did not change notably during static action at lower intensities and, to our surprise, it tended to increase during exercise at higher intensities.

As to muscle architecture, LG has the longest fascicle length, smallest fascicle angle (Kawakami, et al., 1998, Maganaris, et al., 1998, Muraoka and Kagaya 2003). This might lead to the smaller elevation in intramuscular pressure in LG and less blood volume reduction during muscle action. Another possibility for the different behavior in LG might be a lesser contribution to the force generation at the ankle joint. There has been no direct evidence for this, but the study by Kinugasa, et al., (2005)

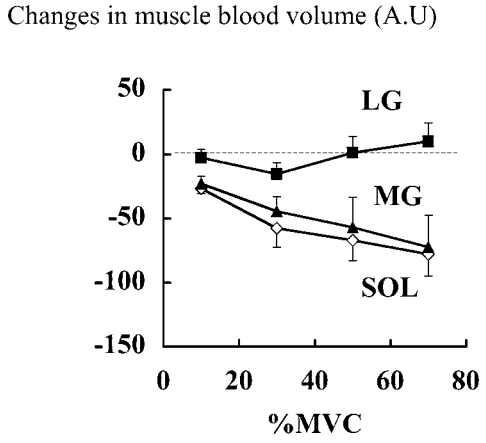

Figure 6 The changes in muscle blood volume in three muscle groups (LG, MG, SOL) during static contraction at different intensities. (Muraoka and Kagaya 2003).

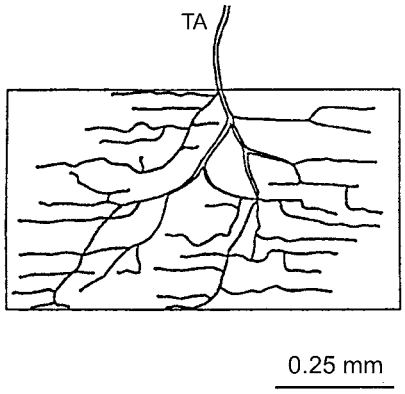

Figure 7 Microvascular unit (MVU) consisting of terminal arteriole and the group of capillaries it supplies (Emerson and Segal 1997)

showed that the activation of the muscles was less (35%) in LG compared to MG (46%). If this finding implies a smaller increase in force in LG than MG with an increase in contraction level, the absence of comparable decrease in blood volume in LG would be attributable to the lower resistance in the artery supplying to LG compared with MG.

However, this explanation was not applicable to different responses in blood volume between LG and SOL because the activation of the SOL was similar to the LG (Kinugasa, et al., 2005). Possibly, different responses in blood volume to a change in the muscle length (Yokozawa, et al., 2002) may be involved

4. Heterogeneity of muscle architecture and circulation within the muscle

As generally accepted, an uneven distribution of muscle fibers rich in capillaries (type I) will cause inhomogeneous blood flow across the whole muscle. There are other aspects of inhomogeneous muscle circulation in the muscle. The first is inhomogeneous muscle architecture. The second is a mismatching of motor unit (MU) and microvascular unit (MVU), which came from a spatial consideration of motor unit and capillary alignment.

The finding that muscle architecture differed among different sites of the same muscle (Maganaris, et al., 1998, Muramatsu, et al., 2002a) will lead to the heterogeneity of muscle circulation or metabolism (Miura, et al., 2001). Miura, et al., (2001) showed that the distal portion of the medial gastrocnemius had larger changes in muscle oxygen saturation and blood volume (measured using NIRS) than the proximal portion had. To elucidate the relationship between muscle architecture and muscle circulation heterogeneity within the same muscles, Miura, et al., (2004) measured architectural properties, oxygen supply, and consumption index in the medial head of the gastrocnemius muscle in vivo using B-mode ultrasound and functional near infrared (NIR) imaging devices. They found that the changes in fascicle length and fascicle angle at the distal portion of the gastrocnemius muscle were greater than those at the proximal portion, and the muscle structural changes were closely related to the changes in the deoxygenated Hb and blood volume. The conclusion was that plantar flexion exercise produced regional differences in oxygenation status consistent with regional differences in muscle architecture.

Spatial considerations of muscle fibers at the single motor unit (MU) level and capillary alignment at the single microvascular unit (MVU) level are interesting from the view point of heterogeneity of muscle circulation. MVU was defined as a terminal arteriole and the group of capillaries it supplies (**Figure 7**) (Emerson and Segal 1997). Each MVU was considerably shorter than the length of skeletal muscle fibers, which means the capillary branching from same MVU is located in a limited region. Furthermore, MVU was not precisely aligned along the muscle fiber(s) (Emerson and Segal 1997), and rather spread to neighboring muscle fiber(s). This finding implies that blood flow cannot selectively

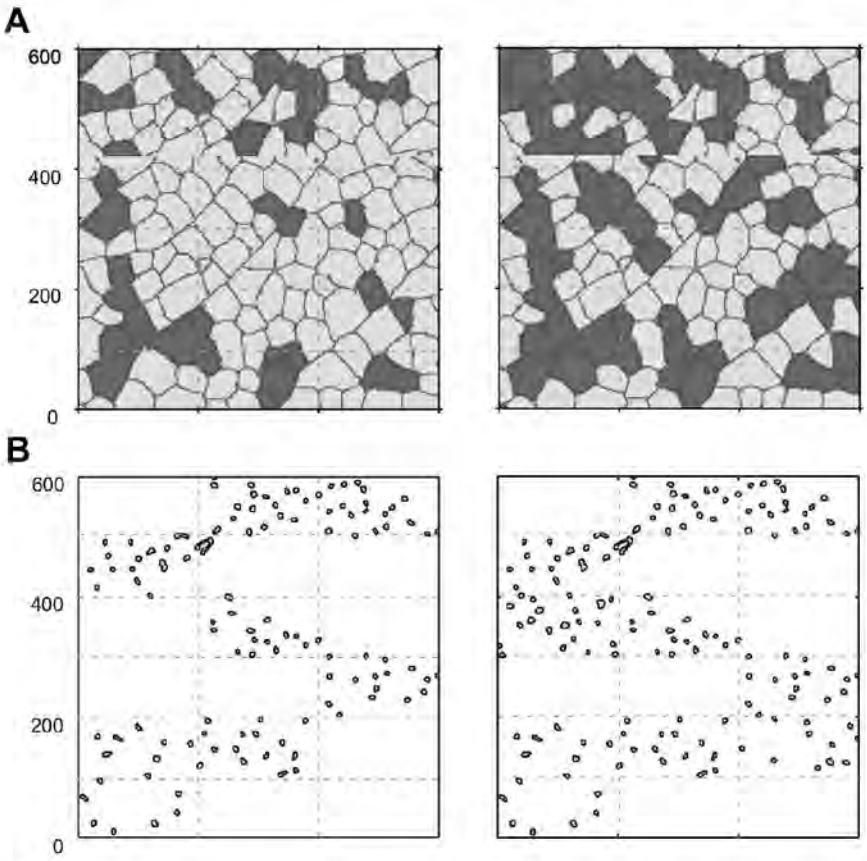

Figure 8 Location of the activated muscle fibers (A) and perfused capillaries (B) at low (left) and high (right) electrical stimulation. The widespread dispersion of motor unit fibers. (Lo, et al., 2003)

increase to a specific muscle fiber or to a particular group of fibers, because whenever any capillary is perfused, all other capillaries in the same MVU are necessarily also perfused (Emerson and Segal 1997, Fuglevand and Segal 1997, Lo, et al., 2003). On the other hand, the muscle fibers belonging to the same MU are distributed diversely within the muscle. Accordingly, a spatial mismatching occurs between perfused capillaries and activated muscle fibers (Lo, et al., 2003) (**Figure 8**). A simulation study by Fuglevand and Segal (1997) demonstrated that the widespread dispersion of MU fibers facilitates complete capillary (MVU) perfusion of muscle at low level activity.

What remains to be shown is whether this spatial mismatching between muscle fiber of the same MU and capillaries of the same MVU differs among different muscles or persons of different physical characteristics.

5. Effect of muscle architecture on the relationship between venous outflow and vasodilation

The finding on blood volume changes in synergist muscles (Muraoka and Kagaya 2003) led us to hypothesize that muscle architecture modifies the muscle pumping effect on circulation. Muraoka and Kagaya (2003) demonstrated that the reduction of blood volume during static plantar flexion was larger in MG and smaller in LG, and the former muscle had a shorter fascicle length and larger fascicle angle than the latter muscle. However, this hypothesis on human subjects has been tested using muscle blood volume changes and no studies directly determined the blood outflow (venous flow) from the muscle due to muscle pump.

Our recent study challenged to estimate the venous outflow at the site of brachial vein when a handgrip exercise was performed (Kagaya, et al.,

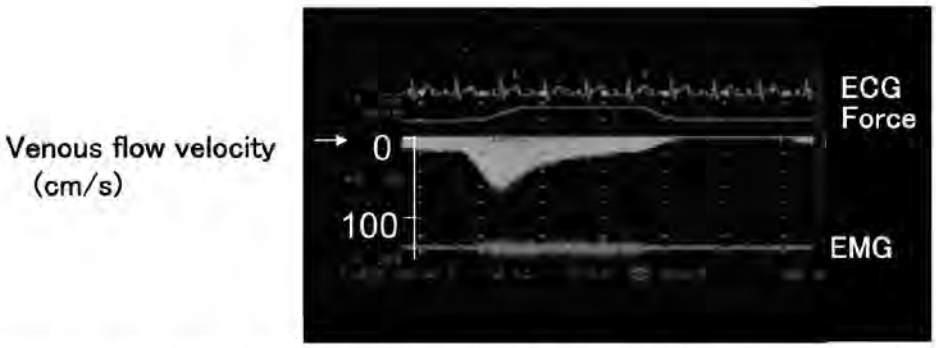

Figure 9 Spectrum of the venous flow velocity in brachial vein at the onset of handgrip exercise. The vertical line s indicates the onset of exercise. The venous blood flow velocity was accelerated immediately after initiation of muscle contraction. (Kagaya, et al., 2003)
ECG, Force, Flow velocity in brachial vein and EMG from forearm flexor muscles are presented from upper to bottom.

2004). **Figure 9** illustrates the spectrum of the venous flow in the vein at the onset of isometric muscle contraction. The venous blood flow velocity was accelerated immediately after initiation of muscle contraction, but thereafter it gradually decreased despite the muscle still contracting at a given force. Therefore, the muscle pump effect was enforced at the very beginning of each contraction.

At the arterial side, the blood flow in the conduit artery was inhibited during the first cardiac cycle at the beginning of isometric muscle contraction when the muscle starts shortening (Kagaya, et al., 2001). This is consistent with a study by Rogers, et al., (1997), which showed the arterial blood flow was inhibited during concentric contraction (shortening) phase. During this phase, the muscle tension was increasing (inhibitory factor), with the muscle fiber shortening (dilatory factor). After the 2nd cardiac cycle, the arterial blood flow was augmented and thereafter remained at a constant level (Kagaya, et al., 2001). Only limited knowledge was obtained as to the coordination of venous and arterial blood flow during exercise.

The next topic we are interested in is the effect of muscle architecture on the relationship between arterial and venous blood flow. However, no evidence has accumulated yet on this topic. Before elucidating this question, the muscle pump effect on vasodilation should be determined, because the results of recent studies are conflicting concerning the effects of muscle pump on vasodilation.

Several studies showed that the muscle pump increased venous emptying and increased the pressure gradient between the artery and vein across the muscle (Shiotani, et al., 2002, Tschakovsky and Hughson 2000, Tschakovsky and Sheriff, 2004). Shiotani, et al., (2002) reported that the muscle pump-dependent venous pressure drop has a potential to increase leg blood flow at least threefold during upright (not in supine position) exercise via the increase in leg perfusion pressure and/or reflex vasodilation in the leg. In contrast, Hamann, et al., (2003) showed that muscle contraction did not give any effect on the maximally vasodilated vasculature by infusing adenosine. Similarly Valic, et al., (2005) concluded in a study using anesthetized dogs that the muscle pump is not a major contributor to the hyperemic response to skeletal muscle contraction.

Considering the effect of muscle structure on intramuscular pressure and muscle blood volume (Muraoka and Kagaya 2003), it is reasonable to suppose that muscle architecture plays an important role in determining venous outflow as well as arterial inflow. Accordingly the balance between arterial blood flow and venous blood flow could be modified due to the difference in muscle architecture. However more information is needed on this topic.

6. Summary

This paper reviews the effects of muscle architecture on muscle circulation with special reference to intramuscular pressure to the vessels and capillary geometry. The subjects discussed in this study were summarized as follows:

1) The lengthening of muscle fiber straightens capillary tortuosity, and further increase in muscle fiber length reduces blood flow by

extending the capillary while reducing its diameter. The direction of the capillary to the fiber long axis will modify the effect of muscle fiber lengthening on the capillary lumen diameter. These relations between the muscle fiber length and capillary geometry may produce heterogeneity in blood circulation across synergistic muscles at rest and during passive stretching.

2) The muscle architecture, such as muscle thickness, muscle curvature, muscle fascicle angle, etc., will change intramuscular pressure, which increases more in short bulging muscle with great curvature of fibers than in long slender muscles with less curvature. These factors of muscle architecture lead to heterogeneous responses in blood circulation across synergistic muscles during contractions.
3) Heterogeneity of muscle circulation was indicated at the distal and proximal portion of the calf muscle. This difference is partly attributable to the difference in the pennation angle of the muscle fascicle. The mismatching/coordination of microvascular unit and motor unit will be an interesting subject to study.
4) Muscle architecture influences venous outflow by changing the muscle pumping action. However, only limited information is available on venous blood flow directly measured on human subjects. The effect of muscle architecture on the relationship between venous outflow and arterial inflow remains to be studied.

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Bilateral prefrontal cortex oxygenation responses to a verbal fluency task: a multichannel time-resolved near-infrared topography study

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Abstract. The letter-fluency task-induced response over the prefrontal cortex is investigated bilaterally on eight subjects using a recently developed compact, eight-channel, time-resolved, near-IR system. The cross-subject mean values of prefrontal cortex oxygen saturation (SO_2) were 68.8±3.2% (right) and 71.0±3.6% (left), and of total hemoglobin concentration (tHb) were 69.6±9.6 μM (right) and 69.5 ±9.9 μM (left). The typical cortical activation response to the cognitive task [characterized by an increase in oxyhemoglobin (O_2Hb) with a concurrent decrease in deoxyhemoglobin (HHb)] at each measurement point is observed in only four subjects. In this subset, the amplitude of the O_2Hb increase and HHb decrease is uniform over each prefrontal cortex area and comparable between the two hemispheres. These findings agree with previous studies using continuous wave functional near-IR spectroscopy and functional magnetic resonance imaging, therefore demonstrating the potential of a time-resolved spectroscopy approach. In addition, a significant increase in SO_2 levels was observed in the right (1.1±0.5%) compared to left side of the prefrontal cortex (0.9±0.5%) (P=0.005). A different pattern of cortical activation (characterized by the lack of HHb decrease or even increased HHb) was observed in the remaining subjects. [DOI: 10.1117/1.1851512]

Keywords: near-infrared spectroscopy; time-resolved spectroscopy; brain; verbal fluency task; cortical activation.

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1 Introduction

Starting almost 27 years ago with the pioneering work of Jobsis,[1] noninvasive near-IR spectroscopy (NIRS) was initially employed to investigate brain oxygenation in neonates and adults both experimentally and clinically, and later to assess muscle oxidative metabolism in pathophysiology (for reviews see Refs. 2–4). In spite of the powerful, high-cost tools for human brain mapping such as positron emission tomography (PET) and functional magnetic resonance imaging (fMRI), since 1993,[5–7] functional NIRS (fNIRS) using a continuous wave (cw) has been largely used to investigate functional activation of the human cerebral cortex (for reviews see Refs. 8–11). fNIRS enables investigation (without discomfort and interference related to the intrinsic limitations of PET and fMRI) of regional changes in oxyhemoglobin (O_2Hb) and deoxyhemoglobin (HHb) concentration in small vessels including capillary, arteriolar, and venular beds of the brain cortex.

The physiological significance of increased O_2Hb and decreased HHb on cortical activation has been extensively investigated in a rat brain model[12] and in humans.[13] O_2Hb is the most sensitive indicator of changes in cerebral blood flow and the direction of the changes in HHb is determined by the degree of venous blood oxygenation and volume. In addition, studies combining either PET or fMRI with fNIRS have demonstrated that changes in oxygenation (reflecting the dynamic balance between oxygen supply and oxygen consumption), measured by fNIRS, correspond to signal intensity increases detected by fMRI (Refs. 14–16) and PET (Refs. 17 and 18).

To date, the most common approach of fNIRS is to measure light attenuation at two wavelengths between a pair of optical fibers set normal to the tissue surface at a known relative distance, to assume a fixed value of the scattering coefficient (μ_s'), and, by applying the Lambert-Beer law, to track the relative concentration changes in HHb and O_2Hb. This rather straightforward technique has been developed over time, resulting in instruments that operate at more wavelengths, with multiple-source and/or multiple-detector geometries. In particular, this latter feature offers the possibility to simultaneously probe different tissue regions to produce functional maps.

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In the last 7 yr, multichannel fNIRS systems have been developed and tested to provide spatial maps[19] (with a spatial resolution of about 0.5 cm) of changes in oxygenation in frontal, temporal, parietal, and visual cortical areas following different stimuli.[20–24] In particular, the prefrontal cortex (the anterior portion of the frontal lobe) and the frontal lobe (the front part of the brain involved in planning, organizing, problem solving, selective attention, etc.), both involved in higher cognitive functions and in the determination of the personality, have been studied using various neuropsychological tests including mental calculation tasks, continuous performance task, Wisconsin Card Sorting task, color-word matching Stroop task, etc.[25–44]

Another cognitive paradigm known to activate the prefrontal cortex is the verbal fluency task (VFT). The VFT is a neuropsycological task that enables assessment of the subject's ability to retrieve nouns based on a common criterion. The letter fluency version is based on a phonological criterion that requires the subject to pronounce as many words as possible beginning with a certain letter. Performances have been regarded to be mainly associated with frontal lobe function, particularly the left hemisphere.[45] During the execution of VFTs, maximum task-induced activation was observed in the left frontal regions, particularly in the left middle prefrontal girus and/or left inferior prefrontal girus using different methods including ^{133}Xe inhalation method,[46] fMRI (Ref. 47), PET (Ref. 48), and single-photon emission computed tomography[49] (SPECT). Some authors,[50–53] using fMRI, have reported task-induced bilateral activation, particularly in the dorsolateral prefrontal and posterior parietal cortex.

To date, few fNIRS data about the prefrontal and frontal lobe involvement during VFT [using one/two-channel cw NIR (NIR_{cw}) systems) are available.[26,30,36,43] The prefrontal cortex of both hemispheres was activated by the VFT, i.e., O_2Hb increased and HHb decreased significantly with respect to the corresponding baselines. Using multichannel fNIRS on both hemispheres, a significant increase in O_2Hb not accompanied by a decrease in HHb was found;[44] conversely, a significant increase in O_2Hb accompanied by a decrease in HHb was found in another study.[38]

The results of these fNIRS studies confirm that the performance of the VFT leads to the activation in specific areas of the prefrontal cortex, without revealing a left lateralized activation. On the other hand, there is no strong evidence that cw fNIRS is sufficiently sensitive to reveal HHb changes, conventionally detected by fMRI.

The key limitations of the cw fNIRS technique are the coupling between the absorption and scattering coefficients (μ_a,μ_s') resulting in the lack of quantitative assessment, sensitivity to artifacts and experimental conditions. A possible way to uncouple μ_a from μ_s' is based on the use of sinusoidally modulated laser sources, and on the measurement of signal phase and amplitude changes induced by propagation. The frequency-domain (FD) technique extracts both the mean μ_s' and μ_a of the probed medium provided that a nontrivial calibration of collection efficiencies is performed. This approach has been successfully applied to measure tissue oxygenation, and has led to the first identification of a rapid change in μ_s' following a cerebral stimulus.[54] The dual approach is the study of photon migration in the time domain and was first introduced *in vivo* by Chance et al.[55] and Delpy et al.[56] Furthermore, the temporal dispersion of a short laser pulse traveling through a diffusive medium can provide both the mean μ_s' and μ_a using a proper model of photon migration. In the past, the cost, size, and complexity of the time-resolved reflectance spectroscopy (TRS) instrumentation have prevented this technique from being effectively employed to study tissue oxygenation.

We have recently reported the development of a compact multichannel TRS tissue oximeter[57] (NIR_{TRS}). This system operates with two wavelengths, two injection points, and eight independent collection points, and has a typical acquisition time of 166 ms. Considering the controversial cw fNIRS results concerning the effects of the VFT on the prefrontal cortex, the aim of this study was to use our eight-channel NIR_{TRS} system to further investigate bilateral effects of the VFT-induced response within the prefrontal cortex.

2 Methods

2.1 *System Setup*

A compact two-source eight-channel NIR_{TRS} system was employed in this study. A pair of semiconductor pulsed lasers (PDL, Picoquant, Germany), working at 685 and 780 nm, with an 80-MHz repetition rate and a 1-mW average power, were used as light sources. Multimode graded-index fibers (50/125 μm) of different lengths and a fiber optics integrated device (VIS/NIR 2×2 fused splitter, OZ Optics, Canada) were used to multiplex in time the output pulses of the two laser heads so as to create two independent injection points. A compact 16-anode photomultiplier (R5900-01-L16, Hamamatsu, Japan) integrated with a 16-channel router (PML-16, Becker&Hickl, Germany) and a PC board (SPC-630, Becker&Hickl, Germany), for time-correlated single-photon counting (TCSPC), were used to detect and acquire time-resolved reflectance curves. Due to 20% optical crosstalk among adjacent channels, only 8 out of 16 channels were used by placing optical fiber on odd channels (1,3,5,...,15). In this configuration, the crosstalk was lower than 3%. The typical measurement time for the parallel acquisition of time-resolved curves from the 8 channels was 166 ms (6 Hz). A detailed description of the system is reported elsewhere.[57] In the most severe configuration for TCSPC, the maximum count rate should not exceed 8×10^5 photons/s (i.e., 0.01 photons detected per signal period with a 80-MHz repetition rate laser). Furthermore, the TCSPC board we employed in this study had 125-ns dead time (equivalent to a maximum acquisition frequency of 8 MHz) and a minimum acquisition time of 0.1 ms. Taking into account that the typical count rate from biological tissues is less than 10^6 photons/s, the combination of the lasers and the TCSPC board sets no practical limits to the detection of photons in TRS.

2.2 *Data Analysis*

Simultaneous estimation of μ_s' and μ_a can be achieved by best fitting time-resolved reflectance curves with a standard model of diffusion theory.[58] Therefore, to reduce dispersion of the fitted absorption coefficient values, we employed the modified Lambert-Beer law.[59] First, for each wavelength, a reference time-resolved reflectance curve $R_0(\rho,t,\lambda)$ was derived by averaging the curves corresponding to an initial rest-

ing period (typically 0.5 min). Fitting of $R_0(\rho,t,\lambda)$ yielded a reference absorption value $\mu_{a0}(\lambda)$, then $\Delta\mu_a(\lambda)$, the variation from the reference value, was derived according to

$$\mu_a(\lambda)=\mu_{a0}(\lambda)+\Delta\mu_a(\lambda), \quad (1)$$

$$\Delta\mu_a(\lambda)=-\frac{1}{vt}\ln\left[\frac{R(\rho,t,\lambda)}{R_0(\rho,t,\lambda)}\right]. \quad (2)$$

Improvement over the standard methods was more effective when the absorption was high. In this condition, standard fitting with the nonlinear least-squares methods yielded high dispersion in the fitted data.[60] A fitting range from 80% of the peak of TRS curve in the leading edge and 1% in the trailing edge of the TRS curve was chosen to estimate $\mu_{a0}(\lambda)$. For the estimation of $\Delta\mu_a(\lambda)$ from Eq. (2), the fitting range was 70 to 1% of both limits in the trailing edge, so as to enhance the contribution of late photons rather than early photons.

Assuming that O_2Hb and HHb are the major chromophores that contribute to tissue absorption, their respective concentrations are easily derived using the extinction coefficient.[61] Indeed water absorption in this spectral region is much lower than hemoglobin absorption.[61] A constant absorption (30%) was attributed to water and subtracted from μ_a prior to calculation of HHb and O_2Hb concentration. The total hemoglobin concentration ($tHb=O_2Hb+HHb$) and tissue oxygen saturation ($SO_2=O_2Hb/tHb$, in percent) could then be derived.

During data analysis an integration time of 1 s was used to increase the SNR. This operation consisted in summing six time-resolved reflectance curves, each of which was acquired with a measurement time of 166 ms. After fitting the time-resolved reflectance curves, a 5-s average was applied to the data (i.e., data in Figs. 2 to 5 in Sec. 3 are represented with an effective sampling time of 5 s). Note that TCSPC uncertainty (i.e., the standard deviation over the average) in the estimation of μ_a is dramatically reduced when sampling time is augmented (either directly by incrementing the acquisition time, or indirectly by summing up several time-resolved reflectance curves acquired with a shorter acquisition time) since the total number of photons per curve is increased.

2.3 *Subjects*

Eight normal, right-handed, healthy volunteers (34.6±8.7 yr) participated in this study. Informed consent was obtained from each subject after a full explanation of the nature of the procedure to be used and the noninvasiveness of the study. Throughout the study, subjects were lying on a comfortable bed in a quiet room. Right-handedness was evaluated by the Edinburgh Inventory of Handedness.[62] Cardiac frequency was monitored by a pulse oximeter (N-200; Nellcor, Puritan Bennett, St. Louis, Missouri) with the sensor attached to the index finger of the right hand. The heart rate did not vary between the pretask and the task periods in all subjects (data not shown).

2.4 *Verbal Fluency*

A 2-min letter version of the VFT was adopted in this study.[30] Following a 2-min baseline (with eyes closed), subjects (preliminarily instructed properly) were asked to produce (overt speech) as many nouns as possible beginning with the letters "S," "P," "F," and "C". Each letter was acoustically presented every 30 s. No repetitions or proper nouns were permitted. Correct verbal responses were recorded for each subject. As a control task, subjects were requested to listen to a 2-min story.

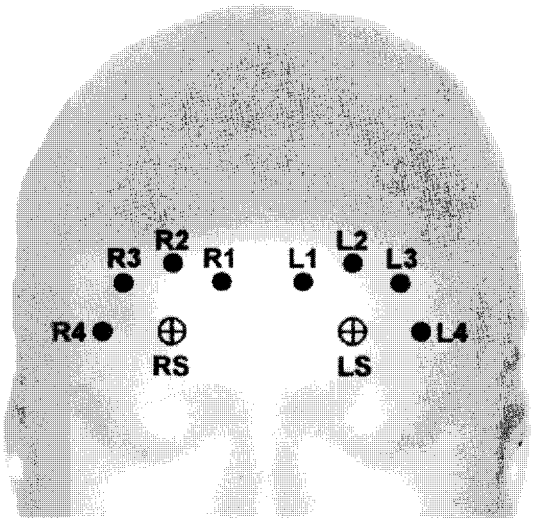

Fig. 1 Schematic representation of the optical probe and the eight measurement sites over the prefrontal lobe. The optical probes were centered at the Fp1 and Fp2 (according to the international 10–20 system for the EEG electrode placement) for the left (L) and right (R) sides (LS and RS), respectively. The source-detector distance was 3 cm.

The optical probe was placed over the head to cover the underlying prefrontal cortex and was centered (according to the international 10–20 system for the EEG electrode placement) at the Fp1 and Fp2 for left and right sides, respectively (Fig. 1). The frontal sinuses are located slightly below the lines between Fp1/Fp2. Only in some cases, the lines overlap the upper edge of the sinus. Therefore, the influence of the frontal sinuses on the NIRS measurements was considered negligible. The source-detector distance was 3 cm. No downward sliding of the fiber holders was observed at the end of the measurements in any subject.

Custom-made fibers holders were designed to keep fibers normally to the forehead by black plastic hollow tubes. Holders were kept in place on the head of the subject by biadhesive tape. The minimum distance between the light source located on the left (right) forehead and detectors placed over the right (left) forehead was 5 cm, to avoid crosstalk between optical signals detected simultaneously in the two areas.

2.5 *Statistics*

Changes (Δ) in SO_2, tHb, O_2Hb, and HHb measured on the prefrontal cortex during the VFT were calculated by the difference between the rest condition (mean value over the 1.5- to 2-min baseline) and the end of the VFT (mean value over the last 30 s). The means and standard deviations of SO_2, tHb, O_2Hb, and HHb values within left and right prefrontal cortex were determined separately and compared.

Statistics evaluation was carried out using the SPSS PC version 12.0 program (SPSS, Inc., Chicago, Illinois). Three-way repeated measures analysis of variance (RMANOVA) was applied to SO_2, O_2Hb, HHb, and tHb as a dependent variable, with factors of side ($df=1$, left and right), measurement point ($df=7$), and condition ($df=1$). All three factors as well as two-way and three-way interactions among factors were included in the model.

When there was a significant main effect or interaction, we performed the RM ANOVA. Significant differences were identified using the Tukey's honestly significant difference multiple comparison test. The paired t test was used to compare the SO_2, tHb, O_2Hb, and HHb values corresponding to each pair of left and right prefrontal cortex positions. The criterion for significance was $P<0.05$.

3 Results

The absolute values (average over the 1.5- to 2-min baseline) of SO_2, O_2Hb, HHb, and tHb for each subject are reported in Table 1. The baseline values (grand average over the eight subjects) of O_2Hb, HHb, and tHb were homogeneous over the right prefrontal area. Some differences were found among the measurement points within the left hemisphere. Grand average SO_2 values of the most lateral measurement points (R4 and L4) were relatively lower than remaining ipsilateral values. Comparing paired measurements points (grand average values) in both hemispheres (R1 versus L1, R2 versus L2, etc.), no difference was found in O_2Hb, HHb, and tHb between left and right sides. Considering the grand average of SO_2 values, only L3 and L4 significantly differed from corresponding contralateral measurement points ($P=0.01$).

During the VFT, the subjects achieved a mean of 33.5 $\pm$10.3 number of correct responses for the four letters, showing similar performances in each of the four letter conditions (S=7.9$\pm$2.4, P=8.6$\pm$3.3, F=8.6$\pm$2.6, C=8.4$\pm$2.6).

The response in terms of prefrontal cortical oxygenation (measured as ΔO_2Hb, ΔHHb, and ΔtHb) to the VFT was variable amongst the subjects investigated. In particular, a typical prefrontal cortex activation response (measured indirectly by fNIRS) upon the VFT was[30] observed only in four (subjects: A, B, C, D) out of the seven subjects (one subjects was excluded from the data analysis due to motion artifacts during the task). Figure 2 shows a single individual (subject A) as a representative of a typical prefrontal cortex ΔO_2Hb, ΔHHb, and ΔtHb response. In this subject, O_2Hb started to increase at the beginning of the VFT to reach a maximum change within the VFT, and it decreased progressively after the end of the task. Concomitantly, HHb decreased (not specularly) during the VFT, and it did not return to the pretask value within the observation time. The amplitude of the O_2Hb increase and HHb decrease was not uniform over the four measurement points within the right or the left side. The corresponding change in SO_2 is also reported in Fig. 2.

The larger increase of SO_2 and O_2Hb in the right compared to left hemisphere (Fig. 2) was no more evident when the response at each measurement site was averaged over the four subjects (A to D) (Fig. 3).

A significant VFT-mediated effect was found in SO_2 ($P<0.001$), HHb ($P<0.0001$), O_2Hb ($P<0.001$), and tHb ($P<0.05$) changes. A significant hemisphere-associated effect was also observed in both SO_2 ($P<0.05$) and HHb ($P<0.01$), but not in O_2Hb and tHb changes. No significant influence of the measurement point factor on fNIRS parameters was found. In addition, no interaction was found between the three factors considered (task, hemispheres, and eight measurement points).

The time course of the grand average over the four subjects of each measured parameter (average of the responses over the four measurement points in the left or right side) is shown in Fig. 4.

The pattern of the O_2Hb, HHb, tHb, and SO_2 response to the VFT was variable among the three remaining subjects, with none comparable to that displayed in Figs. 2 and 3. In these subjects, an increase in SO_2, O_2Hb, and tHb was observed during the task. Concomitantly, HHb decreased very rarely and, in most of the cases, did not change or increased at some measurement points. Furthermore, the O_2Hb, tHb, and SO_2 amplitude increase was not homogeneous over each side of the prefrontal cortex within the same subject. Figure 5 shows an individual (subject F) as a representative of an atypical ΔO_2Hb, ΔHHb, and ΔtHb response over the prefrontal area. Interestingly these three subjects (E, F, and G) had the same VFT performances as the others.

In all subjects, O_2Hb, HHb, tHb, and SO_2 tracings over the 2-min control task were not different from the corresponding baseline tracings.

4 Discussion

Verbal fluency tasks are designed to evaluate the spontaneous production of words beginning with a given letter (letter fluency; syntactic or phonetic association) or words beginning to a given class (category fluency; semantic association), within a limited amount of time.[45] These letter and category fluency paradigms (with a differential brain activation pattern) are frequently used in the assessment of patients with suspected prefrontal disorders. Deficits in word retrieval are probably the most serious impediment to effective communication in aphasics. Therefore, it is particularly important to identify which verbal fluency mechanisms can recover. Regional brain activity during phonological and semantic processing has been studied using fMRI, PET, SPECT, and transcranial Doppler sonography. During the execution of the VFT, maximum task-induced activation was observed in the left frontal regions particularly in the left middle prefrontal girus and/or left inferior prefrontal girus by different methods/techniques such as ^{133}Xe inhalation method,[46] fMRI (Ref. 47), PET (Ref. 48), and SPECT (Ref. 49). Some authors,[50–53] using fMRI, have reported task-induced bilateral activation, particularly on the dorsolateral prefrontal and posterior parietal cortex. However, the category fluency task, and not the letter fluency task, has been reported to provoke a bilateral prefrontal activation response using[63] SPECT.

A recent study[64] evaluating whether VFT may specifically induce relatively greater left- than right-hemispheric activation in the dorsolateral prefrontal cortex has demonstrated that the desired effect could be achieved only in individuals with good performances on the VFT and not by poor performers who showed marked right-hemispheric activation. A significant bilateral blood flow velocity increase in the middle cerebral arteries was observed in response to 13 verbal and visu-

Table 1 Right (R) and left (L) prefrontal cortex SO_2, tHb, HHb, and O_2Hb at the eight measurement points.

Subject	Parameter	R1	R2	R3	R4	L1	L2	L3	L4
A	SO_2(%)	71.6(0.5)	73.9(0.5)	71.9(0.4)	69.4(0.5)	74.2(0.2)	73.0(0.3)	73.2(0.3)	72.7(0.4)
	tHb (μM)	80.3(0.8)	72.3(0.7)	55.6(0.4)	63.4(0.5)	69.3(0.3)	59.2(0.3)	51.2(0.3)	64.5(0.4)
	HHb (μM)	22.9(0.3)	18.8(0.2)	15.6(0.1)	19.4(0.2)	17.9(0.1)	16.0(0.2)	13.7(0.1)	17.6(0.2)
	O_2Hb (μM)	57.5(0.9)	53.4(0.9)	40.0(0.5)	44.0(0.6)	51.4(0.3)	43.2(0.4)	37.5(0.3)	46.9(0.5)
B	SO_2(%)	73.7(0.3)	72.4(0.3)	68.0(0.5)	65.1(0.7)	75.6(0.3)	73.1(0.3)	74.3(0.3)	73.0(0.4)
	tHb (μM)	90.6(0.6)	86.4(0.6)	84.0(0.8)	82.6(0.9)	90.6(0.5)	83.1(0.4)	76.7(0.3)	82.7(0.5)
	HHb (μM)	23.8(0.2)	23.8(0.2)	26.9(0.3)	28.8(0.4)	22.1(0.2)	22.3(0.2)	19.7(0.2)	22.3(0.3)
	O_2Hb (μM)	66.8(0.6)	62.6(0.6)	57.2(0.8)	53.8(1.1)	68.5(0.6)	60.8(0.5)	56.9(0.4)	60.4(0.6)
C	SO_2(%)	69.2(0.3)	69.8(0.5)	68.4(0.4)	69.0(0.6)	71.0(0.3)	69.1(0.3)	70.6(0.3)	69.7(0.5)
	tHb (μM)	85.0(0.5)	77.3(0.6)	72.7(0.5)	72.7(0.7)	83.5(0.3)	77.6(0.5)	73.1(0.3)	71.6(0.4)
	HHb (μM)	26.2(0.2)	23.4(0.3)	23.0(0.2)	22.5(0.3)	24.2(0.2)	24.0(0.2)	21.5(0.2)	21.7(0.3)
	O_2Hb (μM)	58.8(0.5)	53.9(0.8)	49.8(0.5)	50.2(0.8)	59.2(0.4)	53.7(0.5)	51.6(0.4)	49.9(0.6)
D	SO_2(%)	67.5(0.6)	67.3(0.6)	63.5(0.5)	63.3(0.6)	68.7(0.3)	72.8(0.5)	69.4(1.0)	68.8(0.6)
	tHb (μM)	60.9(0.5)	67.6(0.6)	60.4(0.4)	64.5(0.6)	53.4(0.3)	62.9(0.4)	50.5(0.6)	53.8(0.4)
	HHb (μM)	19.8(0.3)	22.1(0.3)	22.1(0.3)	23.5(0.3)	16.7(0.1)	17.1(0.3)	15.4(0.4)	18.9(0.2)
	O_2Hb (μM)	41.1(0.7)	45.5(0.7)	38.4(0.5)	38.1(0.7)	36.7(0.3)	45.8(0.5)	35.0(0.8)	34.8(0.6)
E	SO_2(%)	61.6(0.7)	71.1(0.7)	67.6(0.7)	63.4(0.8)	69.2(0.4)	69.8(0.6)	70.3(0.5)	66.6(0.6)
	tHb (μM)	55.2(0.7)	60.3(1.0)	53.0(0.7)	58.1(0.9)	64.6(0.8)	61.7(1.0)	58.2(0.7)	65.7(1.3)
	HHb (μM)	21.2(0.3)	17.4(0.3)	17.2(0.3)	21.3(0.4)	19.9(0.2)	18.6(0.2)	17.3(0.2)	21.9(0.3)
	O_2Hb (μM)	34.0(0.7)	42.9(1.0)	35.8(0.8)	36.9(1.0)	44.8(0.8)	43.1(1.0)	40.9(0.8)	43.8(1.2)
F	SO_2(%)	72.0(0.3)	74.9(0.4)	75.3(0.4)	76.0(0.4)	79.1(0.3)	77.4(0.4)	76.4(0.3)	76.6(0.4)
	tHb (μM)	44.0(0.3)	63.4(0.6)	65.2(0.7)	69.5(0.6)	58.6(0.4)	70.3(0.4)	63.1(0.3)	72.3(0.5)
	HHb (μM)	12.3(0.1)	15.9(0.1)	16.1(0.2)	16.7(0.2)	12.2(0.1)	15.9(0.2)	14.9(0.1)	16.9(0.2)
	O_2Hb (μM)	31.7(0.4)	47.5(0.6)	49.1(0.8)	52.8(0.7)	46.4(0.5)	54.4(0.6)	48.2(0.3)	55.4(0.6)
G	SO_2(%)	68.7(0.4)	69.2(0.4)	67.4(0.4)	62.5(0.5)	68.5(0.4)	67.4(0.5)	68.5(0.5)	66.4(0.4)
	tHb (μM)	77.4(0.5)	76.5(0.5)	73.1(0.4)	76.7(0.6)	81.1(0.4)	78.6(0.6)	77.8(0.4)	83.8(0.5)
	HHb (μM)	24.2(0.2)	23.6(0.2)	23.8(0.2)	28.7(0.2)	25.6(0.3)	25.6(0.3)	24.5(0.3)	28.1(0.3)
	O_2Hb (μM)	53.2(0.6)	53.0(0.6)	49.3(0.5)	47.9(0.7)	55.5(0.5)	53.0(0.7)	53.3(0.6)	55.7(0.6)

ospatial tasks by using transcranial Doppler sonography.[65] Five verbal tasks showed a significant left-hemispheric lateralization that can best be elicited by linguistic tasks that require active or creative processing of the verbal material such as constructing a sentence with given words or retrieving words. The bilateral increase of blood flow velocity in the middle cerebral arteries on VFT is consistent with the increase of O_2Hb observed during VFT in this study by NIR_{TRS} and in other studies using a one-/two-channel NIR_{cw} systems[26,30,36,43] and by multichannel NIR_{cw} systems.[38,44] Although the increase of O_2Hb on VFT is usually accompanied by a smaller decrease in HHb, in our study, this pattern was not observed in three out of the seven subjects. For this reason the oxygenation response to VFT was averaged over four subjects only (Figs. 3 and 4). However, the letter version of the VFT adopted in our study and the recorded number of correct verbal responses were comparable to those reported in a recent study.[30]

Table 1 (*Continued.*)

Subject	Parameter	R1	R2	R3	R4	L1	L2	L3	L4
H	SO_2(%)	66.9(0.4)	69.2(0.3)	67.1(0.4)	64.9(0.6)	65.9(0.3)	68.0(0.4)	67.6(0.3)	65.0(0.4)
	tHb (μM)	70.1(0.5)	67.0(0.4)	69.4(0.5)	72.8(0.8)	75.1(0.5)	68.9(0.5)	68.2(0.4)	71.8(0.4)
	HHb (μM)	23.2(0.2)	20.6(0.2)	22.8(0.2)	25.6(0.3)	25.6(0.2)	22.0(0.2)	22.1(0.2)	25.2(0.2)
	O_2Hb (μM)	46.9(0.6)	46.4(0.5)	46.6(0.6)	47.2(0.9)	49.4(0.5)	46.9(0.6)	46.1(0.4)	46.6(0.5)
Grand average	SO_2(%)	68.9±3.8	71.0±2.6	68.7±3.5	66.7±4.6*	71.5±4.4	71.3±3.4	71.3±3.1^	69.9±4.0°^
	tHb (μM)	70.4±16.0	71.4±8.5	66.7±10.3	70.0±7.9	72.0±12.9	70.3±8.8	64.9±10.9°	70.8±9.8
	HHb (μM)	21.7±4.3	20.7±3.0	20.9±4.1	23.3±4.3	20.5±4.8	20.2±3.8	18.6±3.9°	21.6±3.8
	O_2Hb (μM)	48.8±12.5	50.7±6.3	45.7±7.2	46.4±6.3	51.5±9.7	50.1±6.3	46.2±7.8°	49.2±8.1

The site number referred to is in Fig. 1.
The numbers in parenthesis represent the SD of the mean values of each fNIRS parameter over the corresponding 1.5- to 2-min baseline.
Grand average data are presented as means±SD.
$N=8$.
*Significantly different from *R2* ($P<0.01$).
°Significantly different from L1 ($P<0.05$).
^Significantly different from the corresponding contralateral one ($P=0.01$).

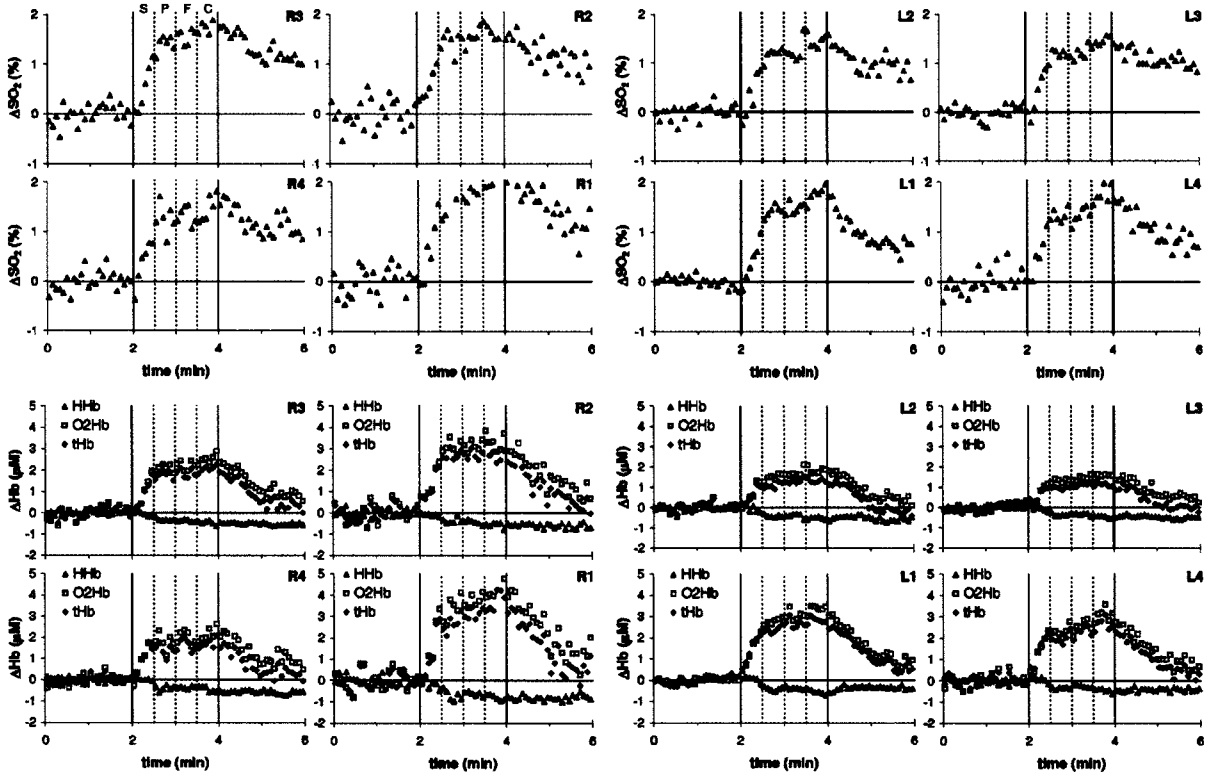

Fig. 2 Typical topographic presentation of the time courses of ΔSO_2, ΔO_2Hb, ΔHHb, and ΔtHb on VFT over eight measurement sites on the right (R) and left (L) prefrontal cortex (subject A). Arrangement of results resembles the measurement positions in Fig. 1. Continuous vertical lines indicate total duration of the VFT, which is in turn subdivided by the three dotted vertical lines in four intervals. Each interval represents the allocated time for each subject to produce as many nouns as possible beginning with the corresponding reported letter (upper left panel).

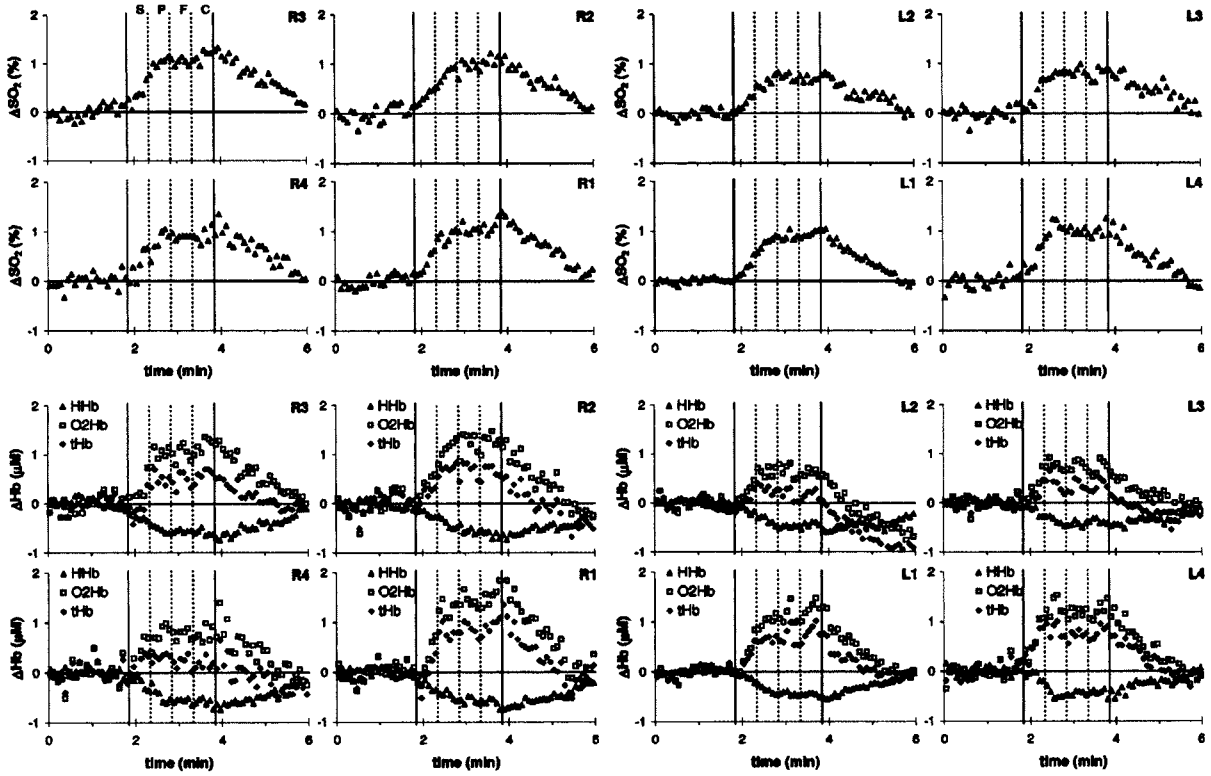

Fig. 3 Topographic presentation of the time courses of ΔSO_2, ΔO_2Hb, ΔHHb, and ΔtHb on VFT over eight measurement sites on the right (R) and left (L) prefrontal cortex. Arrangement of results resembles measurement positions in Fig. 1, expressed as the average over four subjects. Continuous vertical lines indicate total duration of the VFT, which is in turn subdivided by the three dotted vertical lines in four intervals. Each interval represents the allocated time for each subject to produce as many nouns as possible beginning with the corresponding reported letter (upper left panel).

With respect to the amplitude of the cortical activation response between hemispheres, taking into account intersubjects variability, only SO_2 increase during VFT was significantly higher in right ($1.1 \pm 0.5\%$) compared to left prefrontal cortex ($0.9 \pm 0.5\%$) ($P = 0.005$). The VFT-related change in the remaining measured parameters (O_2Hb, HHb, and tHb, as reported by other groups[30,38]) is superimposable over both left and right sides of the prefrontal cortex (Fig. 4). Our results confirm that, in some cases, the oxygenation response to the VFT is bilateral and symmetrical. Recently, hemodynamic differences in the activation of the prefrontal cortex during VFT and attention tasks (letter cancellation and continuous performance test) have been investigated using[43] a two-channel NIRS. While O_2Hb bilaterally increased with a concurrent decrease in HHb during the VFT, both O_2Hb and HHb bilaterally increased during the activation due to the task of attention. It was suggested that HHb measurement may therefore provide an objective index of the subjective effort to pay attention. The impairment of prefrontal lobe functions has been repeatedly documented in major psychiatric disorders, with O_2Hb increases during VFT significantly lower in association with major depressive disorders and bipolar disorders.[36] This result is not explained by differences of performance, since no difference in the number of words answered was found among these three groups. In addition, no significant difference of HHb response was found.[36]

The different cortical activation pattern observed in three out of the seven subjects, characterized by a lack of HHb decrease or even an HHb increase during the VFT (Fig. 5) may be partly explained by the involvement of additional mechanisms (i.e., of attention, association, etc.) besides the specific ones for the letter fluency task. In this manner, other cortical areas (not under investigation) could have been concomitantly activated and/or the oxygen consumption in the investigated area could have been higher[43] than that one observed in the subjects with an activation response characterized by a marked increase in O_2Hb and tHb, and a decrease in HHb. This latter cortical response (found in four out of the seven subjects), defined as the typical one, is interpreted as a mismatch between a major increase in the regional cerebral blood flow (and blood volume) and a minor increase in oxygen consumption over the activated cortical area.[66] On the other hand, the constant level of HHb (found in most measurement points of three out the seven subjects) could have resulted from an increase in the regional cerebral metabolic rate for oxygen, compensated by an increase in the regional cerebral blood flow. Therefore, the increase in HHb (found in some measurement points of three out of the seven subjects) may result from a further increase in oxygen consumption with a consequent mismatch between blood flow increase and oxygen consumption increase this time in favor of the latter one.

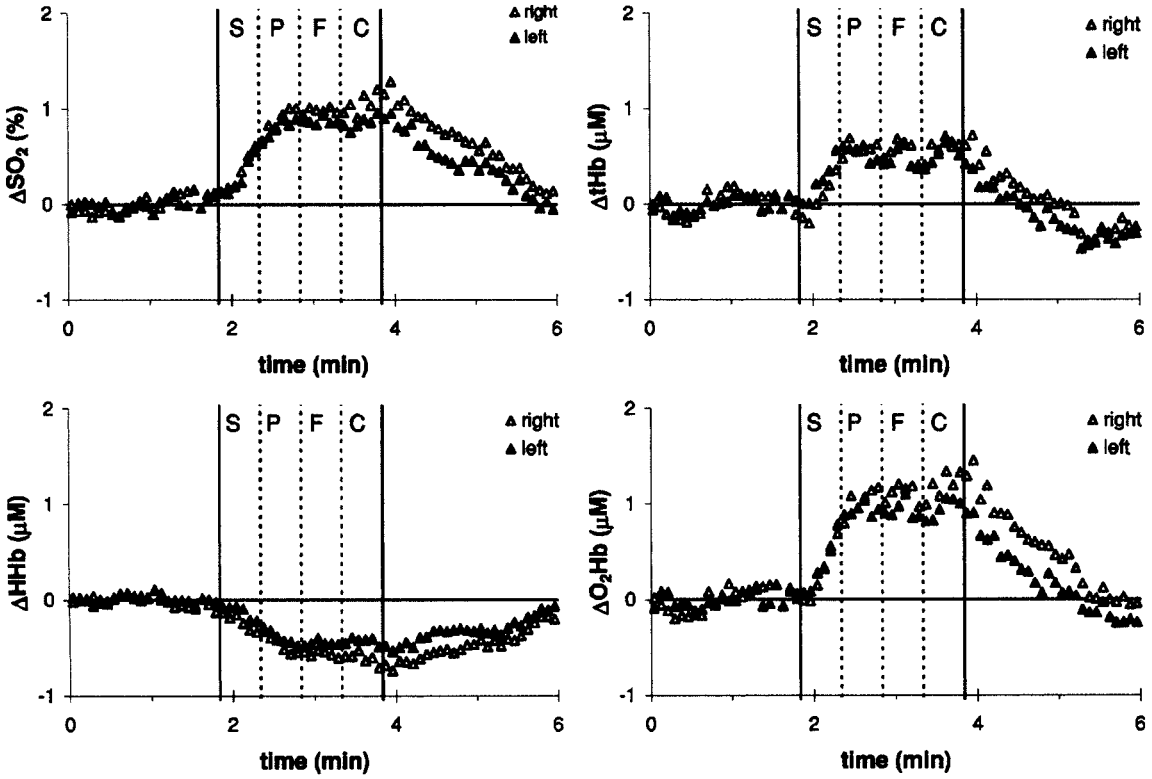

Fig. 4 Grand average over the four subjects of the time course of ΔSO_2, ΔO_2Hb, ΔHHb, and ΔtHb on the VFT. For each subject, the response of each parameter to VFT is reported as the mean of the responses of four measurement points on the right or the left prefrontal cortex. Continuous vertical lines indicate total duration of the VFT, which is in turn subdivided by the three dotted vertical lines in four intervals. Each interval represents the allocated time for each subject to produce as many nouns as possible beginning with the corresponding reported letter (upper left panel).

The lack of HHb decrease may be also explained by the decrease in blood flow velocity probably due to the increased resistance of the capillary venous wind kessel. Indeed, HHb is washed out of the activated cortical area faster than it is generated (typical response), as demonstrated by the increase in blood flow velocity.[65] Another possible reason of a lack of HHb decrease could be the diverse neuroanatomy of the three subjects with respect to the others. Since, in this study the fNIRS measurements were not combined with those from MRI or computed tomography (CT), and/or fMRI, PET, transcranial Doppler sonography, and angiography, it is difficult to provide a concrete interpretation of HHb behavior in the three anomalous subjects (E, F, and G).

In this study, no significant heart rate changes were found during the VFT. Therefore, during the VFT, SO_2, O_2Hb, and HHb changes observed at each measurement point were task-related responses and not the consequence of a generalized increase in cerebral blood flow, as would be expected in the case of an increased heart rate.[22]

A brief summary of current NIRS instrumentation for muscle and brain studies can be found elsewhere.[57] A detailed review on technological advantages/disadvantages of cw, FD, and TRS instrumentation in fNIRS studies has been reported previously.[11] Here, we focus on the advantages and/or disadvantages of using fNIRS in cognitive studies over other functional imaging techniques. First, it is possible to independently quantitate temporal changes in O_2Hb, HHb, and tHb. Furthermore, if TRS or FD are employed, SO_2 can also be estimated, providing a further indicator of brain activation. Second, there is no noise associated with fNIRS measurement techniques, whereas noise associated with fMRI could interfere with auditory stimuli and subject attention levels. Third, a high SNR enables the observation of changes in oxygenation even in response to a single trial, as previously shown.[67] Fourth, fNIRS has fewer artifacts due to head motion than fMRI. Fifth, fNIRS makes it possible to detect overt verbal responses that may provoke artifacts in fMRI. Sixth, fNIRS has a high temporal resolution together with the unique advantage of being compact and transportable, enabling measurements in a natural environment. Conditions under which tests are performed using fMRI or PET do not fit classical neuropsychological test conditions, i.e., sitting at a table or in front of a computer screen in a quite room.

On the other hand, fNIRS measurements are restricted mainly to the cortical surface, the spatial accuracy during focal hemodynamic changes is limited due to the effect of light diffusion and the contribution of extracranial artifacts should be carefully evaluated.[68] A recent study, performed on 17 subjects, has demonstrated that in Fp1 the depth of the cortical surface from the skin is[69] 13.5 ± 2.2 mm. This means that the optical path length differs among individuals by about 5 mm.

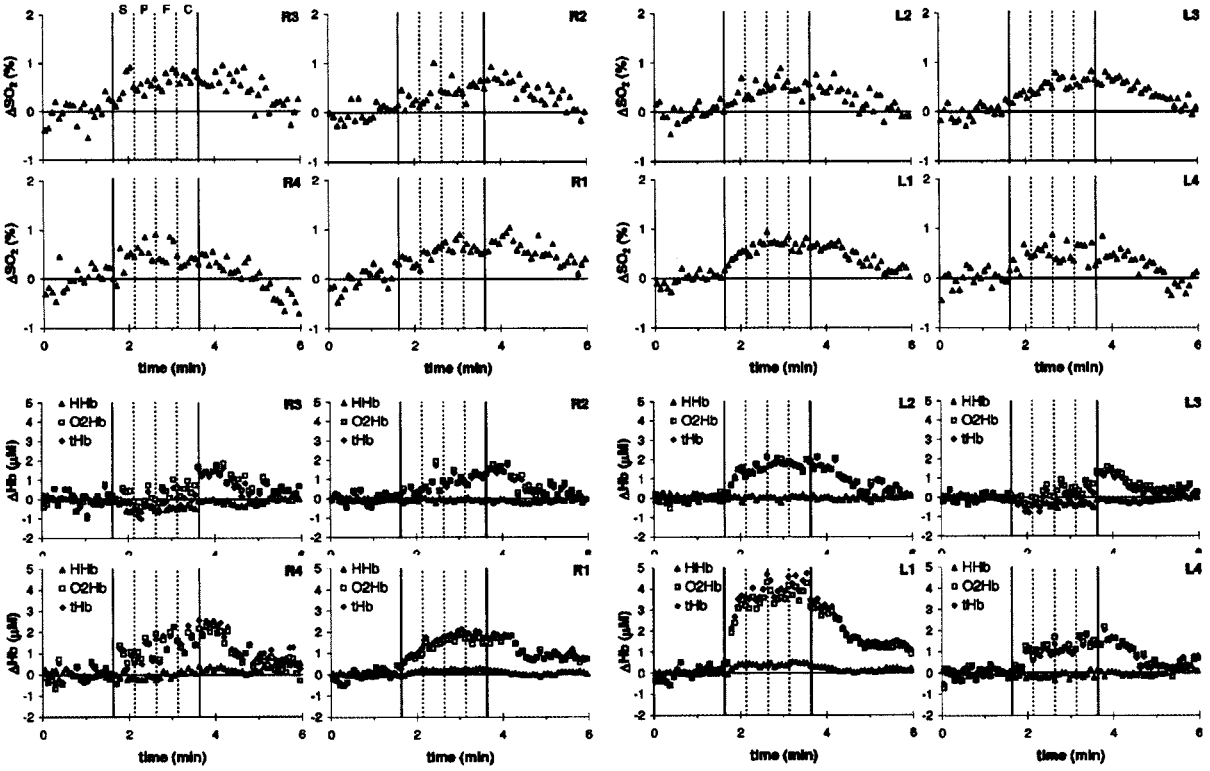

Fig. 5 Topographic presentation of the time courses of ΔSO_2, ΔO_2Hb, ΔHHb, and ΔtHb on VFT over eight measurement sites on the right (R) and left (L) prefrontal cortex (subject F). Arrangement of results resembles measurement positions in Fig. 1. Continuous vertical lines indicate total duration of the VFT, which is in turn subdivided by the three dotted vertical lines in four intervals. Each interval represents the allocated time for each subject to produce as many nouns as possible beginning with the corresponding reported letter (upper left panel).

Different cortical depths among channels can cause a similar problem of varying optical path lengths when a large area is measured by multichannel NIRS. The problems of spatial accuracy, signal contamination by superficial fluctuations, and spatial nonhomogeneity of head tissues could be resolved using multiple source-detector probes and applying new methods of 3-D reconstruction currently under development.[13,24,70] The sensitivity of the NIRS signal to cortical activity changes depends on both the depth of the inner skull and the thickness of the cerebrospinal fluid, as well as the partial path length in the brain and, hence, cannot be predicted from the depth of the brain surface alone.[68,69] Differences in optical path length cause[71] crosstalk between O_2Hb and HHb. As previously suggested, an image reconstruction algorithm that predicts the path length in the activated region of the brain might reduce the crosstalk in the measurement more effectively than a calculation using the mean optical path length.[13]

NIR_{TRS} estimates absolute concentration values (averaged over the investigated tissue volume) of O_2Hb and HHb, from which tHb can be derived. The possibility to map tHb, which strictly relates to tissue blood volume, over a large cortical area may enable regional evaluation of vasodilatation and/or capillary recruitment. Furthermore, by measuring O_2Hb and HHb, NIR_{TRS} enables the quantification of SO_2 in the tissue blood volume considered. Cerebral cortex SO_2 predominantly reflects saturation of the intracranial venous compartment of circulation.[72] SO_2 measurements are extremely important in clinics suggesting potential use of NIR_{TRS} instruments for cortical SO_2 mapping (i.e., to evaluate the cerebrovascular reactivity in the neurovascular diseases and/or to evaluate the efficacy of stroke therapy/rehabilitation). For example, a difference between asymptomatic and symptomatic patients suffering from carotid occlusive disease has been recently demonstrated (in terms of SO_2 increase) using a FD oximeter during a CO_2 reactivity test.[73] For medical applications, the normal range of tHb and SO_2 in the brain must be studied in a large population to determine normal and abnormal value ranges. The cross-subject mean SO_2 values in our study (Table 1) were $68.8\pm3.2\%$ (right) and $71.0\pm3.6\%$ (left) and are similar to those reported using a FD oximeter.[73,74] The cross-subject average tHb values (Table 1) were 69.6 ± 9.6 μM (right) and 69.5 ± 9.9 μM (left) and are also similar to those obtained using a FD oximeter.[74]

It is foreseen that the NIR_{TRS} system may have advantages over NIR_{cw} systems, especially in terms of increased penetration depth. In particular, in contrast to cw systems, in which sensitivity to depth is obtained by increasing the distance between source and detector, the TRS system sensitivity to depth can be obtained at a fixed source detector distance by selecting late photons.[75,76] However, to exploit information encoded in the late photons, it is necessary to make several *a priori* assumptions on the structure of the head (typically modeled as a layered medium consisting of scalp, skull, cere-

brospinal fluid, and brain) and on its optical properties.[76] Currently, however, there is little knowledge of the *in vivo* optical properties of brain tissues, making the interpretation of experimental data difficult in terms of a layered model. Here, we used a homogeneous model for photon diffusion to estimate changes in μ_a as for standard approaches used by cw instrumentation (Hamamatsu NIRO-300, Hitachi ETG-100, etc). Yet, as described in the Sec. 2, we derived $\Delta\mu_a$ by using photons in the tail of the TRS curve that have therefore probed deeper structures, when compared to cw measurements performed at the same source-detector distance.

5 Conclusion

The mapping of brain functions by fNIRS is today no longer a challenge, with promising results obtained using simple cw instruments and more recently even FD systems have been successfully employed. In this paper, we reported the use of a TRS system to monitor brain hemodynamic responses to a cognitive paradigm. For the first time, to our knowledge, we reported the possibility to map SO_2 as well as O_2Hb, HHb, and tHb simultaneously and bilaterally over a large area of the prefrontal cortex at "rest" and during cognitive stimuli, such as the VFT. Furthermore, we reported (in four out of the seven subjects) that after the beginning of the VFT a bilateral O_2Hb increase is accompanied by a HHb decrease. Our results are in agreement with similar experiments performed using cw fNIRS and fMRI, demonstrating the potentiality of a TRS approach. Although the correlation between variables of different neuroimaging techniques must be further elucidated, the clear activation in right and left hemispheres upon a verbal task (such as encoding words) suggests that fNIRS may be better at detecting cerebral activation than other conventional neuroimaging techniques. Finally, considering the necessity to map broader brain areas to better investigate the relationship between different brain regions, work is in progress to improve our instrument replacing the fused splitter with a fiber optics switch, to further increase the number of injection points from two to nine, and reduce the acquisition times to 100 ms. Also, by means of a newly developed photomultiplier tube, it is foreseen to double the number of independent collection channels.

Acknowledgments

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Jpn. J. Phys. Fitness Sports Med. 2006, 55 Suppl. : S213~S216

THE RELATIONSHIP BETWEEN CARDIAC MUSCLE, SKELETAL MUSCLE MASS, AND VESSEL STRUCTURE IN ELDERLY WOMEN

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Abstract

The purpose of this study was to clarify the relationship between left ventricular muscle mass, skeletal muscle volume and vessel structures in elderly women (n=15, 76.0±5.4 years). We measured the thigh muscle thickness, and brachial and common carotid arterial diameter using B-mode ultrasound method. Posterior wall thickness, interventricular septal thickness, left ventricular end-diastolic internal diameter, and aorta artery were measured by B-mode echocardiography. No significant relationship was obtained between brachial and common carotid arterial diameters, and aortic diameter. On the other hand, significant correlation coefficients were obtained between cardiac muscle thickness and thigh muscle thickness ($r=0.674$, $p<0.01$). A significant correlation coefficient was also obtained between the estimated skeletal muscle volume and left ventricular mass [LVmass] ($r=0.542$, $p<0.05$). The slope of regression equation between estimated thigh muscle volume and LVmass in elderly women in this study was ($y=0.11x+75.65$) steeper than in children ($y=0.06x+14.02$) reported previously. These results indicate that the ventricular muscle (LVmass) is closely related to the skeletal muscle volume in ordinary elderly women and skeletal muscle mass at a given LVmass is smaller in elderly women than children.

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key word : LVmass, thigh muscle thickness and ultrasound method

Introduction

Cardio-vascular function is activated by skeletal muscle activities to meet oxygen demands from skeletal muscle tissues. The muscle pump caused by skeletal muscle contraction increases venous return, which in turn increases pre-loading to the heart[4]. One of the major modifications of the vessel with advancing age was widening of the arterial diameter and reduction of blood flow velocity at baseline in peripheral artery[1,7]. In addition, arterial compliance decreases and arterial resistance decreases with advancing age, which resulted in, an elevation in systolic blood pressure, and after-loading to left ventricle.

We hypothesized that the reduction of skeletal muscle volume in elderly women decreases the amount of stimulus to cardiac muscle and vessel structure. However, no previous studies have reported a relationship between cardiac muscle, skeletal muscle mass and vessel structure in elderly women. Only one study exists with respect to this topic[5] conducted on children but not on elderly. They reported that ventricular muscle development is closely related to the development of skeletal muscle in children[5].

The purpose of this study, therefore, was to clarify the relationship between cardiac muscle mass, skeletal muscle and vessel structure, and to elucidate whether the relationship between skeletal and cardiac muscle mass in elderly differs from that in children.

Methods

Subjects and experimental design

Fifteen elderly women, who live in urban part of

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Tokyo, participated in this study after giving their informed consent. Their mean age was 76.0±5.4 years. Their physical characteristics are shown in Table 1. Before voluntarily participating in this experiment, each subject was fully informed of the purpose, protocol, voluntarily participating and associated risk. All the subjects were normotensive, no take medications, and no history of cardiovascular disease.

Physiological measurements

Measurement of skeletal muscle thickness

While standing, the subject's thigh length of the right side was measured as the distance from the lateral epicondyle of the femur to the greater trochanter. The measurement site of the thigh was determined at 50% of its length. Both measurement sites were marked on the dermal surface with a pen. Using a B-mode ultrasound apparatus (SSD-1000, 7.5 MHz, Aloka), we measured layer tissue thickness at 2 sites ; vastus intermedius [VI] and rectus femoris [RF].

Measurement of cardiac dimension

The echocardiographic investigations were carried out at rest in a left lateral decubitus position. B-mode images of the heart were obtained using an ultrasound apparatus (VIVID7, GE) with a 2.5 MHz transducer positioned at the level of the chordar tendinae to exsure simultaneous visualization of the left ventricular posterior wall tickness [LVPWT], the interventricular septal thickness [IVST], the left ventricular end-diastolic internal diameter [LVIDd] and the aorta arterial diameter [AO]. LVmass (g) was calculated by Devereux and Reichek [2], as follows :

$$LVmass = 1.04\{(IVST + LVIDd + LVPWT)^3 - LVIDd^3\} - 13.6$$

Measurement of vessel structure

The blood vessel diameter of the common carotid artery [Cca] and brachial artery [Ba] were measured by B-mode ultrasound method (HP 8500 GP, Hewlett-Packard) with a 7.5 MHz transducer. The longitudinal two-dimensional ultrasound images were obtained using a linear array transducer from 2 different arteries at following sites ; at 1～2 cm proximal to the bifurcation of the common carotid and brachial artery. All the signals were stored on a video cassette recorder (VCR) for later analysis.

Statistics

Pearson's correlation coefficient test was used to determine the relations between cardiac muscles mass and skeletal muscles mass. Differences at $P < 0.05$ were accepted as a significant.

Results

No significant correlation coefficients were obtained among brachial, common carotid and aortic diameters, and between left ventricular end-diastolic internal and aortic diameters. Figure 1 shows the relationship between cardiac muscle thickness and thigh muscle thickness. A significant correlation coefficient was obtained between cardiac muscle thickness (the sum of posterior was thickness and interventricular septal thickness) and thigh muscle thickness (the sum of vastus intermedius and rectus femoris) ($r = 0.246$, $p < 0.05$). The skeletal muscle volume was estimated and its relationship to LVmass in elderly women is illustrated in Figure 2 compared with that in children. A significant correlation coefficients was also obtained between two parameters ($r = 0.360$, $p < 0.05$). The regression equation in elderly women was $y = 0.09x + 108.1$. When LVmass at a given skeletal muscle mass was compared, the elderly women tended to be larger values than that in children[5].

Table 1. Physical characteristics of the subjects

Number of subjects	Age (years)	Height (cm)	Weight (kg)	Number of steps (steps/days)	Consumption (kcal/day)
14	76.0±5.4	148.3±5.3	50.7±8.6	4867±480	1415±40

Values are mean±SD.

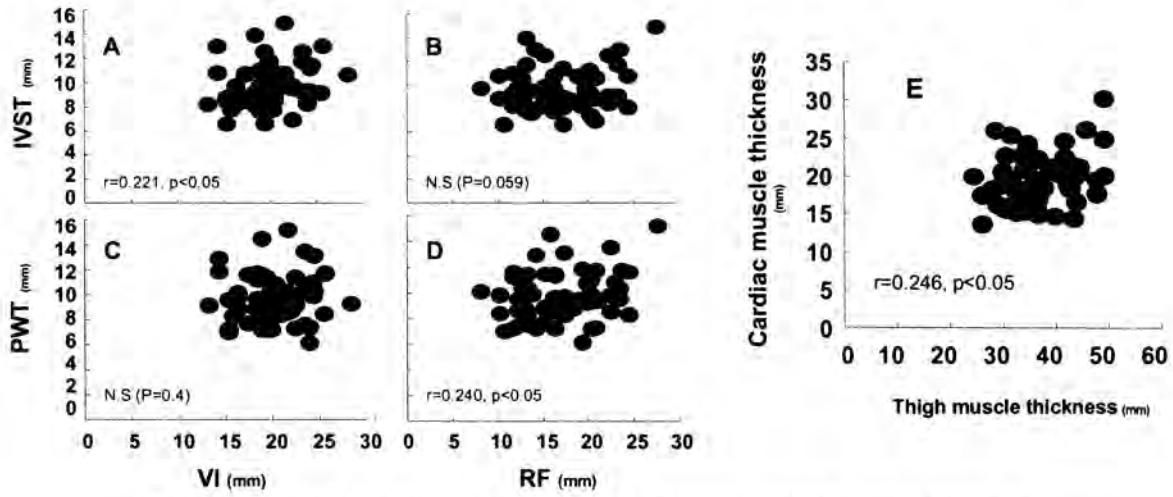

Fig. 1. Relationship between cardiac muscle thickness and thigh muscle thickness.
A, B : VI, RF and IVST, C, D : VI, RF and PWT, E : cardiac muscle thickness (the sum of PWT and IVST) and thigh muscle thickness (the sum of VI and RF)
VI : vastus intermedius, RF : rectus femoris, IVST : inter ventricular septal thickness, PWT : ventricular posterior wall thickness

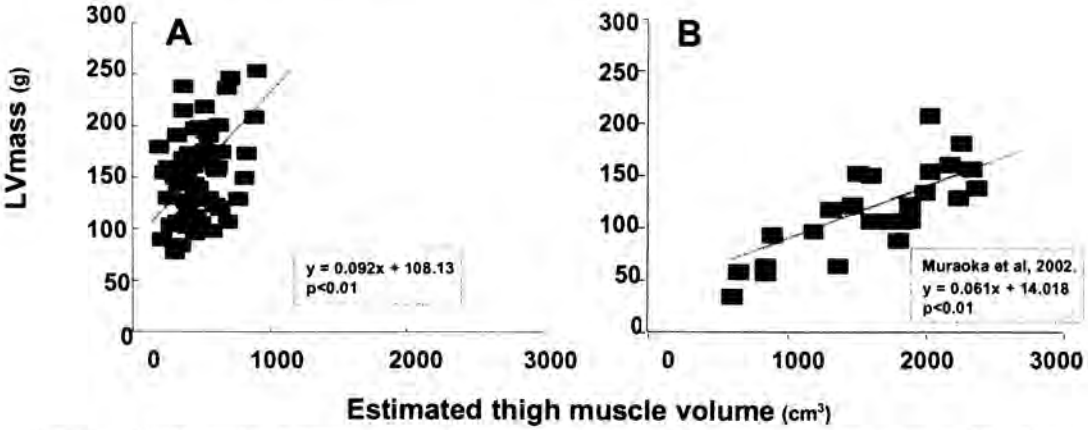

Fig. 2. Relationship between skeletal muscle volume and LVmass in elderly women (76±5.4 years) [A] and children (12±0.8 years) [B].

Discussion

In this study, we estimated left ventricular muscle mass (LVmass), thigh muscle volume and vessel structure in elderly women. The major finding of this study was that cardiac muscle thickness and volume were closely related to thigh muscle thickness and volume in elderly women. This coordinative aging in cardiac muscle and skeletal muscle is functionally important. If the prevention of skeletal muscle atrophy will contribute to maintain stimulus to cardiac muscles, this stimulus makes cardiac muscle mass at a high level. In contrast, $\dot{V}O_2max$ decreases with advancing age[3] and the cardiac index decreases with age[8]. This contributes to the reduction in physiological, functional capacity with advanced age. Radegran and Saltin[6] reported that the common femoral artery diameter correlated to peak pulmonary oxygen uptake during ergometer cycle exercise. Corresponding to the increased oxygen demand, cardiac muscle develops as a way to adapt to the increased blood supply to skeletal muscle tissue. We hypothesized that the reduction of skeletal muscle volume in elderly women decreases the amount of stimulus to cardiac muscle and vessel structure. In this study, the elderly women were surveyed for a physical activity level during consecutive 10 days by using Lifecorder (Szuken CO.). As a result, a sig-

nificant correlation coefficients was obtained between the estimated skeletal muscle volume and physical activity level ($p<0.01$). That means, when the amount of physical activity level is low, the estimated skeletal muscle volume should be small. Therefore, the reduction of cardiac muscle volume with close relationship to skeletal muscle mass will provably be due to the diminished exercise stimulus to the heart and skeletal muscles.

Another finding in this study was that the relationship between cardiac and skeletal muscle mass differed in elderly and children reported previously. During growth, the cardiac muscles developed as shown in following equation ($y=0.06x+14.02$, $p<0.01$). This equation was obtained from the data on children aged 6～17 years old [5]. In this study, the obtained regressions between the estimated skeletal muscle volume and LVmass was $y=0.09x+108.13$. The slope of the regression equation between cardiac and skeletal muscle mass tended to be higher in elderly but did not differ significantly between elderly and children [5]. Therefore, the skeletal muscle mass at a given cardiac muscle volume was smaller in elderly. The linearity between both parameters was obtained when the estimated skeletal muscle mass was lower than 1000 cm^3 in elderly. In contrast, this linearity existed over the wide range of skeletal muscle mass in children.

In conclusion, these results indicate that the ventricular muscle (LVmass) is closely related to the skeletal muscle volume in ordinary elderly women. When this relationship was compared with children reported in the previous study [5], muscle mass at a given LVmass is smaller in elderly women.

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BLOOD FLOW AFTER CONTRACTION OF SHORT DURATION REACHES ITS PEAK BY 3rd CARDIAC CYCLE

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Abstract

The purpose of this study was to elucidate how long it takes to reach peak blood flow after muscle contractions in consideration of the cardiac cycle. Seven healthy female subjects performed two successive dynamic plantar flexions of 1-s duration at 30, 50 and 70% of maximal voluntary contraction (MVC). Based upon the blood flow response after a single contraction, we set up intervals during two successive contractions each corresponding to 10% (10 I), 30% (30 I) and 50% (50 I) of the time required to reach peak blood flow. Upon cessation of contraction, the popliteal artery blood flow ($\dot{Q}$pa) increased progressive, beat-by-beat increase and peaked by the 5th cardiac cycle, for all conditions. The highest peak blood flow among the cardiac cycle was at 3rd cycle in overall data. Peak $\dot{Q}$pa values reached after exercise did not differ among intervals, whereas peak $\dot{Q}$pa value attained after exercise was significantly greater in 50 and 70%MVC than 30%MVC ($p<0.05$). The result indicates that the augmentation of the $\dot{Q}$pa after exercise with short duration differed with the exercise intensity but the timing for reaching peak post-exercise value did not differ in terms of the number of cardiac cycles.

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key word : Peak blood flow, Interval, Popliteal artery

Introduction

Dynamic exercise is characterized by inserting relaxation period between contractions. During this period, the blood flow increased markedly (Barcroft & Dornhost, 1949 ; Kagaya & Ogita, 1992). The magnitude of blood flow increase differed depending on the duration of the relaxation phase, rather than the contraction rate per se (Hoelting et al. 2001). It is also reported that the second contraction of the same intensity made during the period of increased blood flow following the first contraction induced a greater increase in flow than that occasioned by the first contraction alone (Corcondilas et al. 1964). Therefore, the relaxation time should be a causal factor for determination the magnitude of blood flow during dynamic exercise.

To determine the timing of two successive contractions to induce higher blood flow, the duration for reaching peak blood flow after contraction should be clarified. The blood flow early in recovery period from exercise differed between subjects including athletes and nonathletes (Elsner & Carlson, 1962). Therefore, exercise-induced hyperemic response may vary between the subjects, and especially the training status and other factors might influence the duration for the blood flow to reach its peak value.

When we study the duration to reach peak blood flow, we have to consider that arterial blood flow velocity is alternativeiy accelerated and decelerated in accordance with cardiac systole and diastole. Accordingly the time for reaching peak blood flow should be considered from the view point of cardiac cycle.

We hypothesized that the duration for reaching peak blood flow was influenced by the cardiac cycle when we modulate the contraction intervals and the

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exercise intensities. To elucidate the effect of successive contractions on the blood flow, we employed a simple two successive contraction model, which would eable to help understand blood flow response during more complicated continuous contractions. Therefore, the purpose of this study was to elucidate how long it takes for the blood flow to reach its peak value following two successive contractions with respect to the cardiac cycle.

Methods

Subjects

Seven physically active women participated in the study after giving their informed consent. The age, body height and body mass (means±SD) of the subjects were 21.9±0.7 yrs, 162.5±5.8 cm, and 55.4±5.3 kg, respectively. All subjects were free of medical problems. All of the participants gave written consent, on a form approved by the Japan Women's College of Physical Education, after receiving full written and verbal details of the experimental protocol and any potential risks involved.

Experimental protocol

Exercise protocol

All experiments were performed in a supine position. The subjects placed the right foot on the pedal of the ergometer with ankle joint angle at 90° and knee joint at 180°. They pressed the pedal with the ball of the foot to extend the ankle joint to 100°, then relaxed to return it to 90°. Dynamic plantar flexion was performed against the load adjusted to 30, 50 and 70% of maximal voluntary contraction (MVC). Time for lifting and maintaining the load was 1 second, and the cadence was determined by an auditory metronome.

Determination of the relaxation time

Two experiments were conducted in this study (Fig 1). In the first experiment, we investigated popliteal artery blood flow ($\dot{Q}pa$) after single contraction of plantar flexion exercise to determine the duration for reaching peak $\dot{Q}pa$ value. In the second experiment, dynamic plantar flexion of two successive contractions was performed at three different intervals, which were determined based upon first

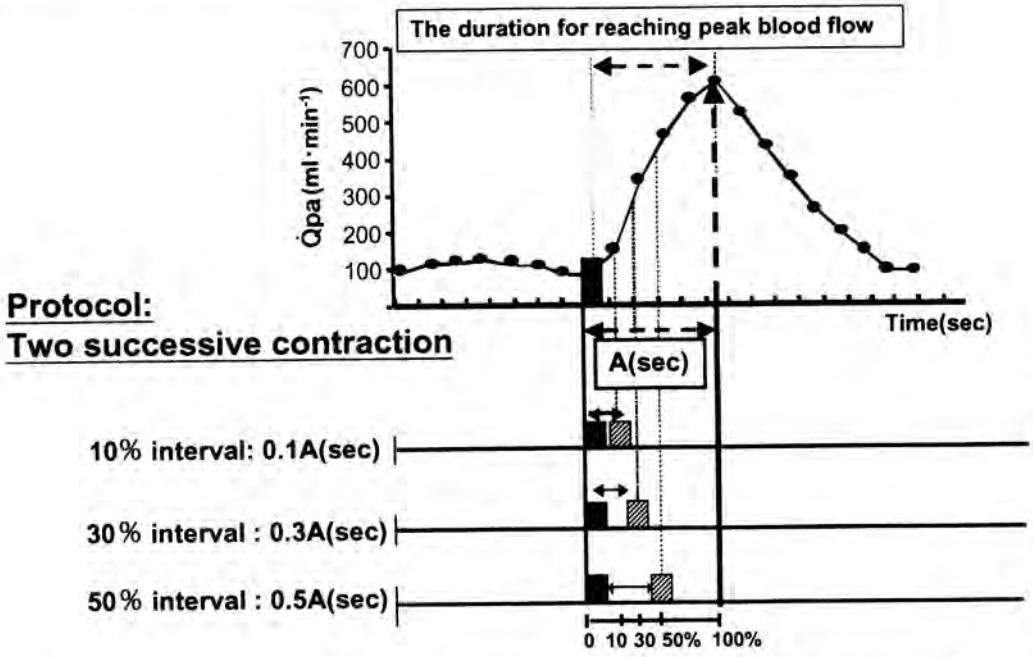

Figure 1. Exercise protcol. The intervals were set up based upon the duration for reaching peak blood flow value in the first experiment on a single contraction of 1-second plantar flexion exercise. The interval between contractions used in this study was time of 10, 30 and 50% of the time reaching peak value.

■: First contraction, ▨: Second contraction

experiment. The intervals between contractions used in this study were corresponding to 10% (10 I), 30% (30 I) and 50% (50 I) of the time required to attain peak blood flow.

Measurement of popliteal artery blood flow

Blood velocity and vessel diameter of popliteal artery were measured using a Doppler and B-mode ultrasound apparatus (HP8500GP) with a 7.5 MHz transducer. Blood velocity signal was obtained for each cardiac cycle. To determine the cross-sectional area of the vessel, the diameter of vessel was adjusted for the relative time periods of the systolic (1/3) and the diastolic (2/3) phases of cardiac cycle. Beat-by-beat $\dot{Q}pa$ was calculated from multiplying FI, HR and πr^2, where FI was flow integral during each cardiac cycle and HR was heart rate obtained from the R-R interval of the electrocardiogram (ECG).

The laboratory temperature and relative humidity were kept at 24℃ and 60%.

Statistical analysis

The values are expressed as mean ± SE. Differences among means obtained from each exercise intervals and from each exercise intensities were evaluated using two-way ANOVA with post hoc comparison using Fischer's PLSD.

Results

The peak $\dot{Q}pa$ was not different among three intervals used in this study {(30%MVC ; 390 ml/min (10 I), 396 ml/min (30 I), 400 ml/min (50 I) : 50% MVC ; 524 ml/min (10 I), 557 ml/min (30 I), 542 ml/min (50 I): 70%MVC ; 542 ml/min (10 I), 538 ml/min (30 I), 582 ml/min (50 I)}. However, the peak $\dot{Q}pa$ differed depending on the exercise intensity. They were significantly higher ($p<0.05$) at 50 and 70% MVC compared with that at 30%MVC.

On the cessation of contraction, the $\dot{Q}pa$ showed progressive, beat-by-beat increase and peaked by the 5th cardiac cycle in exercise at all contraction

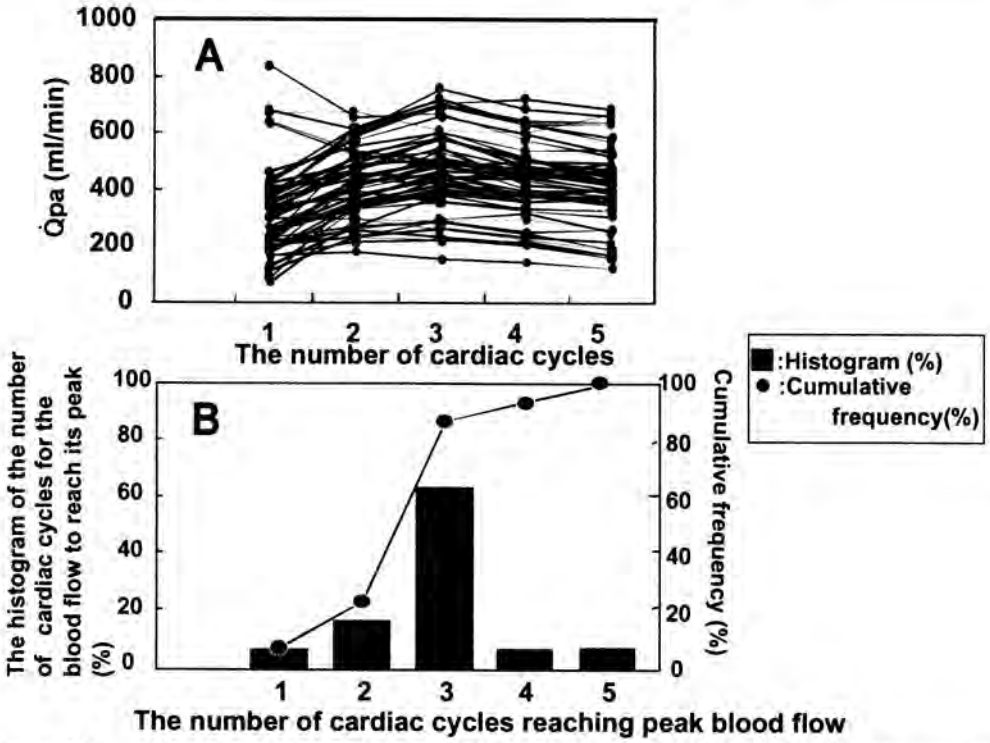

Figure 2 A. The beat-by-beat blood flow after contraction individual value. On the cessation of contraction, the popliteal artery blood flow increased progressive, beat by beat, and peaked by the 5th cardiac cycle, at all contraction frequencies and intensities.

2 B. The histogram and cumulative frequency of the number of cardiac cycles reaching peak blood flow. The most of the cardiac cycle for peak blood flow was 3rd cycle in overall data.

frequencies and intensities (Figure 2A). Figure 2B shows the histogram and cumulative frequency of the number of cardiac cycles for the $\dot{Q}$pa to reach its peak value. The largest occurrence of the peak $\dot{Q}$pa attained was at the 3rd cycle (64%) of the cardiac cycle in overall data.

Tablel shows the range of the duration for reaching peak $\dot{Q}$pa after two successive contractions.

Table 1. The range of the duration for reaching peak blood flow after two successive contraction.

Intensity / Interval	10% interval	30% interval	50% interval
30% MVC	1.8-2.9	2.1-3.1	2.1-3.9
50% MVC	2.0-2.9	0.9-2.9	0.9-2.8
70% MVC	2.2-4.2	2.3-3.5	2.0-3.1

(Second)

Discussion

The major finding of this study was that the blood flow after two successive contractions reached its peak by the 3rd cardiac cycle in 86% of the cases and 64% of overall data at the 3rd cardiac cycle, regardless of different contraction intervals and exercise intensities.

The magnitude of peak $\dot{Q}$pa was significantly higher at 50, 70%MVC compared with that 30%MVC. This might be either due to the number of muscle fibers recruited (Angrep & Saalfeld, 1935) or the production of the tension increased with exercise intensity (Lind & Willaiams, 1979). Moreover, Hamann et al. (2004) indicated that the blood flow response to a single muscle contraction is not solely determined by the work rate performed, but the muscle fiber recruitment contributes independently to changes in blood flow. The increase in exercise intensity influenced the magnitude of peak blood flow but the work rate did not in this study.

The mechanisms of augmentation of the blood flow reported are the consequence of the both mechanical effects of the muscle pump on alteration the perfusion pressure gradient across the capillary bed (Sheriff et al., 1993 ; Rådegran & Saltin, 1998) and the dilation of the resistance vessel by local release of any dilating substances (Corcondilas et al., 1964 ; Brock et al., 1998 ; Rådegran & Saltin, 1998). Immediately after contraction, blood flow started to increase markedly (Corcondilas et al., 1964 ; Brock et al., 1998 ; Naik et al., 1999) and reached the peak values (Tschakovsky et al., 1996). In this study, the $\dot{Q}$pa showed a progressive, beat-by-beat increase and peaked by the 5th cardiac cycle, at all contraction frequencies and intensities in this study. And, the largest occurrence of the cardiac cycle for peak $\dot{Q}$pa was attained at the 3rd cycle in overall data. The duration for reaching peak $\dot{Q}$pa differed in each subject and the number of cardiac cycles for reaching peak blood flow was similar in this study. The duration for reaching peak $\dot{Q}$pa was differed in each subject because of the R-R interval differed by the subjects. However, it is unclear why the largest occurrence reaching peak blood flow was attained 3rd cardiac cycle.

In summary, among three different intervals, the peak blood flow was not different in two successive contractions model used in this study. The peak blood flow at 50 and 70%MVC was significantly higher compared with that of 30%MVC. And, the largest occurrence of the cardiac cycle for peak blood flow was at the 3rd cardiac cycle in all contraction intervals and exercise intensities. The timing for reaching peak blood flow was influenced by the number of cardiac cycles. The finding of this study will contribute to detecting the optimal exercise frequency for the blood flow to increase to a higher level during exercise.

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CHANGES IN BRACHIAL AND FEMORAL ARTERY VASCULAR CONDUCTANCE IN NON-EXERCISING LIMBS DURING HANDGRIP EXERCISE

MUTSUKO YOSHIZAWA[2,3], SHIZUYO SHIMIZU[1,4] and ATSUKO KAGAYA[1]

Abstract

The purpose of this study was to determine the difference in vascular conductance changes in brachial and femoral artery (BVC, FVC) of non-exercising limbs during handgrip exercise at different intensities. Six subjects performed rhythmic handgrip exercise, which consisted of 2-second contraction and 2-second relaxation at the intensities of 15%, 30%, and 45% of maximal voluntary contraction (MVC). Brachial and femoral artery blood flow (Doppler ultrasound method) of non-exercising limbs, blood pressure, and heart rate were measured. The BVC during exercise at lower intensities (15% and 30%MVC) and FVC during exercise at any of three intensities did not change significantly. However, BVC significantly decreased at 45%MVC when the exercise was continued to longer than 60% of maximal endurance time ($P<0.05$). These results suggest that FVC of the non-exercising limb dose not change during handgrip exercise at the intensity lower than 45%MVC, but BVC of the non-exercising limb change during handgrip exercise depending on the exercise intensity and duration.

(Jpn. J. Phys. Fitness Sports Med. 2006, 55 Suppl : S159～S162)

key word : blood flow, exercise intensity, exercise duration, Doppler ultrasound

INTRODUCTIN

Vascular conductance changes in non-exercising limb during regional exercise have been still a matter of issue. Saito et al. (1990) showed that a calf vascular resistance increased during static handgrip exercise, which suggested that the vasoconstriction occurred in the non-exercising limb. In contrast, Fisher and White (2003) suggested that the vasodilatation occurred in non-exercising calf muscles, based upon their observation on calf vascular conductance during isometric exercise of contralateral limb.

A vascular tone is mainly regulated by the sympathetic nerve activity and by direct action of local metabolites on peripheral vessels. The levels of sympathetic nerve activity and muscle metabolisms were modified by the intensity, duration, and mode of exercise (Jensen-urstad et al., 1993 ; Kagaya and Homma, 1997). Additionally, the responses differed depending on the limbs recruited in the exercise. (Ahlborg et al., 1975 ; Taylor et al., 1989). Based upon those findings, it seems likely that the exercise intensity and duration would be very important factor to decide the change of vascular conductance in the non-exercising limb.

The purpose of this study was to determine the change in vascular conductance of brachial artery and femoral artery in non-exercising limbs during exhaustive handgrip exercise at different intensities.

METHODS

Subjects.

Six healthy young females (22.5±1.2 ys) participated in this study after providing their informed consents. The mean (±SD) height and body mass of the subjects were 160.6±6.1 cm and 57.8±5.9 kg, respectively.

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Protocol.

Subjects performed rhythmic handgrip exercise in upright position at .the intensities corresponding to 15%, 30% and 45% of maximal voluntary contraction (MVC). One duty cycle consisted of 2-second handgrip contraction and 2-second relaxation. Following 10-minute rest, they performed the exercise at a constant load until exhaustion. However, exercise was discontinued at 15 minutes when they did not become exhausted The exercise at different intensity was performed on separate day.

Measurements

Blood flow was measured using the Doppler ultrasound method (HP8500-GP, USA) for femoral artery and brachial artery in non-exercising limb. Blood pressure (BP) was measured on a beat-by-beat basis throughout the experiment on contralateral finger (Finapres ; Ohmada, USA). The heart rate (HR) was determined from R-R intervals of the electrocardiogram (ECG). Brachial artery vascular conductance (BVC) and femoral artery vascular conductance (FVC) were calculated as blood flow divided by mean blood pressure (MBP).

Statistical analysis.

Values are presented in the figures as means±SE. Differences between the means were evaluated using one-way analysis of variance for repeated measurements. In the case of a significant F-value, a post-hoc test was performed using the Fisher PLSD. Difference was considered significant when $P<0.05$.

RESULTS

Table 1 shows BVC and FVC at rest and during exercise at 3 intensities.

During exercise at 15%MVC, BVC remained at baseline level, whereas the FVC tended to increase without statistical significance. At 30%MVC, neither FVC nor BVC changed during exercise. At 45%MVC, the BVC decreased significantly during exercise compared with resting level ($P<0.05$) when exercise duration corresponded to 60%, 80%, 100% of endurance time. However, FVC did not change significantly.

DISCUSSION

There are two new findings in this study. The first finding was that the changes in vascular conductance in non-exercising regions were different in brachial artery and femoral artery during handgrip exercise. This finding was consistent with the the result reported by Taylor et al.(1989). They indicated a differential control of limb vascular resistance during rhythmic exercise. In addition, Newcomer et al.(2004) indicated that vascular responses to vasodilator agents were blunted in the leg compared to the forearm. They suggested that these findings could be a consequence of elevated blood pressure in the leg during upright posture.

Table 1. The changes in vascular conductance in non-exercising limbs during rhythmic handgrip exercise.

	Δ Change of vascular conductance					
Duration (% of endurance time)	Rest	20%	40%	60%	80%	100%
Brachial artery						
15%MVC	0	-15.1±7.5	-11.6±12.8	-9.8±12.1	-20.4±8.3	-15.0±8.0
30%MVC	0	-2.9±11.0	-7.3±9.9	8.2±8.2	-8.9±17.7	-4.0±17.4
45%MVC	0	-0.9±18.3	-7.5±15.0	-36.6±8.6*	-22.2±14.3*	-23.1±22.3*
Femoral artery						
15%MVC	0	-17.1±16.3	-30.2±16.6	32.7±16.9	19.9±20.1	40.3±18.5
30%MVC	0	1.51±14.8	-6.51±11.9	-2.11±14.9	2.2±16.4	-5.34±19.8
45%MVC	0	2.1±22.8	17.0±12.2	-9.9±12.1	4.7±27.5	10.2±19.9

Values are means±S. E. M. *Significantly different from Rest

The second finding of this study was that the changes in brachial artery vascular conductance in non-exercising limbs were modified by the exercise intensity and duration. Concerning exercise intensity, we showed that the BVC decreased during exercise at 45%MVC but no significant changes occurred during exercise at 15%, and 30%MVC. In the light of previous finding (Saito et al. 1990), the reduction of BVC at higher intensity is provably mediated by the augmentation of muscle sympathetic nerve activity (MSNA). Further, our study indicated that BVC change was time-dependent; the reduction of BVC occurred during the later phases of exhaustive exercise at higher intensity. These results were also consistent with the changes in vascular resistances in arm and leg during cycling exercise (Kagaya and Homma 1997, Taylor et al. 1989).

In conclusion, the vascular conductance in non-exercising limbs differs depending on the vessels (brachial or femoral), exercise intensity, and duration of exercise. Handgrip exercise at the intensities lower than 45%MVC had no effect on femoral artery vascular conductance. In contrast, the brachial artery vascular conductance in non-exercising limbs decreases when the intensity of contlalateral handgrip exercise was as high as 45%MVC and the exercise was prolonged to more than 60% of the maximal endurance time.

Acknowledgment

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利き腕，非利き腕運動時の筋交感神経反応

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Comparison of Muscle Sympathetic Nerve Activity Response between Dominant and Nondominat Arm Performed Handgrip Exercise

Mitsuru SAITO*, Seika AIZAWA* and Atsunori KAMIYA**

Abstract

The aim of the study was to test whether muscle sympathetic nerve activity (MSNA) response during handgrip exercise performed with the dominant and non-dominant arm was different. Sixteen right handed healthy volunteers were performed two kind of handgrip exercise; intermittent static handgrip for 15 sec repeated ten times in each side arm with maximal voluntary effort and rhythmic handgrip under the forearm circulation arrest with maximal effort followed by two minutes post exercise arterial occlusion (PEAO). MSNA recorded from the tibial nerve using microneurography technique and was expressed as total activity (bursts x burst area: unit). Heart rate and handgrip force was measured simultaneously.

MSNA response during static handgrip was significantly increased at the first handgrip exercise and the elevated activity persisted until ten repetitions while the response was not different between dominant and non-dominant arm. During rhythmic handgrip with ischemia and PEAO, MSNA increased 197 % and 369 % of resting value for dominant and 140 % and 197 % for non-dominant arm respectively, and those differences between dominant and non-dominant arm were significant. Heart rate increased during intermittent handgrip as well as rhythmic handgrip exercise, whereas no significant differences in heart rate response between the arms were found. Mean blood pressure elevated during intermittent handgrip exercise and post exercise ischemia in dominant and non-dominant arm, while the responses were not different between arms. Force output of handgrip was not different between arms in either exercise paradigm.

This study demonstrated that the MSNA response to muscle contraction was different in dominant and non-dominant arm and the difference may be due to the difference in extent of muscle metaboreflex rather than that exercise effort or central command.

Key words: Metaboreflex, Central Command

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Ⅰ　目的

運動時の循環調節に大きな役割を果す交感神経は運動に伴い亢進する．ヒト筋交感神経活動を指標とした交感神経反応の研究から，その活動は運動様式，運動強度，時間，活動筋量，トレーニング，姿勢などの影響を受けることが報告されている[4,14,15,17,18,22,24,27,28]．

これらの研究の多くはハンドグリップ運動を用いて行なわれているが，左右差あるいは利き腕，非利き腕で差があるかどうかについては充分検討されていない．利き腕と非利き腕は日常の使用頻度が異なり[8,20,25]，前腕筋の代謝能や運動時の血流反応に差がみられることが報告されている[8,25]．これらの違いは運動時の筋交感神経反応に影響することが考えられる[20,26]．Sinowayのグループ[26]は疲労困憊に到る律動的ハンドグリップ運動を動脈阻血下で実施した際の代謝受容器反射を比較し，利き腕よりも非利き腕運動時の反応が大きいと報告した．しかし，Saito[20]はラケット競技選手の利き腕，非利き腕の静的ハンドグリップ運動疲労困憊時点の筋交感神経活動を比較し，差を認めなかった．その後，Saito[16]は右利き，左利き被験者を対象に2分間の最大努力静的ハンドグリップ運動および運動後阻血時の筋交感神経活動を比較し，左腕運動の反応が右腕運動時の反応より低くなることを報告した．

このようにハンドグリップ運動時および運動後阻血時の筋交感神経活動が利き腕と非利き腕で異なるかどうかについては一致した見解が得られていない．この原因には運動方法や時間，測定対象者の違いが関係する可能性が考えられる．

運動時の自律神経調節の研究においてハンドグリップ運動を用いようとする際には，運動時の交感神経活動が左右運動で差がないかどうか確かめておくことは，前腕筋を用いたトレーニング効果を確かめる際に重要である．本研究はハンドグリップ運動時の筋交感神経活動が左右側運動時で異なるか確かめることを目的とした．

Ⅱ　方法

A　被験者

健康な右利き成人男子16名を対象とした．彼らの平均年齢，身長，体重はそれぞれ22.8±3.2（SD）歳，169.0±4.7cmおよび63.1±12.1kgであった．利き腕調査はOldfield[9]が報告した15項目の利き腕判定基準を用い，10項目以上が該当すると答えた側を利き腕と判定した．実験に先立ち，研究の目的，危険性について被験者に十分周知した上で，研究に参加する旨の承諾を得た．本研究は「豊田工業大学ヒトおよび動物を対象とする研究」，審査委員会の承諾を得，ヘルシンキ宣言に則り実施した．

B　運動

測定1：間欠的静的ハンドグリップ運動

利き腕と非利き腕では日常的な使用頻度の違いが運動努力に影響するかどうか明らかにする目的で，運動時の代謝受容器反射の影響をできるだけ排除した短時間の静的な最大努力ハンドグリップを行なった．運動は15秒の休止期間を挟んで15秒の収縮を間欠的に左右交互に繰り返した．3分間の安静後，検者の合図に従い一方のハンドグリップを最大努力で15秒間維持したのち15秒間の休止に続いて対側の15秒ハンドグリップ運動を行なう手順で片側それぞれ10回繰り返した．したがって，左右側の運動回数は合計20回，一側では15秒収縮と45秒休止で構成された．測定1では，交感神経記録が途中から記録できなくなった一名を除いて，16名の内15名について解析した．

測定2：動脈阻血下のリズミック運動

活動筋代謝受容器反射を比較する目的で動脈阻血下で1分間に20回の頻度で最大努力の律動的ハンドグリップを実施した．運動は2分間の安静後，運動開始5秒前に上腕部に巻いたカフを200mmHgに加圧し，運動を開始した．ハンドグリップは随意最大努力で最後まで持続するよう指示，さらに加圧を運動後2分間持続した．カフ圧解除後は2分間の回復をとった．16名のうち3名は測定2を実施しなかった．従って，測定1と2の両方を実施したのは13名であった．

測定1，2の運動ともに左右側の運動順序が被験者間で均等になるよう配慮した．測定は仰臥位で，室温24± 1℃の条件で行なった

C　測定項目

筋交感神経活動：筋交感神経活動は微小神経電図法により左膝窩部脛骨神経より記録した．軸直径0.1mmのタングステン針電極を無麻酔経皮的に膝窩部脛骨神経の筋神経束に刺入し，下腿三頭筋支配

の筋交感神経活動を導出した．筋交感神経活動の同定は，心拍に同期した自発性のバースト活動であること，呼吸停止やヴァルサルバ手技で活動が亢進すること，音による覚醒刺激に対しバースト発射リズムが乱れないことを基準にした．とりだした神経活動は作動型前置増幅器で1000倍に増幅し，バンドパスフィルターを介してさらに50-100倍増幅した．神経活動はアナログ積分器により，積分（時定数0.1秒）した．積分した電位をアナログ／デジタル変換し，200Hz（Biopac MP100，USA）でパーソナルコンピュータに取り込み，測定後解析した．

心拍数は胸部から誘導した心電図R-R間隔より求めた．血圧は安静側の第三指にカフを装着し指動脈血圧計（フィナプレス）により測定した．運動開始時や疲労に伴い異常な呼吸停止が起きていないか監視する目的で熱線流量計（RT-H ミナト医科学）を装着した呼吸マスクにより呼吸運動をモニターした．また，運動時には活動筋以外の筋を収縮しないように注意した．これらの測定手順に慣れるため実験に先立つ別の日に測定と同様の手順で練習を行なった．

最大握力は測定前に立位で2回実施し，高い値を最大握力とした．前腕最大周囲長は立位で腕を水平に伸ばし，手掌面を垂直に，手指を伸展した状態で測定した．

D　解析

筋交感神経活動：筋交感神経活動積分波形から筋交感神経活動バースト数とバースト面積を求めた．実験毎に神経電位が異なるためあらかじめ安静時の筋交感神経活動バーストピークの最大値を20単位になるよう基準化し，バースト数とバーストの面積を計測した．

測定1では安静3分のうち最初の2分間の値を基準値とした．間欠的運動時の解析は15秒間の運動と15秒間の休止期に分けて行なった．測定2では安静および回復期は1分毎に，動脈阻血下運動および運動後動脈阻血時の解析は30秒間毎に行なった．いずれの場合にも1分間のバースト数（MSNA-BF）と総バースト活動（バースト総面積：TSNA）として定量化した．心拍数は筋交感神経活動と同様の時間間隔で，血圧は1分間隔で解析した．

ハンドグリップ張力：測定1では，収縮回毎にピーク張力（pHGF）及びハンドグリップ張力曲線で囲まれた面積（ハンドグリップ積分値：iHGF）を算出した．iHGFはハンドグリップ張力が1kgを超えた時点から収縮終了後，ハンドグリップ張力が2分の1まで低下する時点までの面積とした．測定2では一回目のハンドグリップ張力が1kgを超えた時点から最後のハンドグリップ張力が1kgに減衰するまでのiHGFを計測した．

E　統計処理

主効果および左右の比較は繰り返しのある分散分析で検定し，有意の場合にはNeuma-Keule testを用い有意な点を検定した．左右比較には対のあるWilcoxon検定を用いた．危険率5％以下を有意と判定した．結果は，平均値と標準誤差で示した．

Ⅲ　結果

利き腕，非利き腕の最大握力はそれぞれ48.6±2.2kg，44.8±2.3kg，（$p=0.056$）で，利き腕が高い傾向にあったが統計的な差は認められなかった．利き腕，非利き腕の前腕最大周囲長はそれぞれ26.0±0.5cm，25.1±0.4cm（$p=0.0004$）で，利き腕が大きかった．

A　測定1　間欠運動

ハンドグリップピーク張力，iHGFは運動回数とともに低下し．収縮10回目のピーク張力，iHGFは，利き腕，非利き腕がそれぞれ一回目の50％と45％および67％と65％に低下した．ピーク握力およびiHGFの左右運動時の比較では差は認められなかった（図1）．

左右ともに運動時のMSNA-BF，TSNAは有意に増加した（図2）．1回目の収縮ではMSNA-BF平均値は利き腕，非利き腕がそれぞれ安静より110％，74％，TSNAは125％，96％増加した．その後収縮回数を重ねるに伴い増加傾向を示したが，収縮回間の差はみられなかった．10回目の収縮では利き腕，非利き腕MSNA-BF，TSNAはそれぞれ安静より127％，142％，および135％，158％増加した．MSNA-BFおよびTSNA反応を左右の運動で比較した結果ではともに統計的な差は認められなかった．

心拍数は収縮に伴い有意に増加したが，左右差は認められなかった（図2）．

B　測定2　動脈阻血下のリズミック運動

動脈阻血下のリズミック運動のピーク張力およびハンドグリップ張力積分値の左右差は認められなかった（図3）.

MSNAは運動開始30秒から有意に増加し，最後の30秒間のMSNA-BF，TSNA平均値は利き腕運動が安静値よりそれぞれ137%，344%，非利き腕運動が95%，192%増加した（図4）．運動後阻血2分間のMSNAは安静値より高値を示し，利き腕，非利き腕のMSNA-BF，TSNAはそれぞれ安静値の197%，369%および140%，197%であった．分散分析の結果，左右のMSNAに差が認められ（$p=0.0127$），運動および運動後阻血時はともに利き腕運動時が非利き腕運動時より高かった．

心拍数は運動とともに増加したが，運動後阻血時には安静値レベルまで低下した．運動時および運動後阻血時の心拍反応は左右で差は認められなかった．血圧は運動時に増加し，運動後阻血時には安静値より高値を持続したが，左右運動時の差は認められなかった．

Ⅳ　考察

利き腕と非利き腕運動の筋交感神経反応に違いがみられるかどうかを短時間の最大努力の間欠ハンドグリップ運動と動脈阻血下で1分間の最大努力リズ

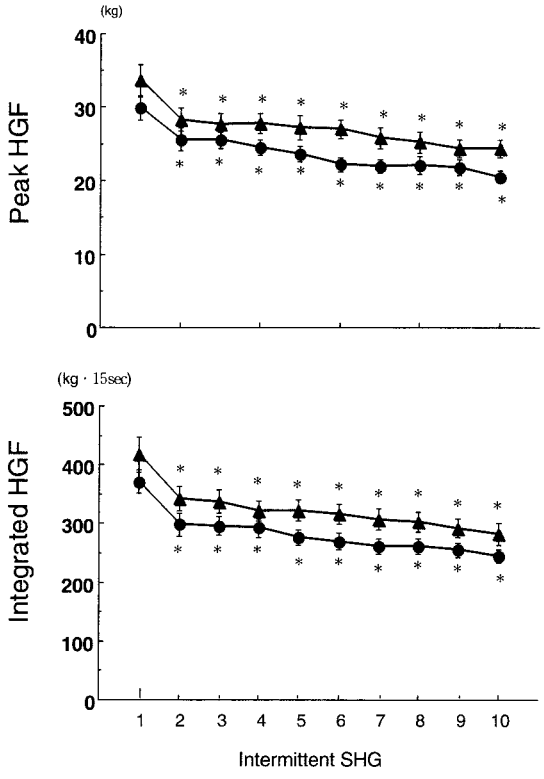

Fig. 1　Comparison of peak and integrated handgrip force between dominant and nondominant arm during intermittent static handgrip exercise.
▲, dominant arm; ●, nondominant arm. HGF, handgrip force; SHG, static handgrip. *$p<0.05$, compared to the first static handgrip.

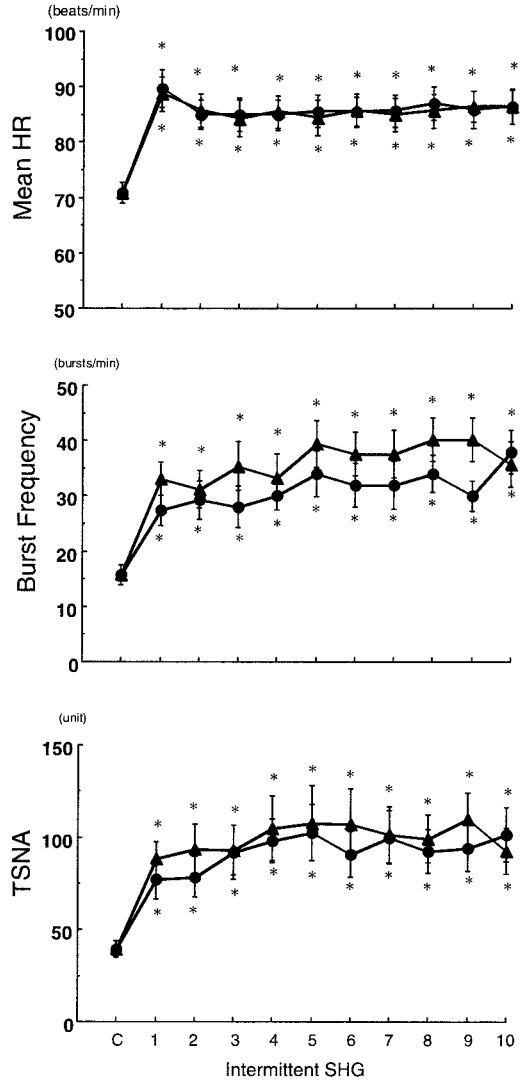

Fig. 2　Comparison of muscle sympathetic nerve activity and heart rate response between dominant and nondominant arm during intermittent static handgrip exercise.
▲, dominant arm; ●, nondominant arm. HR, heart rate; TSNA, total sympathetic nerve activity; SHG, static handgrip. *$p<0.05$, compared to the resting control.

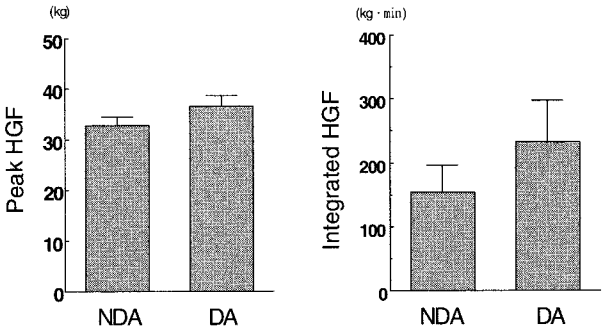

Fig. 3 Comparison of peak and integrated handgrip force between dominant and nondominant arm during ischemic rhythmic handgrip exercise.
HGF, handgrip force; DA, dominant arm; NDA, nondominant arm.

ミックハンドグリップ運動を行なった後の代謝受容器反射について検討した．短時間の強い筋収縮ではMSNA反応の左右差はみられなかったが，1分間の動脈阻血下運動では運動および運動後阻血時のMSNA反応は利き腕運動が非利き腕運動より高くなった．

A　間欠運動

15秒の短時間ハンドグリップ運動では運動の1回目から有意に筋交感神経活動が増加した．運動開始直後のMSNA亢進はセントラルコマンドと筋機械受容器反射が関係する可能性が報告されている[6,29,31]．Herrたち[6]は14秒間の70% MVC運動で運動開始から4－7秒でMSNAが高まることを観察し，これには筋機械受容器反射が関係する可能性を指摘している．本研究の間欠運動は，最大努力で15秒間のハンドグリップを行ない大きな張力を発揮し

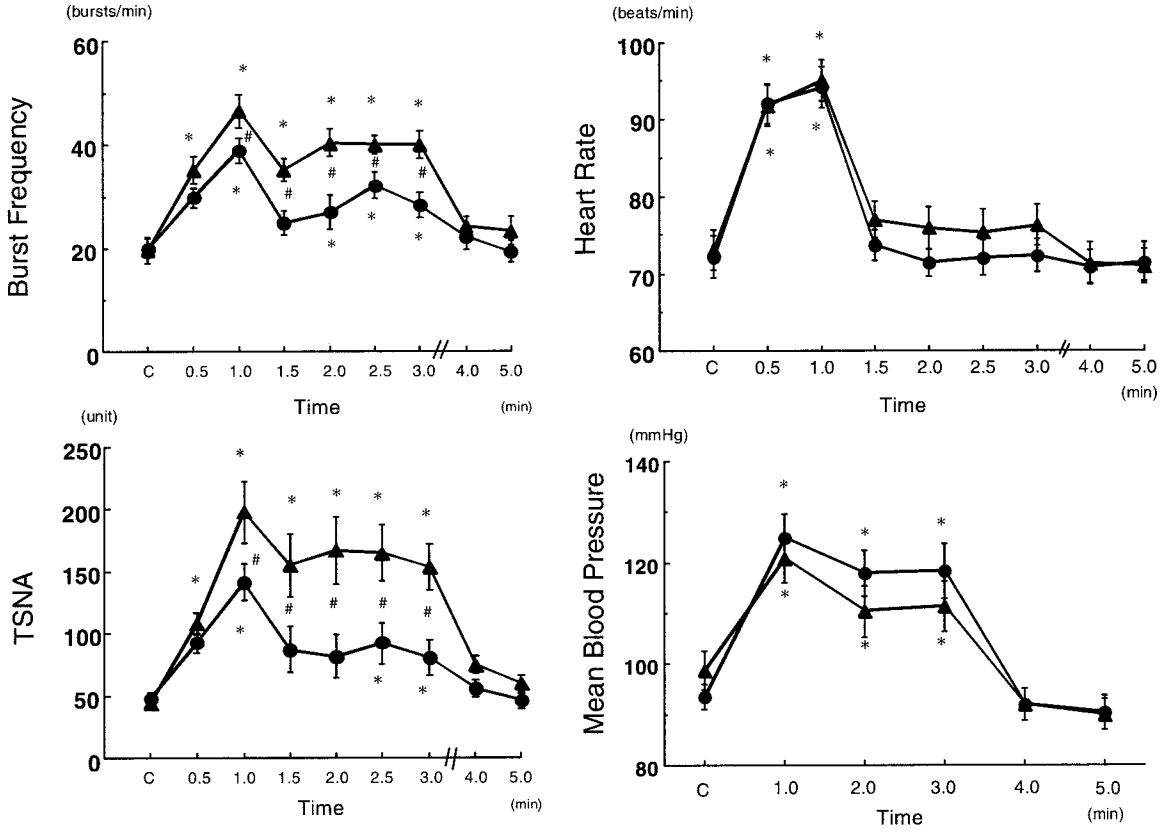

Fig. 4 Comparison of muscle sympathetic nerve activity, heart rate and blood pressure between dominant and nondominant arm during ischemic rhythmic handgrip exercise and post exercise arterial occlusion.
▲, dominant arm; ●, nondominant arm. *, $p<0.05$, compared to the resting control. #, $p<0.05$ dominant vs nondominant arm.

たことから，機械受容器を刺激した可能性が考えられる．しかし，運動時間が15秒で運動後の回復が45秒であったこと，図5に示したように収縮後の運動休止期にはMSNAはすみやかに回復したことから代謝受容器刺激の効果は小さかったと推測される．セントラルコマンドの効果に関して，Victorたち[31]は随意最大握力（MVC）の75%以上の張力発揮で効果がみられるとしている．本研究では75% MVCより僅かに低い張力発揮であったが最大努力で運動するよう指示したことから，セントラルコマンドが筋収縮時のMSNA亢進に関与した可能性が考えられる．

間欠運動において利き腕と非利き腕運動時のMSNA反応の差は認められなかった．この運動パラダイムでは機械受容器反射に関係すると考えられるピーク張力およびiHGFは左右で差は認められなかった（図3）．また，ハンドグリップを行なう際にはいずれの腕でも最大努力で収縮するよう指示し，しかも左右運動時の集中力や疲労の差ができるだけ小さくなるよう左右交互に連続して実施した．したがって，短時間の大きな筋収縮時のMSNA亢進に対する活動筋機械受容器反射とセントラルコマンドの効果は左右で差がみられなかったと考えられる．

間欠運動では，利き腕，非利き腕運動ともに運動回数が進むに従いピーク張力，iHGFが低下したにも関わらず，高いMSNAが持続し，発揮張力とMSNA反応の間に乖離が生じた（図1，2）．この

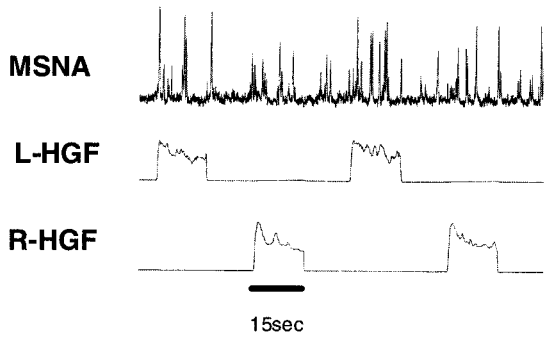

Fig. 5　A portion of neurogram and handgrip forces recordings during intermittent static handgrip exercise.
MSNA, muscle sympathetic nerve activity; L-HGF, left handgrip force; R-HGF, right handgrip force.

原因として，1）運動を最大努力で行なうよう指示したことから大きなセントラルコマンドが最初から最後まで発揮された[31]，2）筋疲労に対する末梢からの求心性神経活動に対抗して中枢からの運動神経活動が増強した[2,19]，3）活動筋の代謝に伴う水素イオン濃度の上昇やアラキドン酸生成物のブラジキニンなどが筋機械受容器を感作し，反射入力が増強された[5,13]ことが考えられる．

B　代謝受容器反射

MSNAに対する代謝受容器反射の効果は1分間の動脈阻血下での最大努力リズミックハンドグリップ運動で検討した．30% MVCの静的ハンドグリップ運動の場合，代謝受容器反射が認められるまでに30-60秒要する[7,24]が，筋収縮張力が高くなるとMSNA亢進は早まり，最大努力の静的ハンドグリップ運動では20秒でMSNAが高まる[4]．リズミックハンドグリップでは，低強度の場合，代謝受容器反射反応は顕著ではないが，収縮張力が高くなると，この反応は充分に生じ，動脈阻血下で同じ張力を発揮している場合には，静的運動に比べて顕著である[17,26,30]．したがって，これらの先行研究の結果を踏まえると，今回用いた1分間の律動的運動は活動筋代謝受容器を充分に刺激したと考える．

運動および運動後阻血時のMSNA-BFおよびTSNAはともに利き腕運動で高値を示したが，運動後阻血時の血圧および心拍数には差が認められなかった．左右でMSNA反応が異なった原因としては，1）代謝受容器刺激物質量（濃度）に差があった可能性が考えられる．しかし，今回は筋組織pHなどの代謝指標を測定しなかったもののハンドグリップ運動の総作業量は両側で差が認められなかったことから，代謝受容器刺激に大きな差があったとは考え難い．2）利き腕と非利き腕で筋線維タイプ分布の異なる可能性．速筋線維分布の高い筋収縮時の血圧反応は分布の低い筋の収縮に比べて大きいことが報告されている[1,33]．また，Saito[14]はハンドグリップ運動と底屈運動時の筋交感神経活動を比較し，速筋線維分布が多いとされる前腕運動（ハンドグリップ）の筋交感神経反応が低屈運動よりが高くなったと報告している．本研究に参加した被験者の利き腕調査では，「大きな力を発揮する側の腕」として利き腕をあげたものがほとんどであった．このような日常生活での使用頻度や使用状況の違いが利

き腕と非利き腕の筋線維分布割合に差をもたらしているかもしれない．3）交感神経活動記録部位の影響．本研究では左脛骨神経から交感神経活動を記録した．運動時のMSNA反応はの四肢で同じとされるが[3,12,22,32]，交感神経活動の指標となるノルエピネフェリン産生量は活動脚と非活動脚で異なる[21]．また，皮膚交感神経活動の指標となる汗腺反応が左右で異なる[10]ことが報告されていることから，MSNA記録を左側脚でおこなったことによる差異も考えられる．この点については今後の課題である．

C　先行研究との比較

運動時の代謝受容器反射は非利き腕にて高くなったと報告したSinowayたち[26]の結果と本研究結果とは異なった．彼らは，両側の運動時の筋組織pHを比較し同程度のであったにもかかわらず，両側間で差が認められたと報告した．本研究では代謝の指標となるpHや乳酸値は測定していないが，ハンドグリップ運動時の運動量に左右差は認められなかったことから，代謝レベルに大きな差がないと考えられる．したがって，Sinowayたち[26]の結果と異なった原因の一つは，彼らはボディービルダーや健常者など異なるグループを用いて検討しており，測定対象群の特性の違いが影響した可能性が考えられる．

動脈阻血下のリズミック運動に対して随意最大努力で行なった15秒間の間欠的ハンドグリップ運動では左右のMSNA反応に差がみられなかった．これはSaitoたち[20]の報告と一致した．Seals[23]は最大握力の40%以上の静的ハンドグリップ運動では発揮張力に関係なく，疲労困憊時点では交感神経活動は同じレベルに達すると報告している．このことは，筋疲労に対して全力を発揮した時と今回実施した間欠的最大努力静的ハンドグリップ運動時では上位中枢からのMSNAに対する効果が同じである可能性を示唆し，この効果が左右運動の差を認めなかった要因であるかもしれない．

D．トレーニングの影響

Sinowayたち[27]，Rayたち[11]は，ハンドグリップ運動のMSNA反応が利き腕より非利き腕で高くなったという結果[26]に基づいて，MSNAに対するトレーニング効果を非利き腕のハンドグリップ運動トレーニングで検討した．その結果，いずれの研究においても利き腕，非利き腕運動のMSNA変化は認めなかった．これに対し，Somersたち[28]は右腕ハンドグリップ運動を用いた持久トレーニングを行ない，静的ハンドグリップ運動時のMSNA反応を比較した結果，右腕運動時のMSNAが有意に低下したことを認めた．しかし，彼らは利き腕については言及しなかった．このように，ハンドグリップ運動を用いた運動時のMSNAに対するトレーニング効果が報告者で異なった背景には，MSNAが運動強度や時間の影響を受けるだけでなく，左右で代謝受容器反応が異なることと関係する可能性が考えられる．しかし，本研究で認められた利き腕と非利き腕運動時のMSNA反応の差が，日常的な使用頻度の違い，すなわちトレーニングの差によるのかどうかについてはさらに検討が必要である．

V　結論

ハンドグリップ運動時の筋交感神経反応が利き腕と非利き腕で異なるかどうかを，15秒間の間欠的最大努力静的ハンドグリップ運動と1分間の動脈阻血下最大努力リズミックハンドグリップ運動後で比較した．間欠的ハンドグリップ運動におけるで筋交感神経活動は，安静時よりも増加したが左右差は認められなかった．動脈阻血下のリズミック運動後代謝受容器反射では，筋交感神経活動は増加したが，左右差が認められ，利き腕運動の反応が非利き腕運動より有意に高値を示した．これらの結果から，利き腕と非利き腕運動時の筋交感神経反応は異なり，この差はセントラルコマンドおよび筋機械受容器反射よりも筋代謝受容器反射の差が関与する可能性が考えられた．

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利き腕，非利き腕運動時の筋交感神経活動に対するレジスタンストレーニングの影響

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Effect of Resistance Training on the Muscle Sympathetic Nerve Responses During Handgrip Exercise

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Summary

Previously, we observed that the metaboreflex increase in muscle sympathetic nerve activity (MSNA) during handgrip exercise was greater in the dominant arm (DA) than in the nondominant arm (NDA) (J Exercise Sports Physiol 13: 29-37, 2006). This study tested whether the MSNA response during handgrip exercise in the NDA is enhanced when forearm use is increased. Ten volunteers trained with a unilateral NDA handgrip exercise, which consisted of three sets of ten 10-second static contractions with maximal effort, 10 seconds apart, five days per week, for four weeks. The subjects performed rhythmic handgripping under forearm circulatory arrest with a maximal effort followed by two minutes of post-exercise arterial occlusion (PEAO) before and after training. MSNA was recorded from the tibial nerve using a microneurography and was expressed as the total activity (bursts × burst area). Handgrip force, heart rate (HR), and blood pressure were measured simultaneously. MSNA during the last 30 sec of the handgrip increased to 425 % for the DA and 337 % for the NDA from the resting value before training and to 485 and 374 %, respectively, after training. The higher levels persisted during PEAO and was greater for the DA than for the NDA, while no significant difference was observed during exercise. The force output of the handgrip during exercise increased in the NDA after training, but not in the DA. No difference in the HR or blood pressure response between the arms during exercise and PEAO was found before and after training.

This study demonstrated that the lower MSNA response to muscle contraction in the NDA did not increase after resistance training, suggesting that it is impossible to change the difference between the DA and NDA with short-term resistance training.

Key words: central command, metaboreflex, dominant & nondominat arm

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Ⅰ．緒言

運動時の筋交感神経活動増加にはセントラルコマンドおよび活動筋感覚受容器反射入力が大きな役割を果す[8,11,14,20]．我々は利き腕と非利き腕運動時の筋交感神経活動を比較し，利き腕運動時の筋交感神経活動が非利き腕運動より高くなり，その差にはセントラルコマンドや活動筋機械受容器よりも活動筋代謝受容器反射入力が深く関わっていることを認めた[15]．この差が生じた原因の一つとして，利き腕と非利き腕の日常的な使用頻度の違いが考えられた．

活動筋代謝受容器反射は活動筋組織における無酸素解糖系活動あるいは筋組織の水素イオン濃度の増加が要因の一つと考えられている[20,24]．例えば，持久トレーニングは運動時の筋交感神経活動反応を抑制するが，これは持久トレーニングに伴い有酸素代謝機能が高まったためと考えられている[21,22]．これに対し，有酸素代謝機能に対して明確な効果を及ぼさないレジスタンストレーニングについて，RayとCarrasco[12]は30% MVCの静的ハンドグリップ運動で効果を検討し，運動時の筋交感神経活動反応に対する有意な効果を認めなかった．彼らが，効果を認めなかった理由として，通常用いられるレジスタンス運動負荷に比べて低い負荷を用いたことが考えられる．

運動時の筋交感神経活動反応は速筋線維分布割合の低い筋群に比べて高い筋群運動時の筋交感神経活動反応が高くなること[13,28]，同様に，速筋線維分布割合の高い人の運動時昇圧反応は分布割合の低い人に比べて大きいことが報告されている[2]．また，運動時の高いセントラルコマンドや発揮筋力は筋交感神経活動反応を増強する[25,26]．これらの結果から，高強度レジスタンストレーニングは筋力発揮や無酸素代謝機能を高め，運動時の筋交感神経活動反応を亢進させる可能性が考えられる．

本研究では，非利き腕運動の筋交感神経活動反応が利き腕運動に比べて低くなった背景には日常の使用頻度差が関係すると考え，高強度レジスタンストレーニングを負荷することで日常的な使用頻度差の解消と筋力向上が非利き腕運動の筋交感神経活動反応を高める，との仮説を検証することを目的とした．

Ⅱ．方法

A．被験者

健康な右利き成人男子10名を対象とした．彼らは先に報告した研究[15]の被験者の一部である．彼らの平均年令，身長，体重はそれぞれ22.5±1.5（SD）歳，168.1±5.3cmおよび64.3±14.4kgであった．実験に先立ち，研究の目的，危険性について被験者に十分周知した上で，研究に参加する旨の承諾を得た．本研究は「豊田工業大学ヒトおよび動物を対象とする研究」，審査委員会の承諾を得，ヘルシンキ宣言に則り実施した．

B．運動：動脈阻血下のリズミック運動

活動筋代謝受容器反射を比較する目的で動脈阻血下で1分間40回の頻度で最大努力の律動的ハンドグリップを実施した．運動は2分間の安静後，運動開始5秒前に上腕部に巻いたカフを200mmHgに加圧し，運動を開始した．ハンドグリップは随意最大努力で最後まで運動するよう指示，さらに加圧を運動後2分間持続した．カフ圧解除後は2分間の回復をとった．このテストをトレーニング前後において実施し，左右の比較を行なった．測定は仰臥位で，室温24±1℃の条件で行なった．

C．トレーニング

トレーニングは非利き腕で行ない，利き腕については，ラケットスポーツなど，通常より使用頻度が多くなる活動を避け，日常生活を送るよう配慮させた．トレーニング内容は10秒間の最大努力静的ハンドグリップ運動を10秒間の休憩を挟んで10回繰り返す手順を1セットとし，1日3セット，週5回実施した．トレーニング期間は4週間とし，握力計を用い，自宅で実施した．被験者には日記形式で一回毎のピーク握力を休息時に記録させ，トレーニング実施状況を確認した．

D．筋交感神経活動

筋交感神経活動は微小神経電図法により左膝窩部脛骨神経より記録した．軸直径0.1mmのタングステン針電極を無麻酔経皮的に膝窩部脛骨神経の筋神経束に刺入し，下腿三頭筋支配の筋交感神経活動を導出した．筋交感神経活動の同定は，心拍に同期した自発性のバースト活動であること，呼吸停止やヴァルサルバ手技で活動が亢進すること，音による

覚醒刺激に対しバースト発射リズムが乱れないことを基準にした．とりだした神経活動は作動型前置増幅器で1000倍に増幅し，バンドパスフィルターを通してさらに50－100倍増幅した．神経活動はアナログ積分器を通し，積分（時定数0.1秒）した．積分した電位をアナログ／デジタル変換し，200Hz（Biopac MP100，USA）でパーソナルコンピュータに取り込み，測定後解析した．

E．その他の測定

心拍数は胸部から誘導した心電図R-R間隔より求めた．血圧は指動脈血圧（フィナプレス）により測定した．呼吸運動は熱線流量計（RT-Hミナト医科学）を装着した呼吸マスクにより監視した．運動時には活動筋以外の筋を収縮しないように注意するとともに，呼吸停止や怒積を行なわないよう注意した．これらの測定手順に慣れるため実験に先立つ別の日に測定と同様の手順で練習を行なった．

最大握力は測定前に立位で2回実施し，高い値を最大握力とした．前腕最大周囲長は立位で腕を水平に伸ばし，手掌面を垂直に，手指を伸展した状態で測定した．

F．測定手順

被験者が来室後，最大前腕周囲径，最大握力を測定した．その後測定用電極等を装着し，横臥位にて筋交感神経活動を導出し，その後測定を開始した．トレーニング前の測定はトレーニング開始の2週間前から二日前の間に実施した．トレーニング後はトレーニング停止後二日から1週間以内に実施した．

G．解析

筋交感神経活動：筋交感神経活動積分波形から筋交感神経活動バースト数とバースト面積を求めた．実験毎に神経電位が異なるため，あらかじめ安静時の筋交感神経活動バーストピークの最大値を20単位になるよう基準化し，バースト数とバーストの面積を計測した．

安静2分間および回復期は1分毎に，動脈阻血下運動および運動後動脈阻血時の解析は30秒間毎に行なった．いずれの場合にも1分間のバースト数（MSNA-BF）と総バースト活動（バースト総面積：TSNA）として定量化した[15]．心拍数は筋交感神経活動と同様の時間間隔で，血圧は1分間隔で解析した．

ハンドグリップ張力：ハンドグリップ運動時のピーク張力（pHGF）および仕事量を計測した．仕事量はハンドグリップ張力曲線で囲まれた面積（ハンドグリップ積分値：iHGF）で表わした．一回目のハンドグリップ張力が1 kgを超えた時点から最後のハンドグリップ張力が1 kgに減衰するまでのiHGFを計測した．

H．統計処理

トレーニング前後および左右の最大筋力，ハンドグリップピーク張力および仕事量はWilcoxon test用いての比較した．運動および動脈阻血下運動の筋交感神経活動，心拍数，血圧反応のトレーニング効果および左右比較は繰り返しのある三元配置分散分析で検定し，有意の場合にはNewman-Keule testまたはWilcoxon testを用いて差を検定した．結果は平均値と標準誤差で示した．危険率5％以下を有意と判定した．

Ⅲ．結果

A．ハンドグリップ張力および仕事量

トレーニング前後において非利き腕（トレーニング側），利き腕（非トレーニング側）の最大握力差は認められなかったが，トレーニング後，非利き腕は8.7%，非利き腕は11.5%，ともに有意に増加した（図1）．

非利き腕の最大周径はトレーニング後有意に増加したが，利き腕の変化は認められなかった．しかし，トレーニング前後において，利き腕の最大周径は非利き腕より大きかった（図1）．

B．阻血下のリズミック運動

トレーニング後，非利き腕の阻血下リズミック運動の仕事量（iHGF）は，13.3%増加したが，利き腕は変わらなかった．トレーニング前後において，仕事量の左右差は認められなかった（図2）．

C．筋交感神経活動

MSNAは運動開始30秒から有意に増加し，運動後阻血では運動時より僅かに低下したが高値を持続した（図3）．

分散分析の結果，トレーニング効果は認められなかったが，左右差が認められた．左右差に関する事

後検定の結果，動脈阻血2分間の平均MSNA-BFおよびTSNAはトレーニング前および後ともに利き腕である非トレーニング側の反応が非利き腕であるトレーニング側より高かった．これに対し，安静および運動時のMSNA-BF，TSNA反応の左右差は認められなかった（図4）．

D．心拍反応

心拍数は運動とともに増加したが，運動後阻血時には安静値レベルにまで低下した．分散分析の結果，心拍反応に対するトレーニング効果および左右差は認められなかった（図5）．

E．血圧反応

血圧は運動時に増加し，運動後動脈阻血時には安静値より高値を持続したが，左右の昇圧反応に差は認められなかった．トレーニング前後の安静血圧および運動，運動後動脈阻血の昇圧反応に差は認められなかった（図5）．

Ⅳ．考察

A．代謝受容器反射

利き腕に比べて低い非利き腕の筋交感神経活動代謝受容器反射がレジスタンストレーニングで高まるのではないかとの仮説で，4週間のハンドグリップレジスタンストレーニングを行なった．その結果，最大ハンドグリップ張力，動脈阻血下ハンドグリップ運動仕事量は有意に増加したが，非利き腕の低い代謝受容器反射の増加は認められなかった．運動後動脈阻血時にはセントラルコマンドは関与しないた

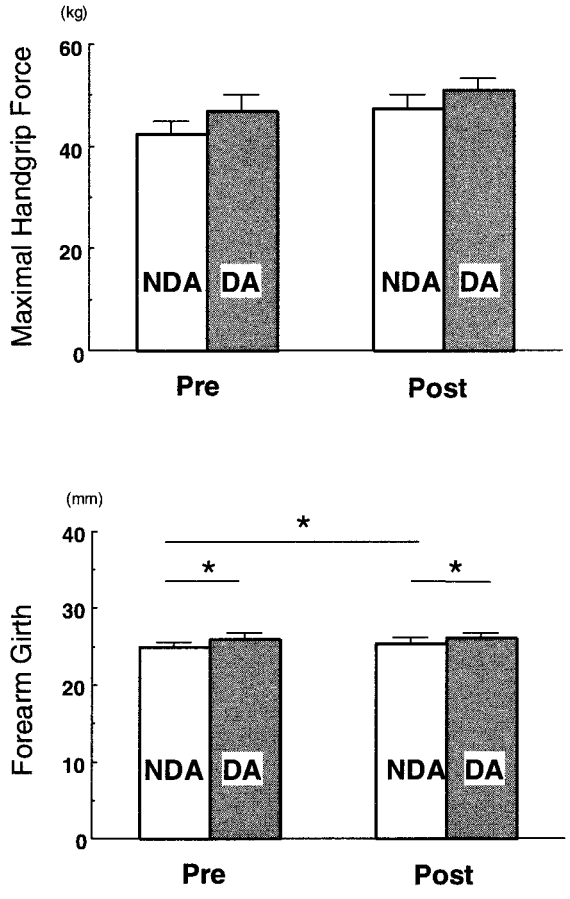

図1　Comparison of the maximal handgrip force and forearm girth between the dominant and nondominant arms pre- and post-training. NDA, nondominant arm; DA, dominant arm.
*p<0.05, pre-training vs. post-training or domnant vs. nondominat arm.

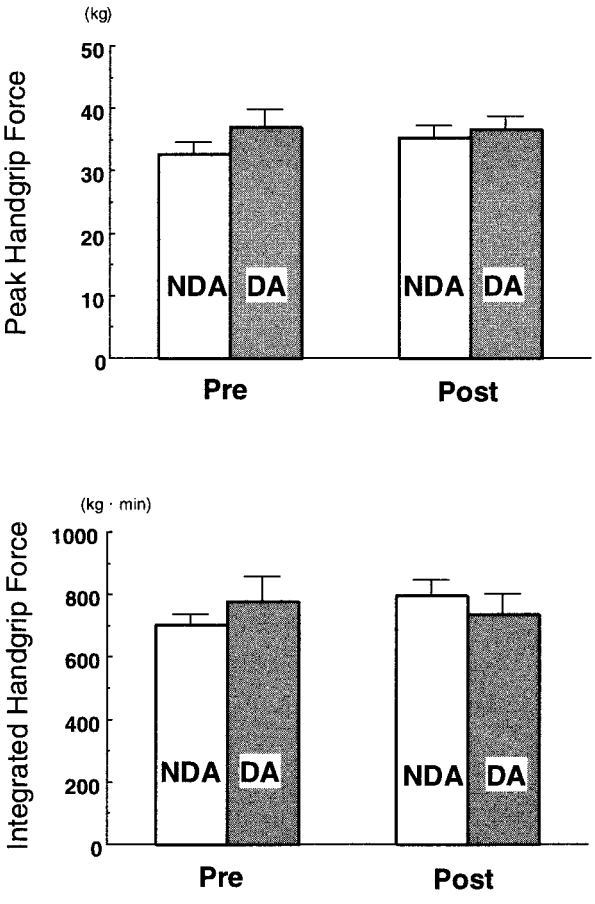

図2　Comparison of the peak and integrated handgrip force between the dominant and nondominant arms during ischemic rhythmic handgrip exercise pre- and post-training.
NDA, nondominant arm; DA, dominant arm.

め[8]，筋交感神経活動増加は筋感覚受容器からの求心性入力増加によると考えられる．さらに，この場合，筋機械受容器の刺激効果はほとんど考えられないので[5]，左右差を生じさせた最も大きな要因は代謝受容器からの求心性入力の差によると考えられる．代謝受容器反射は活動筋量の影響を受ける[19]が，前腕最大周径から推定した活動筋量の差は２％であり，この影響は小さいと考えられる．第二に，代謝受容器刺激の原因となる代謝生成物質の量に違いがみられた可能性[16,24]．本研究では活動筋の代謝水準を示す水素イオン濃度，無機リンや乳酸濃度を測定していないが，非利き腕と利き腕運動の仕事量に統計的差はみられず，有意ではないがむしろ非利き腕の仕事量平均値はトレーニング後，高くなった．したがって，この場合，代謝受容器刺激の差をもたらすほど代謝水準に差があったとは考えられない．第三は，筋線維組成および筋感覚受容器の感受性が左右で異なる可能性．運動性昇圧反応は下肢より上肢で，あるいは遅筋線維より速筋線維分布優位の骨格筋群運動で高くなる[4,28]．また，前腕骨格筋線維組成分布の差異については明らかではないが，利き腕と非利き腕の前腕筋代謝機能の差が認められ[10]ており，これが長期に渡る日常の使用状況の違いから生じている可能性は考えられる[6,10]．第四は，末梢および中枢性神経機構の影響．交感神経中枢からの下行神経線維は両側に分岐して，自律神経遠心性神

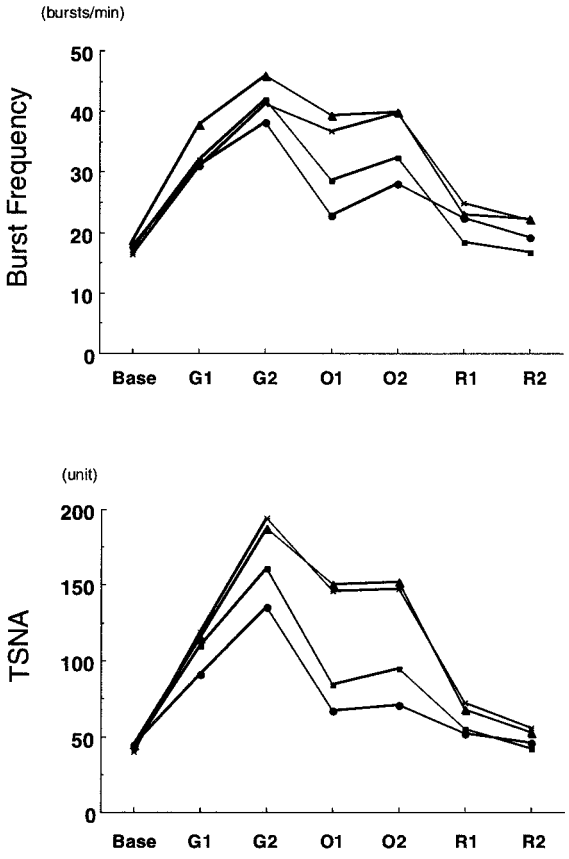

図３ Changes in muscle sympathetic nerve activity in dominant and nondominant arms at rest, during ischemic exercise, and PEAO and recovery pre- and post-training. The top and bottom panels show the MSNA burst frequency and total activity. ▲, dominant arm, pre-training; ●, nondominant arm, pre-training; ×, Dominant arm, post-training; ■, nondominant arm, post-training

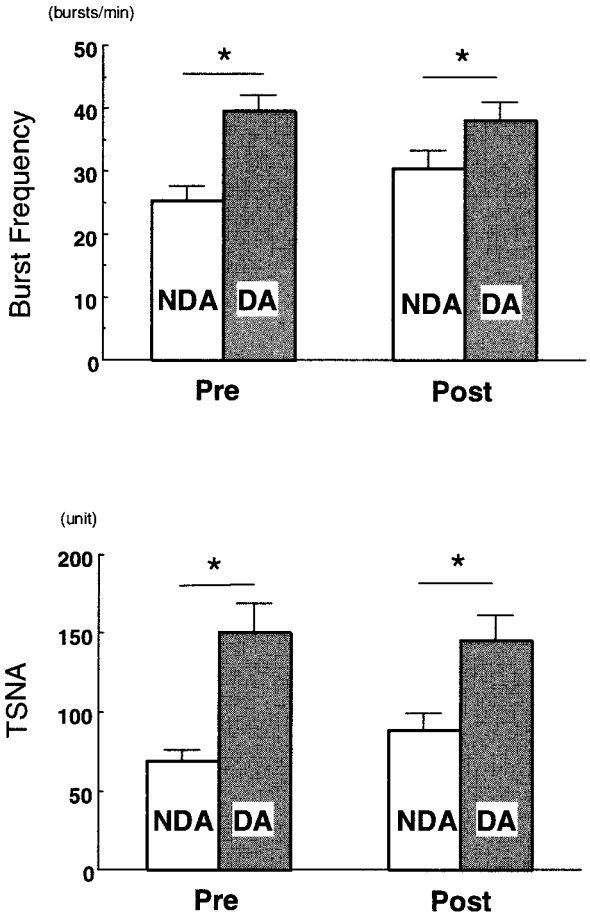

図４ Comparison of the burst frequency and TSNA between the dominant and nondominant arms during two minutes PEAO pre- and post-training.
TSNA, total sympathetic nerve activity.
*$p<0.05$, domnant vs. nondominat arms.

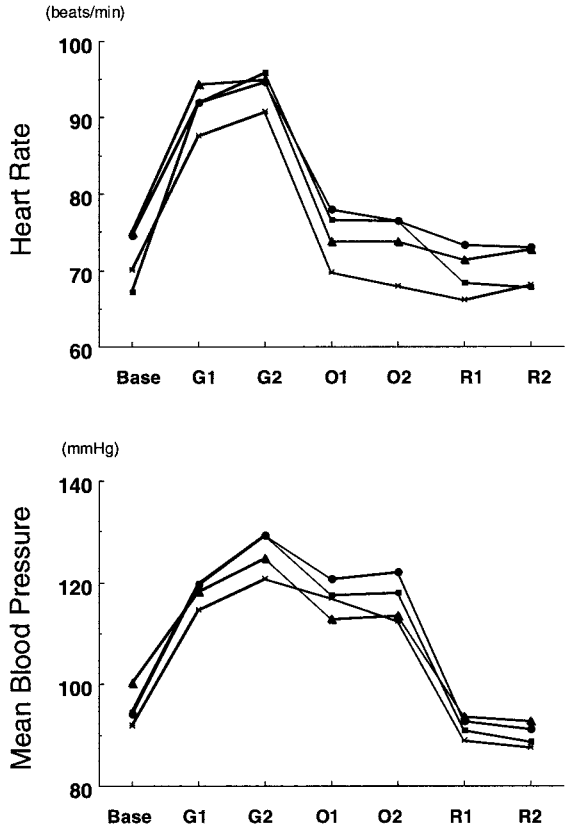

図5　Changes in the heart rate and mean blood pressure in the dominant and nondominant arms at rest, during ischemic exercise, and PEAO and recovery pre- and post-training. The symbols are the same as in Fig. 3.

経活動を地域性に支配し，両側の反応は異なる[3]ことが報告されている．さらに，筋からの求心性線維は対側だけでなく同側にも上行し，両側の線維数は異なる[9]．本研究では，全て左脛骨神経から節後遠心性筋交感神経活動を記録したことから，代謝受容器反射の左右差を生じさせた背景に，これらの遠心性自律神経および体性神経求心性機構が関係した可能性は否定できない．

B．運動時の筋交感神経活動

筋交感神経活動の代謝受容器反射に左右差が認められたのに対し運動時の反応には差は認められなかった．この理由のとしては，最大努力で運動を行なったことから末梢からの反射入力による交感神経活動の左右差が強いセントラルコマンドによる筋交感神経活動亢進効果[25,26]によって隠蔽されたた可能性がある．

C．トレーニング効果

非利き腕の最大握力はトレーニング後増加し，動脈阻血運動の仕事量も有意に増加した．しかし，非トレーニング側である利き腕は，最大握力は増加したが，仕事量は変化しなかった．8週未満の短期間の高強度レジスタンストレーニングによる筋力増加は皮質からの運動神経活動および活動運動単位の増加，神経-筋連関の促通が主体で，筋肥大，速筋線維分布割合の増加は比較的小さい[6]．したがって，今回の4週間のハンドグリップレジスタンストレーニングでは筋の器質的な変化は小さく，皮質からの運動神経活動および活動運動単位の増加，神経-筋連関の促通が主な要因と考えられ[18]，非トレーニング側の最大筋力の増加は中枢および神経筋連関の向上効果が大きいと考えられる．これに対し動脈阻血下運動仕事量は利き腕では増加しなかったがトレーニング側である非利き腕は有意に増加した．おそらく，ハンドグリップ運動を繰り返すトレーニングを行なったことにより，効率的な筋収縮による運動効率の向上[18]，速筋線維の酸化代謝能の改善[23]および末梢性筋疲労に対する耐性向上などが関係したと考えられる．

D．筋交感神経活動と血圧反応

トレーニング前および後において，利き腕の運動後動脈阻血時筋交感神経活動が非利き腕より高値を示したにもかかわらず，平均動脈血圧の差は認められなかった．安静および運動時の交感神経活動は骨格筋，皮膚，内臓などで異なる[17]ことから，骨格筋血管床以外の末梢血管抵抗とのバランスにより，全体として体血圧が一定に保たれ，差が認められなかったと考えられる．

V．まとめ

利き腕に比べて非利き腕の低い代謝受容器反射はレジスタンストレーニングで高まるのではないかのとの仮説で，4週間のハンドグリップレジスタンストレーニングを行なった．トレーニングの結果，最大ハンドグリップ張力，動脈阻血下ハンドグリップ運動仕事量は有意に増加したが，利き腕に比べて非利き腕の低い代謝受容器反射はトレーニング後も変わらず，低値であった．このことは，活動筋代謝受容器反射に対する短期間のレジスタンストレーニング効果が小さいことを示す．したがって，代謝受容

器反射の左右差が生じた背景には長期の使用頻度の違いと，それにともなう前腕筋組成や筋感覚受容器機能の差が生じている可能性が示唆され，この差は，4週間程度のトレーニングでは解消できないと推察される．

謝辞

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Time-dependent modulation of arterial baroreflex control of muscle sympathetic nerve activity during isometric exercise in humans

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Ichinose, Masashi, Mitsuru Saito, Narihiko Kondo, and Takeshi Nishiyasu. Time-dependent modulation of arterial baroreflex control of muscle sympathetic nerve activity during isometric exercise in humans. *Am J Physiol Heart Circ Physiol* 290: H1419–H1426, 2006. First published November 11, 2005; doi:10.1152/ajpheart.00847.2005.—We investigated the time-dependent modulation of arterial baroreflex (ABR) control of muscle sympathetic nerve activity (MSNA) that occurs during isometric handgrip exercise (IHG). Thirteen healthy subjects performed a 3-min IHG at 30% maximal voluntary contraction, which was followed by a period of imposed postexercise muscle ischemia (PEMI). The ABR control of MSNA (burst incidence and strength and total activity) was evaluated by analyzing the relationship between spontaneous variations in diastolic arterial pressure (DAP) and MSNA during supine rest, at each minute of IHG, and during PEMI. We found that *1*) the linear relations between DAP and MSNA variables were shifted progressively rightward until the third minute of IHG (IHG3); *2*) 2 min into IHG (IHG2), the DAP-MSNA relations were shifted upward and were shifted further upward at IHG3; *3*) the sensitivity of the ABR control of total MSNA was increased at IHG2 and increased further at IHG3; and *4*) during PEMI, the ABR operating pressure was slightly higher than at IHG2, and the sensitivity of the control of total MSNA was the same as at IHG2. During PEMI, the DAP-burst strength and DAP-total MSNA relations were shifted downward from the IHG3 level to the IHG2 level, whereas the DAP-burst incidence relation remained at the IHG3 level. These results indicate that during IHG, ABR control of MSNA is modulated in a time-dependent manner. We suggest that this modulation of ABR function is one of the mechanisms underlying the progressive increase in blood pressure and MSNA during the course of isometric exercise.

arterial blood pressure; sympathetic nervous system; integrated circulatory regulation

DURING THE COURSE of isometric exercise, blood pressure, heart rate (HR), and sympathetic nerve activity (SNA) all increase progressively. These cardiovascular responses are thought to be induced by gradual activation of both central command (40) and afferent nerve endings within the working skeletal muscles that are sensitive to the mechanical and metabolic changes that occur during the exercise (28, 29, 39). They are also reportedly modulated by the aortic and carotid baroreflexes (39, 40), although arterial baroreflex (ABR)-mediated cardiovascular control, especially control of SNA during isometric exercise, is not fully understood.

Scherrer et al. (44) showed that ABRs more effectively buffer reflex increases in muscle SNA (MSNA) during isometric handgrip exercise (IHG) than under resting conditions. Moreover, Kamiya et al. (18) reported that ABRs are reset to function at higher arterial pressures, and the sensitivity of their control of MSNA is elevated during both IHG and postexercise muscle ischemia (PEMI). These findings suggest that ABR control of MSNA is modulated during isometric exercise and that time-dependent alterations in ABR function are a key determinant of the MSNA responses during isometric exercise. Consistent with that idea, both the number of MSNA bursts (burst frequency and/or burst incidence) and the MSNA burst strength (amplitude or area of bursts) progressively increase during isometric exercise (42, 43, 46, 47, 51, 52), and both are influenced by ABRs on a beat-to-beat basis (4, 8, 19, 48, 53, 54). Moreover, we recently found that the modulation of the ABR control of MSNA (overall MSNA control) seen during PEMI could be a consequence of altered ABR control of both the occurrence and strength of MSNA bursts (15). Whether and how the ABR-mediated control of the occurrence and strength of MSNA bursts is modulated during isometric exercise have never been examined in humans, however. The purpose of the present study, therefore, was to test our working hypotheses that, in humans, ABR-mediated beat-to-beat controls of the occurrence and strength of MSNA bursts and overall MSNA are all modulated in a time-dependent manner during the course of IHG.

METHODS

Subjects. We studied 13 healthy volunteers (10 men and 3 women) with a mean age of 23 ± 1 yr, a body weight of 62.4 ± 3.1 kg, and a height of 170.1 ± 0.3 cm. None of the subjects was receiving medication, and none smoked. The study, which was carried out in accordance with the Declaration of Helsinki, was approved by the Human Subjects Committee of the University of Tsukuba, and each subject gave informed written consent.

Procedures. After entering the test room, which was maintained at 25°C, each subject adopted a supine position and then performed a maximum voluntary contraction (MVC) using a handgrip dynamometer, from which we determined the 30% MVC. Thereafter, a rapidly inflatable cuff for arterial occlusion was placed on the upper arm, and a microelectrode (see *Measurements*) was inserted manually into the tibial nerve at the popliteal fossa for recording MSNA (43). After MSNA was identified (see *Data analysis* for criteria), the respiratory mask was fitted, and the subject was allowed to rest for at least 15 min before data collection was begun.

The raw data (handgrip force, blood pressure, and MSNA) collected during periods of rest (control), IHG, and PEMI are shown in Fig. 1. Subjects were instructed to maintain a constant rate of breathing (7.5 cycles/min) and a constant tidal volume of 0.7–1.1 liters (previously established as a tidal volume that did not cause dyspnea at a constant respiratory frequency of 7.5 cycles/min) throughout the

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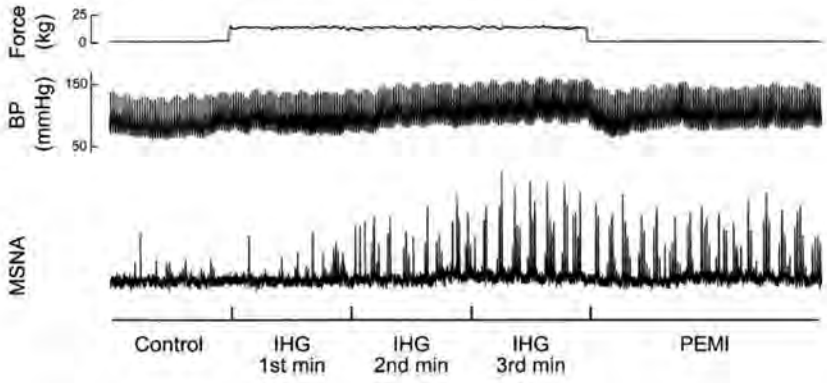

Fig. 1. Raw data showing the recorded variables [handgrip force, blood pressure (BP), and muscle sympathetic nerve activity (MSNA)] during the control period, the isometric handgrip exercise (IHG), and the period of postexercise muscle ischemia (PEMI) in a representative subject.

experiment. Auditory signals and an oscilloscope display of respiratory volume were supplied to assist the subject in this. The purpose of the controlled breathing was to avoid breath holding and Valsalva maneuvers and to keep the effect of breathing on MSNA constant throughout the experiment. Control data were acquired for 4 min before the start of handgrip exercise, after which the subject performed a 3-min IHG at 30% MVC with visual feedback of the achieved force through an oscilloscope display. Five seconds before the cessation of the IHG, the occlusion cuff was inflated to suprasystolic pressure (>240 mmHg) and remained inflated long enough to produce a 4-min period of PEMI. After PEMI, the cuff was deflated. From the 5-min recording made during the recovery period, we used the 4-min-long record starting at 1 min after cuff deflation for analysis.

Measurements. HR was monitored via a three-lead electrocardiogram (ECG). Beat-to-beat changes in blood pressure were assessed by finger photoplethysmography (Finapres 2300; Ohmeda); the monitoring cuff was placed around the middle finger, with the forearm and hand supported so that the cuff was aligned at the level of the heart. The subject wore a mask connected to a respiratory flowmeter (RF-H; Minato Medical Science) for measurement of respiratory flow and tidal volume. The analog signals representing the ECG, blood pressure waveforms, respiratory flow, respiratory volume, and mean voltage neurogram (see below) were continuously recorded on an FM magnetic tape data recorder (MR-30; TEAC). The data were also digitized at a sampling frequency of 400 Hz through an analog-to-digital converter (Maclab/8e; AD Instruments) and fed into a personal computer (Powerbook 1400C; Apple). In addition, individual ratings of perceived exertion (RPE; based on the Borg scale of 6 to 20) were obtained at the end of each minute of IHG (2).

Multiunit muscle sympathetic nerve discharge was recorded using the microneurographic technique. A tungsten microelectrode with a shaft diameter of 0.1 mm and an impedance of 1–5 MΩ was inserted manually by an experimenter into the tibial nerve at the popliteal fossa and then adjusted until MSNA was recorded. The criteria to identify MSNA were spontaneous burst discharges synchronized with the heart beat and enhanced by Valsalva maneuvers or apnea but unaffected by cutaneous touch or arousal stimuli (4, 43, 50). The experimenter did not touch the intraneural electrode once the experimental protocol had begun. The neurogram was fed to a differential amplifier, amplified 100,000 times through a band-pass filter (500–3,000 Hz), and then full-wave rectified and integrated using a capacitance-integrated circuit with a time constant of 0.1 s. The mean voltage neurogram was continuously recorded on FM tape and digitized as described above.

Data analysis. Beat-to-beat heart rate was calculated from the R-R intervals on the ECG. Beat-to-beat systolic and diastolic arterial pressures (SAP and DAP, respectively) were obtained from the arterial pressure waveform. Mean arterial pressure (MAP) was calculated using the equation MAP = DAP + (SAP − DAP)/3.

During the 4-min control period, MSNA bursts were identified by inspection of the mean voltage neurogram while the subject maintained constant breathing. The voltage levels during the periods between bursts were then averaged, and this level was taken as zero. The largest burst occurring during this rest period was assigned a value of 1,000, and MSNA data were normalized with respect to this standard in each subject. The amount of SNA under each condition was expressed as burst frequency (bursts/min) and burst incidence (bursts/100 heartbeats). Burst strength, obtained from the mean area of the MSNA bursts recorded under each condition, was expressed as mean burst strength (arbitrary units). Total MSNA was taken as the product of the mean burst strength and burst frequency. The hemodynamic and MSNA variables were averaged over the 4-min control period, over each minute of the IHG, and over the 4-min PEMI and recovery periods, respectively.

The assessment of ABR modulation of burst incidence, burst strength, and total MSNA has been described in detail elsewhere (15). Briefly, the relationships between DAP and burst incidence, burst strength, and total MSNA during the control period, at each minute of IHG, and during the PEMI and recovery periods were analyzed as follows. *1*) Taking into account the latency from the R wave of the ECG to the sympathetic burst (7), we related the DAP for each individual heart beat to the corresponding MSNA data. Because changes in MSNA correlate closely with changes in DAP, but not with changes in SAP (48), we used DAP in this analysis. *2*) All DAP values measured under each condition were grouped into 1-mmHg bins. In each group, diastoles were inspected to see whether they were associated with an MSNA burst, and we then calculated the percentage of diastoles associated with an MSNA burst (burst incidence per beat). *3*) We used the signal-averaging technique to determine the burst strength and total MSNA for each diastolic-pressure bin (13). The MSNA signals were averaged over a period corresponding to the length of the heartbeat by taking into account the presumed latency from the R wave of the ECG, after which the area under the averaged MSNA signal was calculated. To calculate the burst strength related to each DAP bin (burst strength per beat), only those MSNA signals associated with a burst were selected, and these were averaged to allow us to calculate the area of the averaged MSNA signal using the above-mentioned technique. The total activity related to each DAP bin (total MSNA per beat) was calculated as the area of the averaged MSNA signal created from all the MSNA signals in each bin, whether or not they were associated with an MSNA burst. *4*) The calculated burst incidence, burst strength, and total activity obtained for each DAP bin were plotted against the corresponding DAP, after which linear regression analysis was carried out for each diagram. Because the relationship between MSNA and DAP was often nonlinear at high blood pressures due to complete inhibition of MSNA, regression lines were constructed by using only the linear part of the data. We took the slope of each line as indicating sensitivity of the ABR control of each variable. The points corresponding to the average DAP on the regres-

Table 1. *Arterial blood pressure, HR, and MSNA during the control period, each minute of IHG, and the PEMI and recovery periods*

	Control	IHG1	IHG2	IHG3	PEMI	Recovery
SAP, mmHg	126±3.3†	136±2.8*†	147±3.0*†	161±3.1*	159±2.5*	135±2.5*†
DAP, mmHg	67±2.0†	72±2.1*†	81±2.0*†	92±2.2*†	86±2.8*	69±2.0†
MAP, mmHg	87±2.0†	93±1.6*†	103±1.7*†	115±1.8*	110±2.1*	90±1.6†
PP, mmHg	59±3.3†	64±3.7*†	66±3.7*†	70±3.8*	72±3.4*	66±3.2*†
HR, beats/min	63±3.6	72±3.6*†	75±3.9*†	81±4.5*†	66±3.2	63±2.5
MSNA burst frequency, bursts/min	14.6±1.6†	17.8±1.9†	26.8±3.1*	36.7±2.9*†	29.7±2.3*	15.4±1.7†
MSNA burst incidence, bursts/100 heartbeats	23.1±2.0†	25.0±2.4†	35.8±3.6*†	45.0±2.5*	45.4±3.3*	24.7±2.6†
Mean burst strength, AU	103.0±6.1†	119.3±7.4†	159.2±12.1*	191.6±17.0*†	157.4±10.4*	111.7±10.6†
Total activity (mean burst strength × burst frequency)	1,527±196†	2,215±313†	4,169±537*	6,769±567*†	4,638±464*	1,814±294†
RPE		14.2±0.4	16.6±0.4	19.0±0.3		

Values are means ± SE. PEMI, postexercise muscle ischemia; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; MAP, mean arterial pressure; PP, pulse pressure; HR, heart rate; MSNA, muscle sympathetic nerve activity; RPE, ratings of perceived exertion; IHG, isometric handgrip exercise; IHG1, IHG2, and IHG3 are first, second, and third minute of IHG. *Significant difference from control, $P < 0.05$. †Significant difference from PEMI, $P < 0.05$.

sion lines relating burst incidence or total MSNA to DAP were taken as the prevailing points for a given relationship. Using this approach, we could evaluate ABR control of sympathetic nerve traffic in a way that enabled ABR control of burst occurrence and burst strength to be considered separately. Moreover, if the ABR control of overall MSNA (i.e., total MSNA) is modulated, our approach enables us to examine the underlying relationship between modification of the control of burst occurrence and strength, on the one hand, and modification of the control of total MSNA on the other.

Statistical analysis. Data are presented as means ± SE. Statistical analysis was performed using a one-way repeated-measures ANOVA with Tukey's post hoc test. The characteristics of the ABR relationship between MSNA (burst incidence, burst strength, and total activity) and DAP were determined by least-squares linear-regression analysis. Values of $P < 0.05$ were considered significant.

RESULTS

Basal data. Table 1 shows the changes in arterial blood pressure, HR, and MSNA that occurred during the control period, at each minute during IHG, and during the PEMI and recovery periods. During IHG, the values of SAP, DAP, MAP, pulse pressure (PP), and HR increased progressively. During the subsequent PEMI, the values for SAP, DAP, MAP, and PP were all higher than during the control period, but HR was not different; DAP and MAP were lower than at the third minute of IHG (IHG3), but higher than at the second minutes of IHG (IHG2). At the first minute of IHG (IHG1), there was no significant change from control in any of the MSNA variables. At IHG2, all of the MSNA variables were significantly ele-

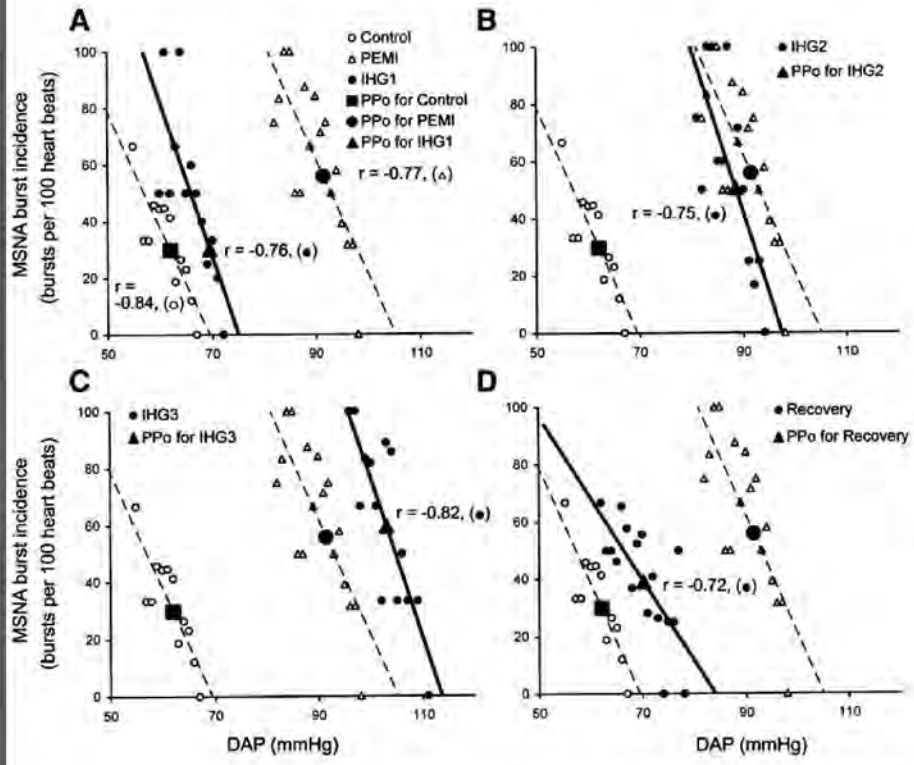

Fig. 2. Linear relationships between MSNA burst incidence and diastolic blood pressure (DAP) during the control period (*A*–*D*, open circles, dashed lines); at the 1st minute of IHG (IHG1; *A*, filled circles, solid line), IHG2 (*B*, filled circles, solid line), and IHG3 (*C*, filled circles, solid line); and during the PEMI (*A*–*D*, open triangles, dashed line) and recovery (*D*, filled circles, solid line) periods in a representative subject. The larger symbols show the prevailing points (PPo) at the indicated times during the experimental protocol.

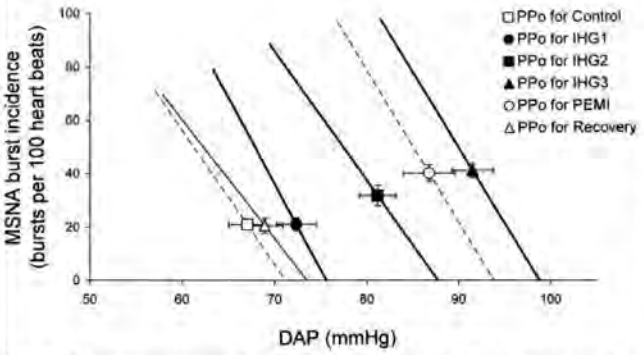

Fig. 3. Group average prevailing points (PPo symbols) with the corresponding mean regression lines relating burst incidence and DAP at the indicated times during the exercise protocol.

vated from control and were increased further at IHG3. During PEMI, all of the MSNA variables remained above control; burst frequency, mean burst strength, and total MSNA were all lower than that at IHG3, whereas burst incidence was comparable to IHG3. During recovery, SAP and PP were still higher than control, whereas DAP, MAP, and HR had returned to control levels. All MSNA variables returned to control levels during the course of the recovery period. RPE gradually increased during IHG, nearly reaching the fatigue level by IHG3.

ABR control of MSNA burst incidence. The linear regression analyses relating burst incidence to DAP for a representative subject are shown in Fig. 2; the group mean prevailing point and the regression lines at each of the indicated times are shown in Fig. 3. The derived variables describing the ABR control of burst incidence are presented for the group in Table 2. All subjects showed significant negative correlations between burst incidence and DAP during the control period, at each minute of IHG, and during the PEMI and recovery periods. During IHG, the linear relationship between burst incidence and DAP was progressively shifted rightward, indicating a time-dependent resetting of ABR operating pressure to higher blood pressures. Then at IHG2, the prevailing point was also significantly shifted upward and was shifted further upward at IHG3. During PEMI, the relationship was shifted back to a blood pressure lower than that at IHG3 but slightly higher than that at IHG2, although the prevailing point remained at the same level as at IHG3. The relationship between burst incidence and DAP and the prevailing point returned to control levels during the recovery period. The slope of the linear regression line relating burst incidence and DAP (sensitivity of ABR control of burst incidence) remained unchanged throughout the experiment.

ABR control of MSNA burst strength. The relation between DAP and burst strength was similar to that between DAP and burst incidence (Fig. 4). During IHG, the linear regression line relating burst strength and DAP gradually shifted rightward. Then at IHG2, it was shifted upward and was shifted further upward at IHG3, as evidenced by the significant increases in mean burst strength (Table 1). During PEMI, the relationship was reset back to blood pressures slightly higher than at IHG2 and was also shifted downward from the IHG3 to the IHG2 level. The relationship between burst strength and DAP returned to control levels during the recovery period. As with burst incidence, the slope of the linear regression line was not significantly changed during the experiment.

ABR control of total MSNA. The linear regression analyses relating total MSNA and DAP for a representative subject are shown in Fig. 5; the group mean prevailing point and regression lines at the indicated times are shown in Fig. 6. The derived variables describing the ABR control of total MSNA are presented for the group in Table 3. All subjects exhibited significant negative correlations between total MSNA and DAP at all of the times examined. As with burst incidence and strength, the relation between total MSNA and DAP shifted progressively rightward during IHG, and the prevailing point was significantly shifted upward at IHG2 and shifted further upward at IHG3. In contrast to burst incidence and strength, however, the slope of the regression line relating DAP to total MSNA became more negative at IHG2 and far more negative at IHG3, indicating increased sensitivity of ABR control of total MSNA. A partial reversal was seen during PEMI. The relation was shifted back to a blood pressure lower than that at IHG3 but slightly higher than at IHG2. The prevailing point was shifted downward from the IHG3 to the IHG2 level, and the slope of the regression line become less negative than at IHG3 and was comparable to that seen at IHG2. The linear relationship between total MSNA and DAP, prevailing point, and those slopes all returned to control levels during the recovery period.

DISCUSSION

The major finding of this investigation is that the ABR control over burst incidence, burst strength, and total MSNA was time dependently modulated during the course of IHG. At IHG1, the linear relationship between DAP and each of the MSNA variables (DAP-MSNA lines) was shifted rightward without significant vertical shift or change in sensitivity of ABR control of MSNA (slope). However, at IHG2, the DAP-MSNA lines were shifted both rightward and upward, and the sensitivity of the ABR control of total MSNA was increased. At IHG3, the DAP-MSNA lines were shifted further rightward and upward, and the sensitivity of the ABR control of total MSNA was increased beyond that at IHG2. Thus the ABR control of MSNA was not uniform throughout the course of IHG.

Table 2. *Derived variables describing the arterial baroreflex control of burst incidence*

	Control	IHG1	IHG2	IHG3	PEMI	Recovery
Slope of incidence line, bursts·100 heartbeats^{-1}·mmHg^{-1}	−5.00±0.40	−6.45±0.86	−4.85±0.51	−5.67±0.33	−5.66±0.51	−4.45±0.39
Correlation coefficient	−0.88±0.02	−0.78±0.03	−0.71±0.02	−0.75±0.02	−0.86±0.02	−0.85±0.02
Prevailing point, bursts/100 heartbeats	21.0±1.55†	21.1±2.37†	31.8±3.69*†	41.3±2.56*	40.2±3.03*	20.6±2.77†

Values are means ± SE. Prevailing point, point on the regression line corresponding to mean diastolic blood pressure. *Significant difference from control, $P < 0.05$. †Significant difference from PEMI, $P < 0.05$.

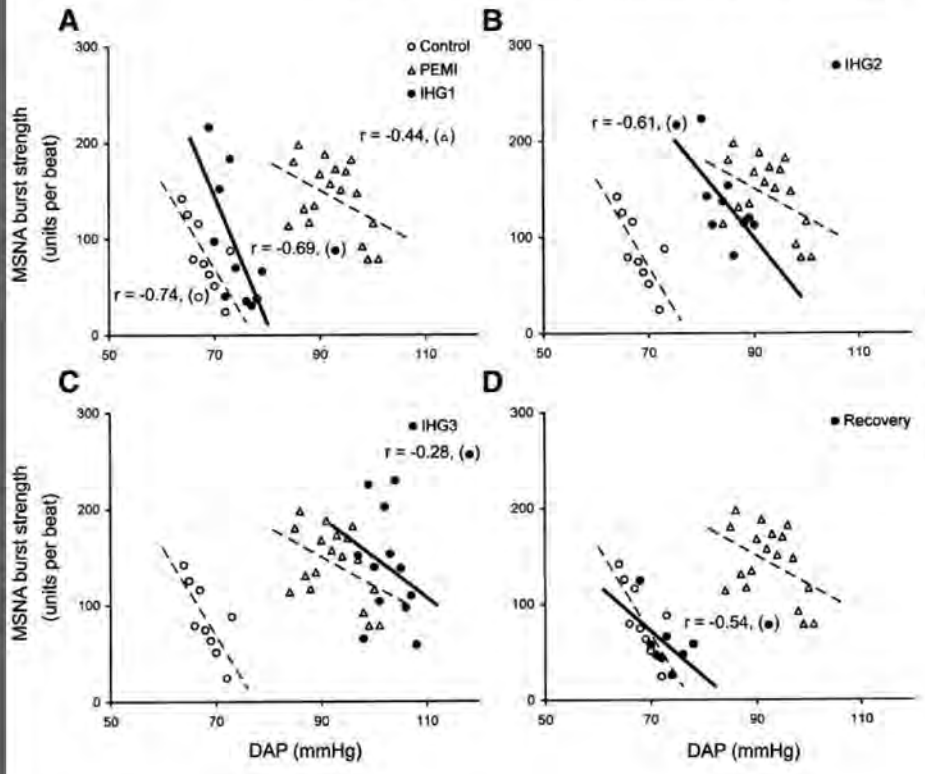

Fig. 4. Linear relationships between MSNA burst strength and DAP during the control period (*A–D*, open circles, dashed line); at IHG1 (*A*, filled circles, solid line), IHG2 (*B*, filled circles, solid line), and IHG3 (*C*, filled circles, solid line), and during the PEMI (*A–D*, open triangles, dashed line) and recovery (*D*, filled circles, solid line) periods in a representative subject.

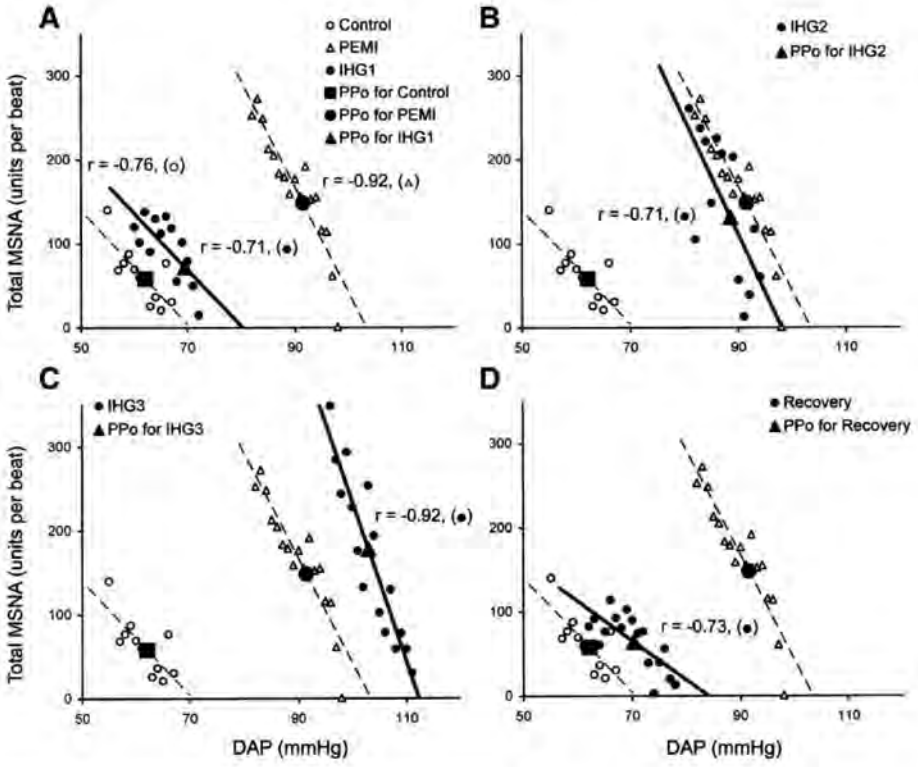

Fig. 5. Linear relationships between total MSNA and DAP in a representative subject. The symbols are the same as in Fig. 2.

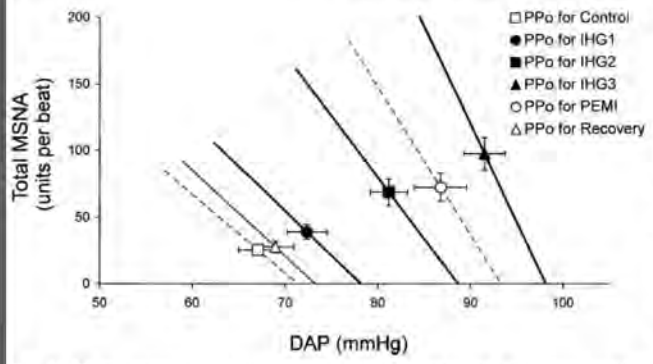

Fig. 6. Group average prevailing points (PPo symbols) with the corresponding mean regression lines relating total MSNA and DAP at the indicated times during the exercise protocol.

It has been suggested that at the onset of exercise, ABR operating pressures are rapidly reset to a higher level (5, 39, 40). The rapid increase in HR and simultaneous increase in blood pressure seen at the onset of exercise are thought to be a consequence of this resetting of ABR (5, 39). In experimental animals (rabbits, cats), moreover, renal SNA increases immediately at the onset of both isometric and dynamic exercise (5, 24, 25), and this, too, is thought to be caused by the rapid resetting of ABR (5, 39, 40). In humans, however, MSNA does not significantly increase until ~60 s after the onset of IHG (at ~30% MVC) (42, 44, 46, 47, 51, 52). Although the mechanism(s) of the difference in the response of renal SNA to the onset of exercise in animals and the response of MSNA in humans is unclear, it could be attributable to species differences (e.g., a difference in adaptation levels to aerobic metabolism) and/or differential regulation of renal SNA and MSNA by exercise (see *Limitations* for more details on this issue). Interestingly, Scherrer et al. (44) showed that within the first minute of IHG (33% MVC), MSNA was increased in subjects receiving nitroprusside to suppress the IHG-induced rise in blood pressure; conversely, MSNA was suppressed in subjects receiving phenylephrine to accentuate the IHG-induced elevation in blood pressure. Those results suggest that the lack of change in MSNA from the resting level at IHG1 is due, at least in part, to ABR control of MSNA. Our finding that the DAP-MSNA relations were shifted rightward (ABR resetting) without a significant vertical shift or change in sensitivity of ABR control of MSNA suggests that, at IHG1, the ABR operating pressures are reset, enabling MSNA to be maintained at the resting level despite an increase in blood pressure.

Rowell and O'Leary (39) hypothesized that two neural inputs, central command and feedback originating within the working muscles, are involved in the resetting of ABR control of SNA during exercise. They postulated that central command resets the ABR operating point to a higher pressure (rightward shift), while the muscle reflex-induced increase in SNA causes a vertical shift in the ABR function curve (relation between blood pressure and SNA). When combined, these two mechanisms would result in parallel upward and rightward resetting such as that seen in the present study. Furthermore, our observation that RPE was 14.2 ± 0.4 at IHG1 suggests that central command was mildly activated at that time, although the muscle metaboreflex would not be, which is consistent with DAP-MSNA relations being shifted only rightward. On the other hand, recent studies investigating the carotid baroreflex control of HR and MAP suggest that central command causes both lateral and vertical shifts in the carotid baroreflex-HR function curve and carotid baroreflex-MAP function curve in humans (10, 33). The difference between those results and ours is likely related to the fact that we investigated ABR control of MSNA, which involves both carotid and aortic baroreflexes. It may be that the effects of central command on ABR control of MSNA differ from its effects on the carotid baroreflex control of MSNA and/or its effects on ABR control of HR and MAP.

Although there is currently no direct evidence, the muscle mechanoreflex is also thought to contribute to the cardiovascular responses at the onset of isometric exercise (29, 39, 40), inducing ABR resetting during isometric exercise in animals (27, 36) and during dynamic exercise in humans (17). Its effect on ABR function during isometric exercise in humans is still unknown, however. The results of the present study suggest that if the muscle mechanoreflex is activated at IHG1 and exerts some effect on ABR function, it may act to reset the ABR operating pressures, but it would not cause a vertical shift of the DAP-MSNA lines or a change in the sensitivity of ABR control of MSNA.

Our findings suggest that activation of the muscle metaboreflex could account for both an upward and rightward shift in the DAP-MSNA relations as well as the increase in the sensitivity of ABR control of total MSNA. This idea is supported by the finding that the time-dependent modulation of the DAP-MSNA relations occurring during IHG persisted during PEMI, a time when the muscle metaboreflex would be activated in the absence of both central command and the muscle mechanoreflex (1, 15, 16, 30–32, 34, 39). The activation of the muscle metaboreflex would presumably be delayed from the onset of IHG by the gradual accumulation of metabolites in the vicinity of the metaboreceptor afferent endings (32, 37, 39, 40, 42, 43, 47, 51, 52), which would account for the almost 60-s latency from the onset of IHG to the onset of sympathetic activation (42, 44, 46, 47, 51, 52). For the same reason, the metaboreflex may not be sufficiently activated at IHG1 to mediate the upward shift in the DAP-MSNA relations and the increase in the sensitivity of ABR control of total MSNA. By IHG2 and

Table 3. *Derived variables describing the arterial haroreflex control of total activity*

	Control	IHG1	IHG2	IHG3	PEMI	Recovery
Slope of total activity line, units·beat^{-1}·mmHg^{-1}	−5.97±0.55†	−6.69±0.65†	−9.24±0.97*†	−14.69±1.76*†	−11.04±0.96*	−6.46±0.83†
Correlation coefficient	−0.86±0.02	−0.73±0.02	−0.75±0.03	−0.77±0.03	−0.88±0.01	−0.82±0.02
Prevailing point, units/beat	25.6±3.21†	39.1±5.39†	69.0±9.94*	97.8±12.04*†	72.5±10.49*	27.9±4.44†

Values are means ± SE. Prevailing point, point on the regression line corresponding to mean diastolic blood pressure. *Significant difference from control. $P < 0.05$. †Significant difference from PEMI. $P < 0.05$.

IHG3, on the other hand, the metaboreflex would be sufficiently activated and involved to mediate the full response.

That the modulation of ABR control of MSNA observed at IHG3 (i.e., rightward and upward shift of DAP-MSNA lines and an increase in sensitivity) was greater than during PEMI indicates that mechanisms other than the muscle metaboreflex (i.e., central command and/or muscle mechanoreflex) are also involved in the modulation of ABR control of MSNA at IHG3. In that regard, our finding that RPE had nearly reached the fatigue level (RPE = 19.0 ± 0.3) at IHG3 indicates that central command should be severely activated by IHG3. According to Victor et al. (52), a mild to moderate level of central command has no effect on MSNA during IHG, whereas MSNA is increased when central command is severely activated. Thus, in addition to the resetting of the ABR operating pressure seen with even mild activation of central command (at IHG1), the severe activation of central command occurring at IHG3 could also account for the upward shift of DAP-MSNA relations and the increase in the sensitivity of ABR control of total MSNA.

During PEMI, the DAP-burst strength and DAP-total activity relations were shifted leftward and downward from those at IHG3 (i.e., back toward control levels). By contrast, the DAP-burst incidence relation was only shifted leftward. That the upward shift in the DAP-burst incidence relation was sustained from IHG3 to PEMI indicates it is mediated mainly by the muscle metaboreflex. In addition, it appears that whereas central command and/or the muscle mechanoreflex may shift the DAP-burst strength and DAP-total MSNA relations both vertically and laterally, they shift the DAP-burst incidence relation only laterally. This suggests that modulation of ABR control of burst occurrence and burst strength by the muscle metaboreflex differs from that by central command and/or muscle mechanoreflex. Although evidence of differential control of the occurrence and strength of sympathetic bursts has been obtained both in animals (20–22) and in humans (14, 15, 19, 49), the mechanism remains unknown (26).

Limitations. There are several limitations to our approach to evaluating ABR control of MSNA on the basis of spontaneous fluctuations in DAP and MSNA. Although a linear relationship between MSNA and DAP has been demonstrated in previous studies (18, 19, 48), spontaneous blood pressure fluctuations are not particularly large, so the ABR stimulus-response range that can be examined using this method is narrow (within 20 mmHg). Although this is a narrower range than is obtained using the neck-chamber technique (6, 16, 53) or invasive pharmacological manipulation (3, 12), a 20-mmHg change in blood pressure is within the physiological range and should be a good reflection of the ABR control of MSNA under physiological conditions. Furthermore, to investigate the reflex effect elicited when two or more inputs are summed (e.g., ABR, muscle reflexes, and central command) it is important to use inputs that are small enough not to cause saturation of the output because of inherent limitations in the effector responses of the system (41). On that basis, our experimental results can be taken as revealing a physiological modulation of the ABR control of MSNA during IHG and PEMI. Moreover, the breathing frequency and tidal volume were fixed throughout the experiment (as far as possible), so the influence of changes in respiration on the modulation of the ABR control of MSNA would have been small.

We also need to consider the potential impact of fixed breathing on the stimulation of peripheral chemoreceptors. It is possible that the fixed breathing prevented the respiratory alkalemia that is reportedly induced by fatiguing isometric exercise (35), and, if so, the activity of peripheral chemoreceptors during IHG in the present study may be greater than during IHG without fixed ventilation. This increase in peripheral chemoreceptor activity may, in turn, enhance the MSNA response and possibly exert an effect on the ABR control of MSNA during IHG. Unfortunately, we measured no blood-gas or acid-base variables, so we can draw no definitive conclusions regarding this issue.

In the present investigation, we measured sympathetic nerve outflow to an inactive skeletal muscle bed and examined the ABR control of that activity during the course of IHG in humans. This does not preclude the possibility that the ABR control of sympathetic outflow and the resultant levels of SNA to other organs differ from the level of MSNA. Because it is known that the regulation of sympathetic outflow to various tissues can be highly differentiated [e.g., differential ABR regulation of renal, lumbar, and adrenal SNA has been demonstrated in rats (45)], our results on MSNA (i.e., levels of SNA and ABR control of SNA) cannot be generalized to SNA in other organs. A more complete understanding of the regulation of SNA mediated by ABR during isometric exercise in humans will require further investigation.

In conclusion, our results show that in human subjects, the ABR control of burst incidence, burst strength, and total MSNA was time dependently modulated during the course of IHG. We suggest that this modulation of ABR function is one of the mechanisms mediating the progressive increase in both blood pressure and MSNA in the course of isometric exercise.

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GRANTS

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FORCE OUTPUT IN MUSCLE FIBERS DURING REPETITIVE STIMULATION IN HUMANS

MIFUYU KAMO[1] and SHIGERU MORIMOTO[2]

Abstract

The evoked force was observed during repetitive electrical stimulation for 3 min on m. vastus medialis. The stimulus frequency was 0.2 Hz, 10 Hz and 20 Hz. The time to peak of twitch was 90.8 ms at 0.2 Hz stimulation. The changes in the evoked force did not represent a constant or a monotonic pattern but were complex at 10 Hz and 20Hz stimulations. At 10 Hz the evoked force represented an initial transient increment (steep peak), then an abrupt decrement followed by a gradual increase (gentle peak) and then a gradual decrease. At 20 Hz the steep phase did not appeared. The magnitude of potentiation was not necessarily large at 20 Hz. These results suggest that a constant discharge rate of motor units cannot maintain constant force development, and "rate coding" is considered to be necessary for keeping a constant force.

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key word : Constant frequency stimulation, Evoked force change, Potentiation

INTRODUCTION

We have reported that the spike interval of motor units (MUs) gradually elongated during the initial period of voluntary isometric contraction at a constant low force level (below 10% maximal voluntary contraction (MVC))[1,2]. Though the developed muscle force was a constant, the MU decreased its firing rate. In order to investigate the contractile property of motor unit at the elongation phase, we observed the changes in the evoked force of muscle fibers under electrical stimulation at two constant frequencies, one high and one low, within motor unit firing rates.

METHODS

Experiments were performed on m. vastus medialis in six volunteers. In a sitting posture ; the knee angle of the subject was set at 90 degrees by strapping the ankle joint with a belt connected to the force transducer. Muscle fibers were stimulated transcutaneously at the motor end-plate zone for 3 min. The electrical stimulation was a square pulse of 1ms duration. To select stimulus intensity, we obtained the relationship between the time to peak of twitch (CT) and stimulus intensity, and employed the minimum level of stimulus intensity at which the CT became constant (even though the intensity increased). We employed three stimulation frequencies, 0.2 Hz, 10 Hz and 20 Hz. The 0.2 Hz was selected to observe twitch responses. The 10 Hz was chosen as it correspond to almost the lowest firing rate of motor units, and 20 Hz because as it correspond to almost the highest. The evoked electrical response (M-wave) was recorded from the fascicle by bipolar surface electrodes. The evoked force and M-wave were recorded on a digital audiocassette tape using a PCM data recorder.

RESULTS

1) Twitch response observation at 0.2 Hz stimulation

CT of twitch response was 75～90 ms in the tested fascicles. In an additional experiment, we observed the twitch response of single MUs with recruitment threshold force (Fth) below 4%MVC by using spike trigger averaging method. The CT of MUs was in the range from 75 to 85 ms.

2) Changes in the evoked force at 10 Hz and 20 Hz stimulation

The evoked force was not constant at both fre-

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quencies. The evoked forces of 10 Hz stimulation were incompletely fused tetanic contraction. The peak evoked force changed complexly, with an initial transient increment, an abrupt decrement, and a gradual increase followed by a gradual decrease. The gentle peak appeared at about 15 secs. On the other hand, at 20 Hz the initial transient peak did not appear, the evoked force steeply fused by 200 ms, and then gently increased for about 10 sec before decreasing. The magnitude of potentiation was not necessarily large at 20 Hz.

DISCUSSION

In general, during percutaneous electrical stimulation MUs are recruited in a reversed sequence compared with voluntary contraction; that is, from fast type to slow type MUs. However, the size and the morphological organization of the axonal branches can also influence the order of activation[3]. In the present study, we employed the stimulus intensity at which CT leveled off in the relationship between CT and stimulus intensity. Additionally, the CT of the stimulated fascicle was similar to the CT of the single MUs with Fth below 4%MVC. Therefore, in our experiments, slow type MUs were also activated during repetitive stimulation.

The force response in human muscle fascicle to constant frequency stimulations were not constant but had complicated changes. Our findings suggest that in voluntary contraction the constant of spike interval of MUs cannot keep a constant muscle force. Gradual elongation of MUs spike interval lowers and/or flattens the gentle peak because the elongation decreases the degree of force summation. The rate coding of MUs is an important mechanism in keeping a constant force.

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Principles, Techniques, and Limitations of Near Infrared Spectroscopy

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Abstract/Résumé

In the last decade the study of the human brain and muscle energetics underwent a radical change, thanks to the progressive introduction of noninvasive techniques, including near-infrared (NIR) spectroscopy (NIRS). This review summarizes the most recent literature about the principles, techniques, advantages, limitations, and applications of NIRS in exercise physiology and neuroscience. The main NIRS instrumentations and measurable parameters will be reported. NIR light (700–1000 nm) penetrates superficial layers (skin, subcutaneous fat, skull, etc.) and is either absorbed by chromophores (oxy- and deoxyhemoglobin and myoglobin) or scattered within the tissue. NIRS is a noninvasive and relatively low-cost optical technique that is becoming a widely used instrument for measuring tissue O_2 saturation, changes in hemoglobin volume and, indirectly, brain/muscle blood flow and muscle O_2 consumption. Tissue O_2 saturation represents a dynamic balance between O_2 supply and O_2 consumption in the small vessels such as the capillary, arteriolar, and venular bed. The possibility of measuring the cortical activation in response to different stimuli, and the changes in the cortical cytochrome oxidase redox state upon O_2 delivery changes, will also be mentioned.

Dans la dernière décade l'étude du cerveau et le muscle humain énergique a subi un changement radical, grâce à l'introduction progressive de techniques non invasifs, y compris

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proche infrarouge (NIR) spectroscopy (NIRS). Cette revue résume la littérature la plus récente des principes, les techniques, les avantages, les limitations, et les applications de NIRS dans la physiologie d'exercice et neuroscience. Les instrumentations principales de NIRS et les paramètres mesurables seront rapportés. La lumière de NIR (700–1000 nm) pénètre des couches superficielles (la peau, subcutaneous gros, le crâne, etc.) et ou est absorbé par chromophores (oxy- et la deoxy hémoglobine et myoglobine) ou dispersé dans le tissu. NIRS est une technique non invasif et relativement bone marché optique qui devient un instrument largement utilisé pour mesurer de tissu O_2 saturation, les changements dans le volume d'hémoglobine et, indirectement, le flux de sang de cerveau muscle et le muscle O_2 consommation. Le tissu O_2 saturation représente un équilibre dynamique entre O_2 consommation de provision et O_2 dans les petits vaisseaux tel que le capillaire, le lit de arteriolar et venular. La possibilité pour mesurer l'activation de cortical en réponse aux stimuli différents, et les changements de l'état de redox de oxidase de cytochrome de cortical sur O_2 changements de livraison, seront aussi mentionnés.

Introduction

Starting with the pioneering work of Jobsis over 25 years ago (1977), noninvasive near-infrared (NIR) spectroscopy (NIRS) has been used first to investigate experimentally and clinically brain oxygenation, and later muscle oxidative metabolism in pathophysiology (for a review, see Boushel and Piantadosi, 2000; Boushel et al., 2001; Ferrari et al., 1997; Madsen and Secher, 1999; McCully and Hamaoka, 2000; Owen-Reece et al., 1999). In the last decade, NIRS has also been largely used to investigate the functional activation of the human cerebral cortex (for a review, see Hoshi, 2003; Obrig and Villringer, 2003). The aim of this review is to summarize the most recent literature about the principles, techniques, advantages, limitations, and applications of NIRS in exercise physiology and neuroscience.

The physical principles of NIRS have been reported previously in detail (Delpy and Cope, 1997; Rolfe, 2000; Strangman et al., 2002a). Briefly, NIR light (700–1000 nm) penetrates skin, subcutaneous fat/skull, and underlying muscle/brain, and is either absorbed or scattered within the tissue (Figure 1). The relatively high attenuation of NIR light in tissue is due to: (a) O_2-dependent absorption from chromophores of variable concentration, i.e., hemoglobin (Hb), myoglobin (Mb) (in the muscle only), and cytochrome oxidase; (b) absorption from chromophores of fixed concentration (skin melanine); or (c) light scattering. Several types of NIRS equipment, based on different NIRS methods, are commercially available (Table 1). Table 2 reports the parameters measurable by NIRS. Each type of NIRS device has different characteristics, as outlined in Table 3. The choice of the NIRS device is determined by the type of information requested.

The length that light travels through the medium (optical pathlength) is longer than the distance between the source and the detector because of the scattering effects of different tissue layers. Single-distance continuous wave (CW) photometers measure only the changes in O_2Hb and HHb when a constant differential pathlength factor (DPF) is included to calculate the pathlength [DPF × (source-detector separation)]. Some muscle and brain DPF values have been published (Delpy and Cope, 1997; Zhao et al., 2002). Considering that pathlength cannot change more than 10% (Ferrari et al., 1992), single-distance CW photometers mea-

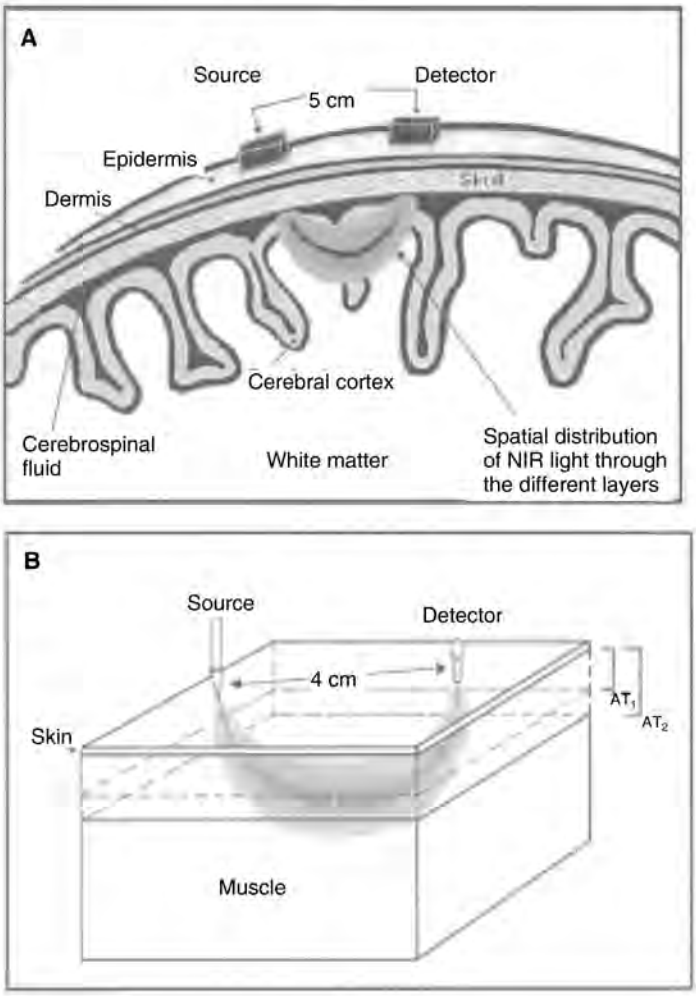

Figure 1. Schematic representation of NIR light traveling through (A) the head and (B) the muscle. Spatial distribution of light flux through the different tissue layers of the head or limb (due to complex light scattering) is simulated using the optical properties of skin, skull, cerebrospinal fluid (CSF), gray matter, white matter, adipose tissue, etc. The detected signal comes mainly from hemoglobin located in small vessels (< 1 mm diameter) such as the capillary, arteriolar, and venular bed (or from the intracellular myoglobin in the case of the limb). Panel B indicates the penetration depth of NIR light depends on adipose tissue thickness. In particular, the light goes deeper in the muscle tissue in the case of low subcutaneous fat (AT_1) and reaches the shallow region of the muscle tissue in the case of high subcutaneous fat (AT_2).

Table 1 Main NIRS Instruments

Instrument	Technique	# of chan.	Company	Technical reference
Photometers				
RunMan*	Single-distance CW	1	NIM, USA	Chance et al., 1992
HEO-100*	Single-distance CW	1	OMRON, Japan	Shiga et al., 1995
NIRO-500	Single-distance CW	1	Hamamatsu, Japan	De Blasi et al., 1994
OXYMON	Single-distance CW	≥2	Artinis, Netherlands	Colier et al., 1995 van Beekvelt et al.,2002
Oximeters				
NIRO-300	Multi-dist. CW (SRS)	2	Hamamatsu, Japan	Suzuki et al., 1999
OM-100	Multi-dist. CW (SRS)	2	Shimadzu, Japan	Quaresima et al., 2001b
INVOS	Multi-dist. CW (SRS)	2	Somanetics, USA	Thavasothy et al., 2002
OxiplexTS	Multi-dist. PMS	2	ISS, USA	Franceschini et al., 2002
TRS-10	TRS	1	Hamamatsu, Japan	Oda et al., 2000
Imagers				
ETG-100	CW	24	Hitachi, Japan	Kennan et al., 2002b
Imagent	PMS	16	ISS, USA	Wolf et al., 2002b
Monstir	TRS	32	UCL, London, UK	Hebden et al., 2002
POLIMI	TRS	8	Politecnico, Milan, Italy	Cubeddu et al., 2002
CT imager	TRS	64	Shimadzu, Japan	Hoshi et al., 2000

Note: CW = continuous wave; PMS = phase modulation; SRS = spatially resolved spectroscopy; * = wearable instrument; TRS = time-resolved spectroscopy

sure quite accurately the changes in O_2Hb and HHb. These instrumentations, however, cannot measure tissue O_2Hb saturation. Spatially resolved spectroscopy (SRS), time-resolved spectroscopy (TRS), and phase modulation spectroscopy (PMS) can calculate tissue O_2Hb saturation.

The brain/muscle volume measured by the different NIRS approaches is still controversial. However, it is generally accepted that, for a source-detector separation of 3 cm, the region of maximum brain/muscle sensitivity will be found between the source and detector fiber tip location, and roughly 1.5 cm below the surface of the skin, though a banana-shaped region of sensitivity extends both above and below this depth (Strangman et al., 2002a). Kohri et al. (2002), combining spatially- and time-resolved spectroscopy, estimated the contribution ratio of the cerebral tissue to whole optical signals at the source detector distance of 3 and 4 cm as 55 and 69%, respectively.

Different methods for NIRS signal quantification, NIRS advantages/limitations, and applications have been extensively reviewed (Boushel and Piantadosi

Table 2 Parameters Measured Directly and Indirectly by NIRS

Parameter	Units	Modality	MDE	Reference
Δ O_2Hb	A.U., μM×cm,	D	yes	Delpy and Cope, 1997
Δ HHb	μM		yes	Delpy and Cope, 1997
Δ tHb			yes	Delpy and Cope, 1997
OI			yes	Grassi et al., 1999
Tissue O_2 saturation	%	D (by SRS)	yes	Quaresima et al., 2002b
		D (by PMS)	yes	Franceschini et al., 2002
		D (by TRS)	yes	Oda et al., 2000
sVO_2	%	I (by VOM)	no	Yoxall et al., 1997
		D	no	Franceschini et al., 2002
Muscle BF	$ml \cdot 100ml^{-1} \cdot min^{-1}$	I (by VOM)	no	De Blasi et al., 1994
		I (by ICG)	yes	Boushel et al., 2000b
Muscle VO_2	$ml \cdot 100g^{-1} \cdot min^{-1}$	I (by VOM)	no	De Blasi et al., 1994
		I (by AOM)	no	De Blasi et al., 1993
Recovery time	seconds	D	no	Chance et al., 1992
Muscle compliance	$ml \cdot L^{-1} \cdot mmHg^{-1}$	I	no	Binzoni et al., 2000
Cerebral BV	$ml \cdot 100ml^{-1}$	I (by O_2 swing)		Owen-Reece et al., 1999
Cerebral BF	$ml \cdot 100ml^{-1} \cdot min^{-1}$	I (by O_2 swing)		Owen-Reece et al., 1999
		I (by ICG)		Owen-Reece et al., 1999

Note: Δ = relative changes from zero; tHb = Δ O_2Hb+Δ HHb; OI = oxygenation index (Δ O_2Hb- Δ HHb); MDE = measurable during exercise; sVO_2 = venous O_2 saturation; BF = blood flow; BV = blood volume; VO_2 = oxygen consumption; A.U. = arbitrary units; D = directly; I = indirectly; SRS = spatially resolved spectroscopy; PMS = phase modulation spectroscopy; TRS = time resolved spectroscopy; VOM = venous occlusion method; AOM = arterial occlusion method; ICG = indocyanine green.

2000; Boushel et al., 2001; Ferrari et al., 1997; McCully and Hamaoka, 2000; Strangman et al., 2002a). Briefly, the main limitations of NIRS measurements are due to: (a) the interference of skull thickness or adipose tissue thickness (ATT) on brain or muscle measurements, respectively; (b) the controversial unknown contribution of myoglobin to the muscle NIRS signal; (c) the effect of blood volume changes on the tissue pathlength, and then on the observed sample volume; (d) the difficulty of predicting how much of an observed NIRS signal change is due to brain vs. scalp blood flow, or (e) simultaneous changes in flow and volume.

In a recent theoretical study of light propagation in adult head models by using a Monte Carlo simulation, Okada and Delpy (2003) studied the effect of the superficial tissue thickness on the partial optical pathlength in the brain and on the

Table 3 Characteristics of NIRS Devices

	Single-distance	1–2 Channel Oximeters			Imagers		
	CW Photometers	SRSCW	PMS	TRS	CW	PMS	TRS
[O_2Hb], [HHb], [tHb] (μM)	changes #	changes #	absolute value	absolute value	changes #	absolute value	absolute value
Scattering & absorption coefficient and pathlength measurement	no	no	yes	yes	no	yes	yes
Tissue O_2Hb saturation (SO_2, %)	no	yes	yes	yes	no	yes	yes
Penetration depth with a 4-cm source-detector separation	low	low, deeper for SO_2	deep	deep	low	deep	deep
Sampling rate (Hz)	≤100 Hz	≤6 Hz	≤100 Hz	≤6 Hz	≤100 Hz	≤50 Hz	1 Hz
Spatial resolution (cm)	n.a.	n.a.	n.a.	n.a.	≤0.5 cm	≤0.5 cm	≤0.5 cm
Instrument size	very small	small	small	medium	bulky	bulky	bulky
Instrument stabilization	no	no	no	required	no	no	required
Transportability	easy	easy	easy	easy	feasible	feasible	feasible
Instrument cost	low	moderate	moderate	high	very high	very high	very high
Caution for eye exposure to coherent sources	no	no	no	yes	yes	yes	yes
Stable optical contact	critical	good	good	good	critical	good	good
Precise anatomical localization	no	no	no	no	scarce	scarce	scarce
Telemetry	feasible	feasible	not easy	not easy	not easy	not easy	not easy
Discrimination between cerebral and extracerebral tissue (scalp, skull, CSF)	n.a.	n.a.	feasible	feasible	n.a.	feasible	feasible
Possibility to measure deep brain structures on newborns	feasible	feasible	feasible	feasible	feasible	feasible	feasible

Note: CSF = cerebrospinal fluid; CW = continuous wave; n.a.= not available; PMS = phase modulation spectroscopy; SRS = spatially resolved spectroscopy; tHb = O_2Hb+HHb; TRS = time resolved spectroscopy; $^{\#}$= when differential pathlength factor (DPF) is included to calculate the tissue pathlength [= DPF × (source-detector separation)].

spatial sensitivity profile. The mean optical pathlength (measurable by time-resolved spectroscopy and phase modulation spectroscopy) increases when the skull thickness increases, whereas the partial mean optical pathlength in the brain decreases when the skull thickness increases. The partial optical pathlength (at a source-detector distance of 3 cm) depends mainly on the depth of the inner skull surface whereas the spatial sensitivity profile is significantly affected by the thickness of the cerebrospinal fluid layer. Moreover, an analysis was developed by another group for changes in mean time of flight (instead of changes in attenuation) to reduce the cross talk for the layers of cortical activation (Uludag et al., 2002).

The influence of ATT on light propagation in leg muscles has been examined by a diverse number of researchers. More recently, Matsushita et al. (1998) concluded that NIR light penetrates shallow regions of muscle under the skin and subcutaneous fat even when the ATT is 1.5 cm.

The NIRS technique is unable to differentiate between the signal attenuation due to Hb and Mb because the absorbency signals of these two chromophores overlap in the NIR range. Within a given volume of muscle there are differences in concentration of both Hb and Mb and in their binding capacities (i.e., Hb has four times more oxygen binding sites than Mb). Little data is available on the Hb/Mb ratio in the human muscles. On the basis of these studies, Mb is on average 4 mg/g wet tissue in human gastrocnemius (Mancini et al., 1994) and 4.5 mg/g in vastus lateralis (Masuda et al., 1999). Although the NIRS sample volume is unknown, considering a muscle blood volume of about 10% one can estimate its weight as a confounding factor at 10% of the whole Hb signal, an amount that may be considered negligible.

Tran et al. (1999) first demonstrated by ^{1}H-magnetic resonance spectroscopy (MRS) that oxy-Mb desaturation kinetics matches the NIRS signal. Richardson et al. (2002) found that at rest the intramuscular O_2 stores (measured by the appearance of ^{1}H-MRS -deoxy-Mb signal during suprasystolic cuff occlusion) begin to decrease after 4 min, and that maximal Mb desaturation is achieved after 8 min. Conversely, at rest the intramuscular O_2 stores, as measured by NIRS during suprasystolic cuff occlusion, begin to decrease immediately after the beginning of the occlusion and the maximal desaturation is achieved after 5–6 min (Komiyama et al., 2001). During high intensity exercise, Mb typically desaturates to only 50% of the level attained during cuff occlusion (Wittenberg & Wittenberg, 2003), and muscle oxygenation, as measured by CW NIRS, typically desaturates to about 90% of the level attained during the cuff occlusion (Grassi et al., 2003).

Overall these data would suggest that, in the case of a short quadriceps maximal voluntary contraction, the measured value of the vastus lateralis O_2 saturation reflects predominantly (at least 80%) the weighted mean of arteriolar, capillary, and venular O_2Hb saturation. The remainder can be attributed to the contribution of Mb oxygen saturation. Nevertheless, more combined ^{1}H-MRS and NIRS studies are needed to clarify not only the issue of the contribution of Mb to the NIRS signal, but also the kinetics and the amount of Mb desaturation during exercises with different workloads (Conley et al., 2000).

As discussed by McCully and Hamaoka (2000), not all published studies found a good correlation between muscle oxygenation by NIRS and venous blood O_2 saturation (Costes et al., 1996; Hicks et al., 1999; MacDonald et al., 1999).

During a prolonged exercise, venous blood O_2 saturation initially decreased but did not increase as muscle oxygenation did. McCully and Hamaoka proposed several possible explanations, i.e., change in the calibration curve due to blood volume changes, and a shift of the weighted average of the NIRS signal toward capillaries. In support of the effect of apparent sample volume during prolonged exercise, some studies have shown that the magnitude of the partial recovery in muscle oxygenation during exercise was reduced during hypoxia (Costes et al., 1996; MacDonald et al., 1999). This is because during hypoxia the overall O_2 saturation and the gradients along the vascular trees are reduced, and thus the shifts in blood volume between compartments will affect fewer NIRS measurements (McCully and Hamaoka, 2000).

NIRS Instrumentation and Measurable Parameters

Several types of NIRS equipment, based on different NIRS methods, are commercially available (Table 1). The advantages and disadvantages of the different NIRS approaches have been reviewed (Delpy and Cope, 1997; Hoshi, 2003; Rolfe, 2000; Strangman et al., 2002a). Most of the commercial instruments utilize CW light in combination with a modified Lambert-Beer law (Delpy and Cope, 1997) to measure changes in O_2Hb and HHb (Figure 2). In a scattering medium such as biological tissue, quantification of the NIRS signal is difficult and different methods have been proposed; one of the most reliable is the spatially resolved spectroscopy (SRS). SRS and time/phase-resolved instruments are the only ones to provide the measurement of average tissue O_2 saturation.

In SRS, which uses CW light and a multidistance approach, the slope of NIR light attenuation vs. distance is measured at a distant point from the light input, from which the absolute ratio of O_2Hb to the total Hb content (tHb), and hence average tissue O_2 saturation ($SRS\text{-}O_2$), can be calculated using the photon diffusion theory (Suzuki et al., 1999). $SRS\text{-}O_2$ represents a dynamic balance between O_2 supply and O_2 consumption in tissue capillaries, arterioles, and venules, because in larger blood vessels NIR light is fully absorbed by the high hemoglobin concentration. From anatomical studies of the brain, the ratio of venule to total vessel volume ranges from 2/3 to 4/5 (van Lieshout et al., 2003). Because about 5% of the blood is in the capillaries and about 20% in the arterioles, NIRS measures mainly the local venous O_2Hb saturation.

NIRS instruments have been validated in vivo by several researchers using different experimental modalities. Boushel et al. (2001) found that $SRS\text{-}O_2$ of the vastus lateralis was inversely related with the femoral arterio-venous O_2 ($a\text{-}vO_2$) difference during dynamic knee extension exercise in normoxia, hypoxia, and hyperoxia.

Recently several groups have begun to use multichannel CW imaging systems that allow the generation of images of a larger area of the subject's head and muscle with high temporal resolution (up to 10 Hz), and thereby the production of maps of cortical and muscle oxygenation changes (Miura et al., 2001; Obrig and Villringer, 2003; Quaresima et al., 2001a, 2002a). The noninvasive cortical NIR images can be obtained in straightforward setups that can be easily combined with other functional methods, in particular EEG. Multichannel brain NIR imaging has

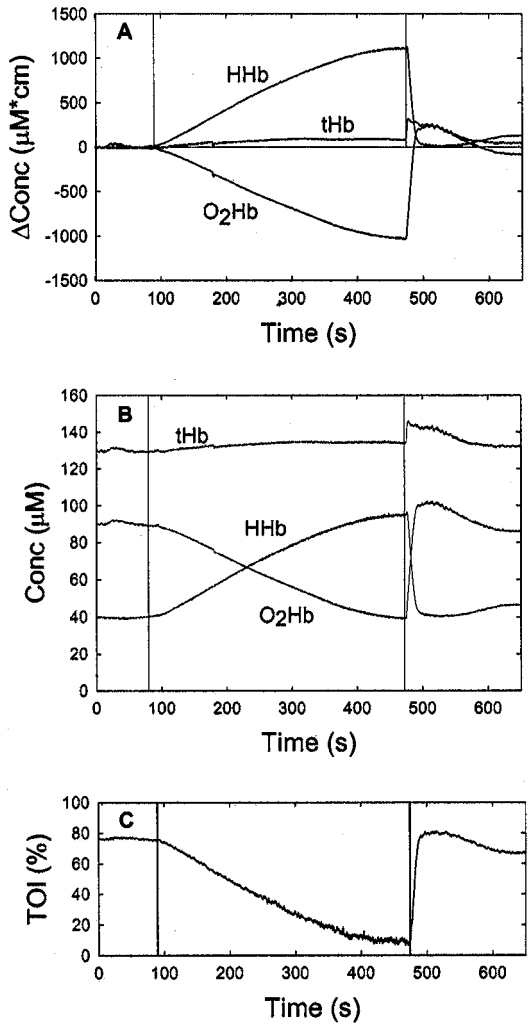

Figure 2. Typical time course of brachioradialis muscle oxygenation measured during arterial occlusion by different NIRS technologies: (A) single-distance continuous wave spectroscopy; (B) phase modulation spectroscopy and/or time resolved spectroscopy; and (C) spatially resolved spectroscopy. Vertical lines indicate the duration of arterial occlusion provoked inflating (250 mmHg) the cuff positioned around the arm. Time course of concentration changes (expressed in μM×cm, when DPF is not included) in O_2Hb, HHb, and tHb measured by single-distance continuous wave photometers (Panel A). Time course of tissue O_2 saturation (TOI, %) measured by continuous-wave spatially resolved spectroscopy, phase-modulation spectroscopy, and time-resolved spectroscopy (Panel C). Time course of absolute concentration (expressed in μM) of O_2Hb, HHb, and tHb measured only by phase modulation spectroscopy and time resolved spectroscopy (Panel B).

two major advantages: it can address issues concerning neurovascular coupling in the human adult, and can extend functional imaging approaches to the examination of the diseased brain. Unfortunately, there are few commercially available imagers, they are quite expensive, and most of them lack U.S. Food and Drug Administration approval.

Although many interesting studies have been performed with multichannel CW systems, the lack of pathlength determination limits the accuracy of the results (Ferrari et al., 1992). Imagent (ISS Inc., Urbana, IL) is a new device that allows the measurement of O_2Hb and HHb concentration maps in tissue via phase modulation. The device works by emitting NIR light into tissue at known distances from a detector. Light of two different wavelengths is used and the light is modulated at a radio frequency of 110 MHz. The collected light is measured and processed and the absorption and scattering coefficients of the medium are determined. Once the absorption and scattering are determined, the assumption that Hb is the only significant absorber is applied and the O_2Hb and HHb concentrations are calculated.

Absolute concentrations of O_2Hb and HHb also can be measured by TRS. For this purpose, a number of companies and academic institutions have been developing multichannel TRS systems (Cubeddu et al., 2002; Hillman et al., 2001; Hoshi et al., 2000). Recently, an 8-channel portable instrument based on TRS has been developed and tested for monitoring spatial changes in calf O_2Hb saturation during dynamic plantar flexion exercise with a sampling time of 200 ms (Cubeddu et al., 2002). A 32-channel TRS optical imaging instrument has been developed by the University College of London principally to study functional parameters of the brain of a newborn (Hillman et al., 2001). Images representing the internal scattering and absorbing properties of the arm, as well as images revealing physiological changes during a simple finger flexion exercise, were presented (Hillman et al., 2001). 3-D images of the newborn infant brain with a cerebral haemorrhage predominantly located within the left ventricle have recently been generated (Hebden et al., 2002).

However, there is a number of tradeoffs when using these multichannel systems, including poor spatial resolution (about 5 mm), difficulty with precise anatomical localization, and relatively poor penetration and localization depth. All the parameters measurable directly and indirectly by the NIRS devices, based on different approaches, are reported in Table 2.

MUSCLE O_2 CONSUMPTION (VO_2) AND BLOOD FLOW (BF)

The utility to measure VO_2 has also been demonstrated. For example, VO_2 can be measured in the arm or in the leg by calculating the rate of conversion of O_2Hb to HHb during a period of tourniquet-induced ischemia (De Blasi et al., 1993). VO_2 can be measured at rest and during forearm maximal voluntary contraction (MVC) achieved with and without vascular occlusion. The MVC, performed during vascular occlusion, caused a complete desaturation in 10–15 sec, which was not followed by any further desaturation when the second contraction was performed. No difference was found in VO_2 measured during MVC with and without vascular occlusion. The relationship between VO_2 in the soleus muscle and the level of isometric exercise expressed as % of MVC was investigated by Colier et al. (1995).

A linear relationship was found between the VO_2 and the level of exercise. More recently, Sako (2001) examined the validity of the VO_2 method. Subjects performed two bouts of dynamic handgrip exercise, once for the NIRS measurement and once for the ^{31}P-MRS measurement as a standard. There was a physiologically significant correlation ($r = 0.965$) between the VO_2 values measured by the two methods.

Several recent studies have suggested that the NIRS VO_2 method could be useful not only for examining regional differences, but also changes over time between muscle groups as a function of training. NIRS in combination with ^{31}P-MRS was used to assess muscle bioenergetics (Binzoni et al., 1998; Boushel et al., 1998). Energy metabolism and interstitial fluid displacement were studied in the human gastrocnemius during three subsequent 5-min ischaemia-reperfusion periods (Binzoni et al., 1998). VO_2 in the muscle region of interest, as estimated by NIRS, was approximately 8 μmol/100g/min. Phosphocreatine (PCr) and ATP concentrations did not change over the whole experimental period. Forearm flexor muscle VO_2 was measured during ischemia at rest and rhythmic handgrip at 15% and 30% of MVC, postexercise muscle ischaemia, and recovery (Boushel et al., 1998). The oxygenation of the forearm flexor muscles closely reflected the exercise intensity and metabolic rate determined by ^{31}P-MRS, but not the rate derived from flow and the a-vO_2 difference.

As suggested by Boushel et al. (1998), this discrepancy is due to the limitations in sampling venous blood representative of the flexor muscle capillaries. Using ^{31}P-MRS and NIRS simultaneously, it was found that the initial rate of finger flexor deoxygenation during immediate postexercise ischemia (exercise: 5-min submaximal isotonic grip exercise at 10–40% of MVC) was a reflection of muscle VO_2 (Hamaoka et al., 1996).

NIRS has also been successfully applied for the simultaneous measurement of forearm BF (FBF) and VO_2 (FVO_2) by inducing a 50-mmHg venous occlusion (De Blasi et al., 1994). FBF data were validated by strain-gauge plethysmography (De Blasi et al, 1994: Homma et al., 1996). Therefore, NIRS provides the particular advantage of obtaining the concomitant evaluation of FBF and FVO_2, allowing a correlation between these two variables by a single maneuver without discomfort for the subject. The FVO_2 values obtained by using the venous occlusion method correlated with the FVO_2 values obtained by using the arterial occlusion method ($r^2 = 0.66$, $p < 0.01$) (De Blasi et al., 1997). VO_2 and BF in resting and exercising forearm (sustained isometric handgrip exercise) were examined via NIRS and the results were compared with those via the global muscle VO_2 data and FBF derived from the Fick method and plethysmography (van Beekvelt et al., 2001b). This study concluded that NIRS is an appropriate tool for providing information about local VO_2 and local FBF because both place and depth of the NIRS measurements reveal local differences that are not detectable by the more established, but also more global, Fick method.

These methods were also successfully used to estimate FBF and FVO_2 during venous occlusion imposed at rest and immediately after handgrip exercise with incremental loads (5–30% of MVC) (Homma et al., 1996). Quantitative measurements of regional muscle BF at rest and during exercise were also possible using NIRS and a light-absorbing tracer, indocyanine green (ICG). This invasive method

has been applied to evaluate the circulatory responses to exercise along with the assessment of SRS-O_2 (Bangsbo et al., 2000; Boushel et al., 2000a, 2000b).

OTHER PARAMETERS MEASURABLE ON MUSCLES

Muscle venous saturation (SvO_2) can be estimated with NIRS by applying a venous occlusion and measuring changes in O_2Hb vs. tHb (Yoxall et al., 1997). More recently, another method for the measurement of SvO_2, based on the respiration-induced oscillations of the NIR absorption in tissues, has been reported (Franceschini et al., 2002). In the vastus medialis and vastus lateralis muscles, a good agreement was found between SvO_2 measured with the new method and SvO_2 measured with the venous occlusion method (average deviation of 0.8%).

The recovery time reflects the balance of O_2 delivery and O_2 demand in the localized muscles following muscle work, and it can be interpreted as a measure of the time for repayment of O_2 and energy deficits accumulated during intense exercise by tissue respiration under ADP control (Chance et al., 1992). Recovery time can be measured also after tourniquet-induced ischemia (McCully et al., 1994; Sahlin, 1992). McCully et al. (1994) investigated simultaneously PCr and muscle oxygenation during the recovery phase from isokinetic plantar flexion. Muscle reoxygenation approximated submaximal PCr recovery and was not different between maximal and submaximal exercise, demonstrating that ^{31}P-MRS measurements of PCr recovery and NIRS measurements of recovery of muscle oxygenation provide similar information.

A method has been developed to measure the compliance of the microvascular superficial venous system of the lower limb by NIRS (Binzoni et al., 2000). This method is complementary to strain-gauge plethysmography, which does not allow compliance to be distinguished between deep and superficial venous or between venous and arterial compartments. Hydrostatic pressure (P) changes were induced in a calf region of interest by head-up tilt of the subject from alpha = –10 to 75 deg. For $P \leq 24$ mmHg, the measured compliance, based on NIRS data of tHb, HHb, and O_2Hb, reflects essentially that of the superficial venous system. For $P \geq 24$ mmHg, no distinction can be made between arterial and venous volume changes. However, by following the changes in O_2Hb and HHb in the P range from –16 to 100 mmHg, it seems possible to assess the characteristics of the vasomotor response of the arteriolar system. These results were later explained by Binzoni et al. (2003) in a study in which it was demonstrated (via a NIRS dye dilution technique) that a reduction in blood flow is responsible for the limited O_2Hb concentration increase during the tilting maneuver from 0 to 60 deg.

Since adipose tissue interacts with the NIR light, the monitored muscle oxygenation changes are underestimated if adipose tissue thickness is not taken into consideration. There are reports demonstrating that adipose tissue affects in vivo quantitative NIRS, especially BF and VO_2 in skeletal muscle (van Beekvelt et al., 2001a). A negative correlation was found between VO_2 and adipose tissue thickness (also Binzoni et al., 1998). No correlation was found between MVC and VO_2, nor between MVC and adipose tissue thickness, indicating that the contraction force did not confound the results. The main conclusion of these studies was that adipose tissue thickness has a substantial confounding influence on in vivo NIRS measurements, and that it is essential to incorporate this factor into NIRS muscle

studies in order to justify comparisons between different muscle groups. Recently an algorithm capable of correcting for the influence of the subcutaneous fat layer has been proposed (Niwayama et al., 2000); however, it is not included in the commercial units.

TISSUE OXIMETRY

Madsen and Secher (1999) reviewed brain oximetry studies based on NIRS. Caveats of cerebral oximetry include insufficient light shielding, optode displacement, and a sample volume including muscle or the frontal sinus mucous membrane. The relative influence from the extracranial tissue is minimized by optode separation and correction for an extracranial sample volume, or both. The natural pigment melatonin and also water are of little influence to spectroscopic analysis of cerebral oxygenation, whereas bilirubin systematically lowers brain oxygenation and attenuates the detection of changes in cerebral oxygenation. The application of intracranial NIRS in adults has been hampered by concerns over contamination from extracranial tissues.

A typical SRS system like the NIRO-300 (Hamamatsu Photonics, Hamamatsu City, Japan) provides continuous online measurements of O_2Hb and HHb concentration changes and a calculated tissue O_2 saturation named TOI. Al-Rawi et al. (2001) confirmed the anatomic source of TOI in the adult cranium on patients undergoing carotid endarterectomy. A change in TOI was predominantly associated with internal carotid artery clamping. When TOI changed during external carotid artery clamping, there were significant changes in blood pressure, or extracranial-to-intracranial anastomosis was evident. In the absence of such variables, the sensitivity of TOI to intracranial and extracranial changes was 87.5% and 0%, respectively, and specificity was 100% and 0%, respectively.

Two SRS oximeters, NIRO-300 and OM-200 (Shimadzu, Tokyo, Japan), were compared with regard to the measurement of O_2 saturation values in two forearm muscle groups at rest and during arterial occlusion. There was a significant correlation between the muscle O_2 saturation values obtained at rest using the two oximeters, whereas these values were significantly different during arterial occlusion (Komiyama et al., 2001). Thus, although there was good agreement between muscle O_2 saturation values measured using the two oximeters, the operating range (i.e., the interval within which the instrument works reliably) of the tissue oximeters should be recognized and indicated. Thavasothy et al. (2002) compared the cerebral cortex oxygenation as measured by the NIRO-300 and the INVOS 5100 (Somanetics, Troy, MI). Both monitors demonstrated similar changes in response to hyperoxia and hypocapnia (coefficient of variance for FiO_2 0.45 = 10.0%, FiO_2 1.0 = 10.1%, hypocapnia = 14.5%).

Cerebral oximetry found several interesting clinical and physiological applications (for a review, see Madsen and Secher, 1999). For example, van Lieshout et al. (2003) investigated cerebral oxygenation during syncope, and Imray et al. (1998) studied cerebral regional O_2 saturation in subjects ascending rapidly to 4,680 m. Also muscle oximetry found several interesting applications. For example, Boushel et al. (2000a) investigated calf and peritendinous oxygenation during dynamic exercise, and Quaresima et al. (2002b) studied oxygen resaturation of thigh and calf muscles after two treadmill stress tests.

CORTICAL CYTOCHROME OXIDASE REDOX STATE

NIRS assessment of the redox state of mitochondrial cytochrome oxidase Cu_A could be a valuable technique for monitoring intracellular O_2 delivery. Although the NIRS hardware has been refined and the algorithms (used to deconvolute the light absorption signal) have been improved, recent years have seen lively discussion in the literature on the possibility of measuring cortical cytochrome oxidase by NIRS. Conversely, this measurement cannot be done on muscle tissue because of the Mb interference. Hoshi (1997) found in rats that O_2-dependent redox changes in cytochrome oxidase occur only when O_2 delivery is extremely impaired.

To improve the accuracy of this measurement, most of the recent studies employed a multiwavelength detector. Quaresima et al. (1998) determined the relationship between the redox state of mitochondrial cytochrome oxidase Cu_A and Hb oxygenation on newborn piglet brain. The large reductions in the Cu_A redox state during anoxia (1.8 μM) were caused by a decrease in the rate of O_2 delivery to the cytochrome oxidase O_2 binding site; the small oxidations (0.2 μM) during hypercapnia were likely due to the effects of metabolic changes on the redox state of Cu_A rather than to increases in the rate of O_2 delivery. In the same experimental animal model, Cooper et al. (1999) used mitochondrial inhibitors (cyanide) to demonstrate that cytochrome oxidase NIRS can measure mitochondrial dysfunction. The O_2 dependency and precision of cytochrome oxidase signal from full spectral NIRS of the piglet brain was measured during brief anoxic swings at both normocapnia and hypercapnia (Springett et al., 2000a). A minimal interference between the Hb and Cu_A signals was found in this model, the Cu_A oxidation state was independent of cerebral oxygenation at normoxia, and the oxidation after hypercapnia was not the result of increased cerebral oxygenation.

Changes in Hb oxygenation and oxidation state of cytochrome oxidase were measured simultaneously with phosphorus metabolites using ^{31}P-MRS by applying a transient anoxia (Springett et al., 2000b). During the onset of anoxia, there was no change in either PCr concentration or the oxidation state of the Cu_A centre of cytochrome oxidase until a substantial fall in cerebral Hb oxygenation occurred, at which point the Cu_A centre reduced simultaneously with the decline in PCr. The concomitant reduction of Cu_A and decline in PCr can be explained in terms of the effects of the falling mitochondrial electrochemical potential. From these observations it was concluded that, at normoxia, oxidative phosphorylation and the oxidation state of the components of the electron transport chain are independent of cerebral oxygenation, and that the reduction in the Cu_A signal occurs when O_2 tension limits the capacity of oxidative phosphorylation to maintain the phosphorylation potential.

De Visscher et al. (2002) demonstrated that nitric oxide does not inhibit cerebral cytochrome oxidase after brief anoxia or during reoxygenation after a brief anoxic period. Although these are very interesting results, the validity of the cytochrome signal has been questioned as it could easily be overwhelmed by the Hb signal. Using a piglet model, Sakamoto et al. (2001) found that the cytochrome signal as presently measured by scanning NIRS is highly dependent on hema-tocrit.

Several human visual cortex cytochrome oxidase studies have been performed by the Villringer's group. For example, Wobst et al. (2001) investigated the vascu-

lar and metabolic response to brain activation in human primary and adjacent secondary visual cortex. Using NIRS they were able to measure concentration changes in the redox status of the cytochrome-c oxidase. Predictions of cellular and vascular oxygenation responses to visual stimulation were good for 6- to 24-s stimuli duration under the assumption of a linear transfer characteristic.

CEREBRAL BLOOD FLOW AND CEREBRAL BLOOD VOLUME

Methods of using NIRS to achieve absolute quantification of cerebral blood flow (CBF) and cerebral blood volume (CBV) by a transient hypoxia have been developed in neonatal intensive care and have also been applied in adults (see Owen-Reece et al., 1999, for a review). However, these methods were questioned because, for example, they give systematically different CBV readings and large intersubject variability (see Newton et al., 1997; van de Ven et al., 2001; Wolf et al., 2002a). Therefore, these methods have found a scarce application in clinics. Roberts (1998) described a novel noninvasive method for repeatedly measuring CBF during cardiopulmonary bypass on children with NIRS using ICG, injected into the bypass circuit, as an intravascular tracer. The method was compared with microsphere injection in piglets undergoing cardiopulmonary bypass.

More recently, CBF was estimated using NIRS and pulse dye-densitometry after intravenous ICG injection (Gora et al., 2002). Arterial and cerebral changes in ICG concentration were measured using pulse dye-densitometry and NIRS, respectively. The precision was improved using a deconvolution algorithm (coefficient of variation of 10.1%). The precision of this method has been improved by applying the Fick principle in both integral and differential forms using a linear regression technique to improve the precision of calculated values of CBF (Springett et al., 2001). In addition, the differential method allowed the venous outflow to be calculated, giving further information on the state of the capillary bed.

The same group (Brown et al., 2002) more recently has developed a method that allows, after ICG injection, quantitative measurement of CBF, CBV, and mean transit time (MTT). Measurements of CBF, CBV, and MTT were made on piglets in normocapnia, hypocapnia, and hypercapnia to test the technique over a range of hemodynamic conditions. The accuracy of the new approach has been determined by direct comparison with measurements made using a computed tomography technique. No significant difference was found between computed tomography and NIRS measurements of CBF, CBV, and MTT (Brown et al., 2002).

Hopton et al. (1999) developed an integration method to measure CBV in adults by using ICG. After bolus injection, concentration-time integrals of cerebral tissue ICG concentration measured by NIRS were compared with corresponding integrals of the cerebral blood ICG concentrations estimated by high-performance liquid chromatography of peripheral blood samples. Multichannel NIRS with ICG was preliminarly used to measure regional CBF in the temporal lobes of infants (Kusaka et al., 2001). Since the application of ICG in the adult human critically depends on differentiation between extra- and intracerebral vascular compartments, Kohl-Bareis et al. (2002) investigated the latency and shape of the change in absorption of a bolus of ICG traveling through the cerebral vasculature using frequency-domain and multidistance measurements. Based on measurements of both

the photon's mean time of flight (phase) and the intensity, the results revealed the differentiation between an upper layer (skin and skull) and a lower layer (brain). The bolus in the deeper tissue layers had a peak of about a 10-s width, while the change in absorption in the upper layers shows a much longer recovery time. This was in qualitative agreement with magnetic resonance imaging results using a gadolinium bolus (Kohl-Bareis et al., 2002).

Recently, changes in cerebral O_2Hb and HHb were compared to corresponding changes in CBF and CBV as measured by positron emission tomography (PET) (Rostrup et al., 2002). Changes in CBV measured with both techniques were significantly correlated to CO_2 levels. However, ΔCBV(NIRS) was much smaller than ΔCBV(PET). Rostrup et al. (2002) concluded that while qualitatively correct, NIRS measurements of CBV should be used with caution when quantitative results are needed.

Cortical Activation (Functional NIRS)

Neuroimaging techniques, such as functional MRI (fMRI) and PET, monitor task-related neuronal activations in the brain indirectly through the associated neurovascular/metabolic responses. fMRI and PET measure local changes in brain hemodynamics induced by motor, visual, cognitive, or perceptual tasks. Moreover, fMRI and PET measures are characterised by a uniform highly spatial resolution (millimetres or less) and a poor temporal resolution (about 1 s). Conversely, EEG, magnetoencephalography (MEG), and NIRS measure instantaneously the current flows induced by synaptic activity or the cortical hemodynamics. Recently techniques have been developed that, in the context of brain anatomy visualized with structural MRI, use both hemodynamic and electromagnetic measures to arrive at estimates of brain activation with high spatial and temporal resolution. These methods range from simple juxtaposition to simultaneous integrated techniques. Their application has already led to advances in our understanding of the neural bases of perception, attention, memory, language, etc. Further advances in multimodality integration will require a better understanding of the coupling between the physiological phenomena underlying the different signal modalities.

NIR optical topography is the simultaneous acquisition of O_2Hb and HHb changes from an array of optical fibers on the scalp to construct maps of cortical activity. The oxygenation response typically expected over an activated cortical area consists of a decrease in HHb accompanied with an increase in O_2Hb of two- to threefold of magnitude. NIRS and fMRI both allow noninvasive monitoring of cerebral cortical HHb responses to various stimuli. Kleinschmidt et al. (1996) first measured simultaneously cerebral oxygenation changes during human brain motor activation by fMRI and one-channel fNIRS. fNIRS and fMRI measurements showed good correlation in young and elderly subjects during a motor task (Mehagnoul-Schipper et al., 2002).

Toronov et al. (2001) investigated human brain hemodynamics by simultaneous NIRS and fMRI mapping during a periodic sequence of stimulation by finger motion and rest. Both methods revealed a good co-location of the brain activity centers. While rough spatial correspondences with maps generated from fMRI were found in these experiments, the amplitude correspondences between the two

recording modalities have not been fully characterized. Recently, strong correlations were found between fMRI changes and all optical measures, with O_2Hb providing the strongest correlation (Strangman et al., 2002b).

NIRS has been used to monitor child and adult brain function in a wide variety of tasks. A recent review covers the literature on intrinsic optical signal and the functional brain NIRS imaging studies of the past few years (Obrig and Villringer, 2003). In this research field, Kennan et al. (2002b) demonstrated that optical topography could be used to determine lateralization of prefrontal areas to a language task that has been validated by fMRI. Kennan et al. (2002a) also demonstrated that optical topography can be used to simultaneously detect and characterize the hemodynamic responses associated with an "oddball" auditory stimulus, and that corresponding electrical event related potentials (ERP) could be acquired simultaneously using conventional scalp recordings. In addition to the measured electrical response, the hemodynamic localization was consistent with fMRI studies, which showed significant activation in the temporal and parietal cortical regions.

This study showed the regions of peak hemodynamic activity that were in closest proximity to areas of peak electrical activity. This was the first demonstration of simultaneous ERP electrical recording and noninvasive optical mapping in human subjects. The same group also demonstrated, by using a global hyperoxic or mild hypoxic challenge, that it is possible to normalize the activation response in terms of the fractional changes in CBV, tissue oxygenation index, and O_2 extraction ratio, which are independent of the optical pathlength (Kennan and Behar, 2002).

Maps of concentration changes in O_2Hb, HHb, and tHb of the visual and motor cortices were generated via a frequency-domain NIRS during stimulation using a reversing checkerboard screen and palm-squeezing, respectively (Wolf et al., 2002c). In the visual cortex the patterns of O_2Hb and HHb were linearly correlated in 13 of 24 locations. The patterns of the O_2Hb and HHb traces over the motor cortex looked different. The O_2Hb reached its maximum change a few seconds before the HHb reached its minimum. Patterns of O_2Hb and HHb differed among cortex areas. This implies that the regulation of perfusion in the visual cortex differs from that in the motor cortex. There is evidence that the cerebral metabolic rate for O_2 increases substantially in the visual cortex, while this is not the case for the motor cortex (Wolf et al., 2002c).

The literature on the fast intrinsic optical signal is quite controversial (Obrig and Villringer, 2003). Millisecond changes in the optical properties of the human brain during motor stimulation were recently detected using frequency-domain NIRS (Wolf et al., 2002b). During a motor stimulation task, highly significant signals were found which were directly related to neuronal activity and exhibited much more localized patterns than the slow hemodynamic signals.

Chance et al. (1993) first reported observations of NIR absorbance changes attributable to repetitive tHb changes in response to stimulation in the human brain frontal region by a cognitive process. These responses were observed as low-frequency recurrence of changes by Fourier transform analysis. Toronov et al. (2000) studied the motor cortex hemodynamics in human subjects at rest and under motor stimulation conditions using a multichannel near-infrared tissue spectrometer (ac-

quisition time of 160 ms per map). The main findings were: (a) the amplitude of the hemodynamic response to the motor stimulation was comparable to the amplitude of the fluctuations at rest; (b) the spatial patterns of the O_2Hb and HHb responses to the stimulation were different; and (c) the hemodynamic response to stimulation showed a spatial localization and a level of phase synchronization with the motor stimulation that depended on the stimulation period.

Obrig et al. (2000) investigated slow spontaneous oscillations in cerebral oxygenation in the human adult's visual cortex. Both the spectral power and the phase relationship between O_2Hb and HHb were analysed. Spontaneous vascular and metabolic low frequency oscillations (LFO) centered around 0.1 s^{-1} and very LFO (VLFO) centered around 0.004 s^{-1} were reproducibly detected by NIRS in the human adult brain. Their respective power differed between O_2Hb and HHb. Either frequency (LFO and VLFO) was altered in magnitude by functional stimulation of the cortical area examined. Their spectral characteristics and their response to hypercapnia corresponded to findings with transcranial Doppler sonography and fMRI.

Recently Fantini (2002) presented a model that describes the effect of physiological parameters such as the speed of BF, local O_2 consumption, capillary recruitment, and vascular dilation and constriction on Hb concentration and O_2 saturation in tissue. This model suggests that the superposition of asynchronous contributions from the arterial, capillary, and venous Hb compartments may be at the origin of observed out-of-phase oscillations of the O_2Hb and HHb concentrations in tissue.

Perspectives

On average, one article a day is reported on MEDLINE about the in vivo applications of NIRS. Most are clinical studies. However, many researchers have been using NIRS in exercise physiology (see accompanying symposium papers by Bhambhani and by Neary) and neuroscience. Since oxidative metabolism is the dominant source of energy for skeletal muscle, the possibility of investigating it noninvasively in exercising muscles and following its modification in response to specific training or rehabilitation programs is of great interest. Recently the combination of ^{31}P-MRS with NIRS has enhanced the opportunity to measure local muscle oxidative metabolism noninvasively during exercise (Binzoni et al., 1998; Boushel et al., 1998; Cerretelli et al., 1997). Moreover, NIRS in combination with surface electromyography can shed light on one of the possible causes of muscle fatigue (Miura et al., 2000). Human brain mapping is one of the key areas of neuroscience research. From this point of view, functional NIRS is giving a unique contribution considering that it has several advantages over existing technologies (MRI, PET, etc.) for brain imaging (Hoshi, 2003; Obrig and Villringer, 2003).

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VASTUS LATERALIS METABOLIC RESPONSE TO EXPLOSIVE MAXIMAL ISOMETRIC LEG PRESS EXERCISE

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1. INTRODUCTION

Explosive force production is considered as an additional class of strength tests.[1] An important rationale for testing explosive force production has been the short time available for production in various athletic and other activities. The most applied test is the rate of force development (RFD) during which the subject exerts his maximal force in an explosive way. RFD can be assessed as the maximal slope of the recorded force-time curve or as the slope after a fixed time following the initiation of the contraction.[2] Leg press is one of the common core exercises that are utilized by athletes to enhance performance in sport. In particular, leg press exercise develops the upper leg, because it works the quadriceps, the hamstrings and the gluteus maximum. This exercise is normally performed on a machine where the legs press against a weighted platform. Muscle bioenergetics during explosive muscle strength has not been clarified yet.[3]

Near infrared spectroscopy (NIRS) is becoming a widely used instrument for measuring tissue O_2 status.[4] In fact, NIRS is a non-invasive and relatively low cost optical technique that offers the advantage of being less restrictive (no limitations on the type of exercise to be performed), more comfortable and suitable than ^{31}P-MRS for monitoring (with high temporal resolution, up to 100 Hz) oxygenation (then indirectly oxidative metabolism) of multiple muscle groups.[5]

This study aimed at measuring *vastus lateralis* (VL) muscle O_2 saturation (SmO_2) response to a single very short-duration static (maximal voluntary force, MVF) leg press exercise.

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2. METHODS

Seven male volunteers (23±2 years; 79±9 kg) were recruited for the experiments. The experimental procedures were explained, and all the subjects gave their informed consent. The subjects were physically active (although none were engaged in daily, intensive or specific training programs) with no history of serious lower extremity (specifically ankle or knee joint) injury. Leg press strength was measured on a commercial leg press equipped with strain gauge to convert analog force signal, sampled at 100 Hz, to digital signal and stored on a PC. The subjects were positioned on the sledge of the leg press with the knee ankle adjusted at 110° (Fig. 1). The waist was fixed and the subjects were allowed to stabilize their upper body by holding on to handles attached to the leg press. The position of each subject was documented so that it was identical for the duration of the protocol. Testing was only performed on the dominant leg.

Figure 1. Experimental setup.

A warm-up period of 10 min on a treadmill preceded the testing session itself. Each subject (accustomed to the testing procedure) performed five static leg press exercises with his maximal voluntary effort. For each trial, subjects were thoroughly instructed to act "as forcefully and as fast as possible". Interval between the bouts was about 15 min. During later offline analysis the trial with the maximum static leg press strength was selected. The following force parameters were considered: maximum isometric force output, duration of leg press exercise, and RFD. RFD was calculated using the maximal slope of the force time curve (Δforce/Δtime). Normalized force output values were determined as force relative to maximum force (expressed as % of MVF). The reported data are referred to the bout associated with the best developed force.

NIRS measurements were performed (sampling rate: 6 Hz) with a NIRO-300 oximeter (Hamamatsu Photonics, Japan). The optical probe (consisting of one emitter and one detector 4.5 cm apart), supported by a rigid rubber shell, was firmly attached to the skin of the main body of VL by a double-sided adhesive sheet. The rigid rubber shell, in turn, was secured by a soft and elastic bandage. To identify the exact site for the

positioning of the rubber shell, each subject performed preliminary leg contractions. Pen-marks were made on the skin to check for any sliding of the probe during the exercise. No sliding of the probe was observed at the end of the measurements in any subject. NIRS data were collected and transferred on-line to a computer for storage and subsequent analysis. SmO_2 was measured as tissue oxygenation index (TOI, %). TOI reflects the local balance between O_2 supply and O_2 consumption. Blood volume changes were measured as total hemoglobin changes (tHb, μM*cm). Adipose tissue thickness (ATT) underlying the monitored VL area was measured with a skinfold caliper. Adipose tissue thickness was 4.2±0.9 mm. Considering that ATT was less than 6 mm, it can be assumed that TOI variations reflect the metabolic changes occurring mainly at the muscle level.

3. RESULTS

Static leg press exercise duration and maximal force output (corrected for body mass) were 3.3 ± 0.5 s and 18 ± 2 N/kg, respectively (Table 1). The normalized profile of force output for all subjects is reported in Fig. 2.

Table 1. Force output and *vastus lateralis* TOI values measured over explosive static leg press exercise.

Subject	EXERCISE			TOI (%)			Time to min TOI (s)
	Duration (s)	Max Force (N)	RFD (N/s)	Baseline	End exercise	Minimum	
1	4	1050	2416	71	57	35	4
2	3	1195	4413	73	74	56	7
3	3	1264	5286	75	76	49	10
4	3	1328	6651	71	68	47	7
5	3	1224	2822	65	64	43	9
6	3	1190	8855	70	60	44	10
7	4	1445	3433	66	56	19	3
Mean±SD	**3.3±0.5**	**1242±123**	**4839±2299**	**70±4**	**65±8**	**42±12*#**	**7±3**

RFD: rate of force development. Time to min TOI: the time (after the end of exercise) at which TOI reached its minimum value. *: significantly different from baseline (P= 0.0003); #: significantly different from the end of exercise (P= 0.0001).

Figure 3 shows the VL oxygenation pattern observed in 2 out the 7 subjects (#2, 3). TOI was unchanged over the 3-s exercise and started to drop immediately after the exercise end. In the remaining 5 subjects, TOI was stable only over the first 1.5-2 s of the exercise; thereafter, TOI started to decline (5.3 ± 2.3 %/s) (Fig. 4). In all the subjects, TOI was reduced by 40 ± 16 % (in correspondence to TOI minimum value: 42 ± 12 %) in 7 ± 3 s after the end of the exercise (Table 1).

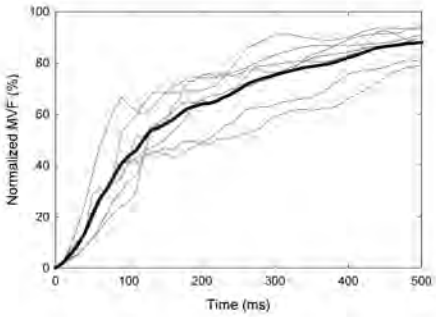

Figure 2. Time course of normalized maximal voluntary force (MVF, %) at the onset of the static leg press exercise. The solid line represents the average over the 7 subjects.

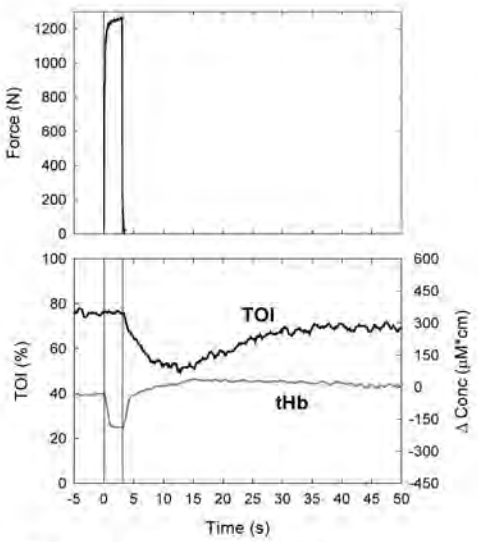

Figure 3. Time course of leg force output (upper panel), and *vastus lateralis* TOI and tHb (lower panel) before, during, and after static leg press exercise (subject #3).

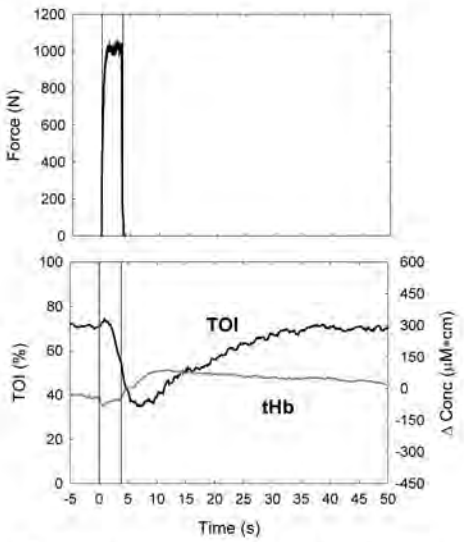

Figure 4. Time course of leg force output (upper panel), and *vastus lateralis* TOI and tHb (lower panel) before, during, and after static leg press exercise (subject #1).

4. DISCUSSION

To the best of our knowledge, this is the first time that NIRS has been employed to assess SmO_2 in leg muscle during single very short trials of static leg press exercise. This non-invasive optical method has been found suitable for evaluating the metabolic response in exercising muscles.[5] It is well known that there are 3 distinct yet closely integrated processes that operate together to satisfy the energy requirements of skeletal muscle. The anaerobic energy system is divided into alactic and lactic components, referring to the processes involved in the splitting of the stored phosphagens, ATP and phosphocreatine (PCr), and the nonaerobic breakdown of carbohydrate to lactic acid through glycolysis. The aerobic energy system refers to the combustion of carbohydrates and fats in the presence of O_2. The interaction and relative contribution of the energy systems during single bouts of maximal exercise has not been clarified yet. Most recent research suggests that energy is derived from each of the energy-producing pathways during almost all exercise activities.[3] The duration of maximal exercise at which equal contributions are derived from the anaerobic and aerobic energy systems appears to occur between 1 to 2 min and most probably around 75 s, a time that is considerably earlier than has traditionally been suggested.[3] TOI data reported in Fig. 3 suggest that during the 3-s static leg press exercise, the main contributor of the energy system to the exercising VL muscle was represented by the anaerobic-alactic one. On the other hand, the initial decline of TOI within the first 3-s of exercise (Fig. 4) suggests that the lactic component of the anaerobic system was already involved, and/or O_2 was even utilized by VL. The aerobic pathway (oxidative metabolic response) starting after the end of the exercise period was evident in both the observed oxygenation patterns (Fig. 3 and 4). In this case TOI dropped to reach its minimum value and returned slowly to the pre-exercise value as a consequence of O_2 utilization for regenerating ATP, then for replenishing the PCr stores. The variability of the VL metabolic response, observed amongst the subjects, could be in part explained by the diverse performance of the subjects (Fig. 2).

In conclusion, this study suggests that NIRS could be used to: 1) profile in each muscle group the aerobic and anaerobic energy system contribution during a single bout of maximal exercise; 2) follow alteration of the profile as function of specific aerobic or anaerobic training or rehabilitation programs.

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Differences in exercising limb blood flow variability between cardiac and muscle contraction cycle related analysis during dynamic knee extensor

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Aim. **Blood flow in peripheral conduit arteries during steady-state, dynamic exercise, can be estimated noninvasively with Doppler ultrasound, by measuring the conduit arterial diameter and the mean blood velocity averaged over consecutive cardiac beat-by-beat cycles (BB_{cycle}) or muscle contraction-relaxation cycles (CR_{cycle}). The precise impact fluctuations in the 1-BB_{cycle}- or 1-CR_{cycle}-rate may impose on the average blood flow measurements has previously not been clearly defined. The hypothesis investigated in the present study was that the blood flow measurements obtained, and its variability, during exercise, may differ between the 1-BB_{cycle} and 1-CR_{cycle} at incremental exercise intensities; as the BB_{cycle}-measurements may be influenced by transient alterations in heart rate; whereas the CR_{cycle}-measurements are dependent on the muscle contraction-relaxation frequencies independent of the exercise intensities *per se*. The main purpose was therefore to determine if fluctuations in blood flow for 1-BB_{cycle} and 1-CR_{cycle}varies at incremental exercise intensities (work rates) using the one-legged dynamic knee-extensor exercise (DKE) model.**

Methods. **Limb femoral artery blood flow (LBF) was determined, for 1-BB_{cycle} and 1-CR_{cycle}, in 8 healthy male subjects during 4-min of steady-state DKE at 60 contractions per minute at 10, 20, 30 and 40 W. The variability of LBF was determined from the coefficients of variation (CV_{LBF}).**

Results. **The CV_{LBF} for the CR_{cycle}-measurements at each work rate were similar (P=NS). The CV_{LBF} for the BB_{cycle}-measurements were higher (P<0.05) at 40 W compared to at 10 W. Furthermore, the CV_{LBF} for the 1-BB_{cycle} was higher (P<0.05) than for the 1-CR_{cycle} at 30 and 40 W, despite almost identical mean LBF values for the BB_{cycle}- and the CR_{cycle}-measurements at each exercise intensity.**

Conclusions. **The present data suggests that estimates of LBF at slightly higher exercise intensities such as above 30 W, for a few number of consecutive BB_{cycle}, renders a higher variability than for CR_{cycle}-measurements. This may consequently result in slight over- and under-estimations of LBF compared to the CR_{cycle}-measurement.**

KEY WORDS: Cardiac beat - Doppler ultrasonography - Dynamic knee-extensor exercise - Flow variability - Muscle contraction-relaxation cycle.

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Accurate measurements of limb blood flow (LBF) during exercise, by non-invasive measures, are of great importance. In previous studies using high

time resolution Doppler ultrasound recordings, blood flow velocity measurements have been methodologically evaluated for both the conduit common femoral artery during leg exercise [1-6] and the brachial artery during forearm exercise.[7-9] When making such measurements it is, however, important to consider the impact that the muscle contraction-relaxation and cardiac rhythm may have on the average blood flow estimates obtained.

Rhythmic muscle contractions *per se* induce an oscillatory blood flow response.[4, 10] This results due to the effects of central cardiac and blood pressure (BP) related factors, superimposed on the influence of peripheral muscle contraction-relaxation induced variations in intramuscular pressure, in combination with peripheral vasodilation.[5, 10] The rationale in previous studies for estimating steady-state LBF during exercise have been to reduce the influence of the cardiac beat-by-beat cycle (BB_{cycle}) and muscle contraction-relaxation cycle (CR_{cycle}) related fluctuations in blood flow by averaging over a long enough period of time.[5, 8] Such average values of blood flow in peripheral conduit arteries during steady-state exercise have been methodologically estimated by integrating the Doppler ultrasound samplings over consecutive cardiac BB_{cycle} or muscle CR_{cycle}. This have yielded coefficients of variation (CV) of approximately 5%, thus in the range of the normal physiological variation, and comparable to measurements using the thermodilution technique.[4, 5, 8, 9, 11] As the interest in focus in most of these studies were steady-state measurements, minor fluctuations in the blood flow estimates occurring for each muscle contraction-relaxation cycle or cardiac pumping beat-by-beat cycle were not of great concern. However, when studying transitional changes in blood flow it is of great importance to know to what extent the cardiac beat-by-beat- and muscle contraction-relaxation-averaged estimates may influence the measurements obtained.

The sampling duration of the measurements is one of the key factors influencing the variability in the obtained blood flow value during exercise. The duration of single muscle contraction-relaxation cycles are, however, constant at different work rates unless altered deliberately. As a consequence, the blood flow variability determined for single muscle contraction-relaxation cycles are similar in between different work rates.[5] The CV in LBF for the BB_{cycles} at incremental exercise intensities may, however, show a greater variability as the duration of the BB_{cycles} may vary as heart rate increase for the incremental exercise intensities. The hypothesis investigated in the present study was therefore that the BB_{cycles}-induced blood flow variability may be greater than the CR_{cycle}-induced blood flow variability; which previously have not been systematically studied. Understanding this may contribute to making more accurate peripheral arterial blood flow measurements during exercise and provide further insights into the regulatory mechanisms of blood flow. The purpose of the present study was therefore to examine the femoral arterial LBF variability for single 1-BB_{cycle} and 1-CR_{cycle} measurements at incremental exercise intensities (10-40 W) utilizing the one-legged, dynamic, knee-extensor exercise (DKE) model.

Materials and methods

Experimental design

Eight healthy male volunteers (mean±SEM, range) with an age of 26.8±1.4 years (22-36 years), height of 183.1±2 cm (174-190 cm), and weight of 77.5±2.8 kg (64-90 kg) participated in the study. They were informed about the experimental procedures, potential risks and discomfort, and that they could withdraw at any time without any consequences. All subjects provided written informed consent to participate in the experiments approved by the Ethical Committees of Copenhagen and Frederiskberg (KF-01-013/96).

The subjects were familiarized with the one-legged, DKE model [11, 12] before starting the experiments. They exercised at 60 contractions per minute (cpm) at external work rates of 10, 20, 30 and 40 W. The hamstring muscles were allowed to fully relax so that the knee-extensors solely performed the work. The thigh was positioned horizontally and the lower leg moved to a knee angle of ~150 degrees, where 180 degrees corresponds to a fully extended knee. Belts attached to a seat fixed the upper body and both thighs. The external work rate was calculated according to the dynamic knee-extensor ergometer model,[11, 12] defined as: external work rate (W)=[contraction frequency (cpm)/60 s]×[distance of a knee-extensor revolution (6 m)]×[load mass (kg)×9.81 (m/s^2)]. The specific weights applied at the loads of 10, 20, 30, and 40 W were 0.167, 0.333, 0.5, and 0.667 kg, respectively.

All experiments for each subject were performed

within one day and the recovery time between the DKE bouts was sufficient to allow blood flow to return to control level. LBF was measured for ~4 min at steady-state, which was reached after 3 min of DKE as previously described.[4, 5, 10] The contraction rhythm was maintained by following the pace of a visible and audible metronome, and by visualizing the contraction frequency displayed in real time on a monitor.

Measurements of mean blood velocity (MBV), blood flow, BP and muscle force

MBV and flow measurements in the common femoral artery have previously been validated and shown to produce accurate absolute values at rest and during DKE.[4] The measurements were performed with a Doppler ultrasound (model CFM 800, Vingmed Sound, Horten, Norway) equipped with an annular phased array transducer (Vingmed Sound, Horten, Norway) probe (11.5 mm diameter). It operated at an imaging frequency of 7.5 MHz and variable Doppler frequencies of 4-6 MHz (high-pulsed repetition frequency mode, 4-36 kHz). The site of vessel diameter determination and blood velocity measurements in the common femoral artery was distal to the inguinal ligament, but above the bifurcation into the superficial and profunda femoral branch. This location minimizes turbulence from the bifurcation and influence of blood flow from the inguinal region. In addition, the dimension of the arterial diameter is unaffected by the contraction and relaxations *per se* at this site proximal to the exercising muscles. Heart rate and the systolic and diastolic femoral artery diameter were measured in relation to the ECG on the Doppler ultrasound monitor. The mean vessel diameter was calculated in relation to the temporal duration of the BP curve as [(systolic diameter values±1/3)+(diastolic diameter values±2/3)].[4] The diameter measurements were obtained under perpendicular insonation.

Resting vessel diameter measurements were used to calculate LBF during rest and DKE, since the diameter has been found not to vary significantly between rest and steady-state exercise.[3-5, 13-17] Blood velocity was measured with the probe at the lowest possible insonation angle, always less than 60 degrees.[18] The mean value of the insonation angle was ~46.5±1.1 degrees, and remained constant throughout the experiments for each individual subject. The probe position was stable and the sample volume was placed in the center of the vessel, and then adjusted to cover the width of the diameter. Background noise caused by turbulence at the vascular wall was reduced with a low-velocity rejection filter. Steady-state LBF was calculated by multiplying the cross-sectional area [area=$\pi\times(\text{diameter}/2)^2$] of the femoral artery, with the amplitude (signal intensity) weighted MBV (angle corrected, time and space-averaged signal); where LBF=MBV×area×6×10^4 (L/min). The constant 6×10^4 is the conversion factor from m/s to L/min.[4] Mean LBF was expressed by averaging all sampling data for the individual subjects. Maximum LBF was determined by averaging the 20 highest sampling values for the BB_{cycle} and CR_{cycle}, respectively. Minimum LBF was determined by averaging the 20 lowest sampling values for the BB_{cycle} and CR_{cycle}, respectively. Operator (intraobserver) variability was minimized by extensive training with the Doppler ultrasound equipment during rest and DKE. By continuously sampling the blood velocity at an acquisition rate of 1 kHz small transients in normal physiological arterial blood velocity and flow can be detected with a high temporal resolution. The minimum value of the CV for MBV determined by repeated measurements represented the criteria for quality control of operator technique at rest.[5, 19]

Peripheral arterial BP was monitored continuously with a finger-cuff photoplethysmography device (Finapres™, Ohmeda 2300, Englewood, USA) placed on the middle finger of the left hand. The finger cuff was maintained next to the inguinal ligament in a fixed position at the level of the femoral artery. Mean arterial BP was calculated by integrating the BP curve over time. Kicking muscle force was measured using a strain gauge. The variation in muscle force was taken to represent oscillations in the intramuscular pressure, as these parameters temporally correlate well during DKE.[4, 10, 20] Measurements were continuously performed before exercise and during 4 min of DKE. The data were continuously stored in a computer using a MacLab data acquisition system (Chart v.3.5.7 software, ADInstruments, Sydney, Australia).

Muscle CR_{cycle} and cardiac BB_{cycle} related LBF variability

The LBF variability was determined for each cardiac BB_{cycle} and for each muscle CR_{cycle} during steady-state DKE, as illustrated in relation to the BP and force tracings (Figure 1). The CV for LBF (CV_{LBF}) were calculated from the MBV measurements for the 1-CR_{cycle} and for the 1-BB_{cycle} during DKE (Figure 1).

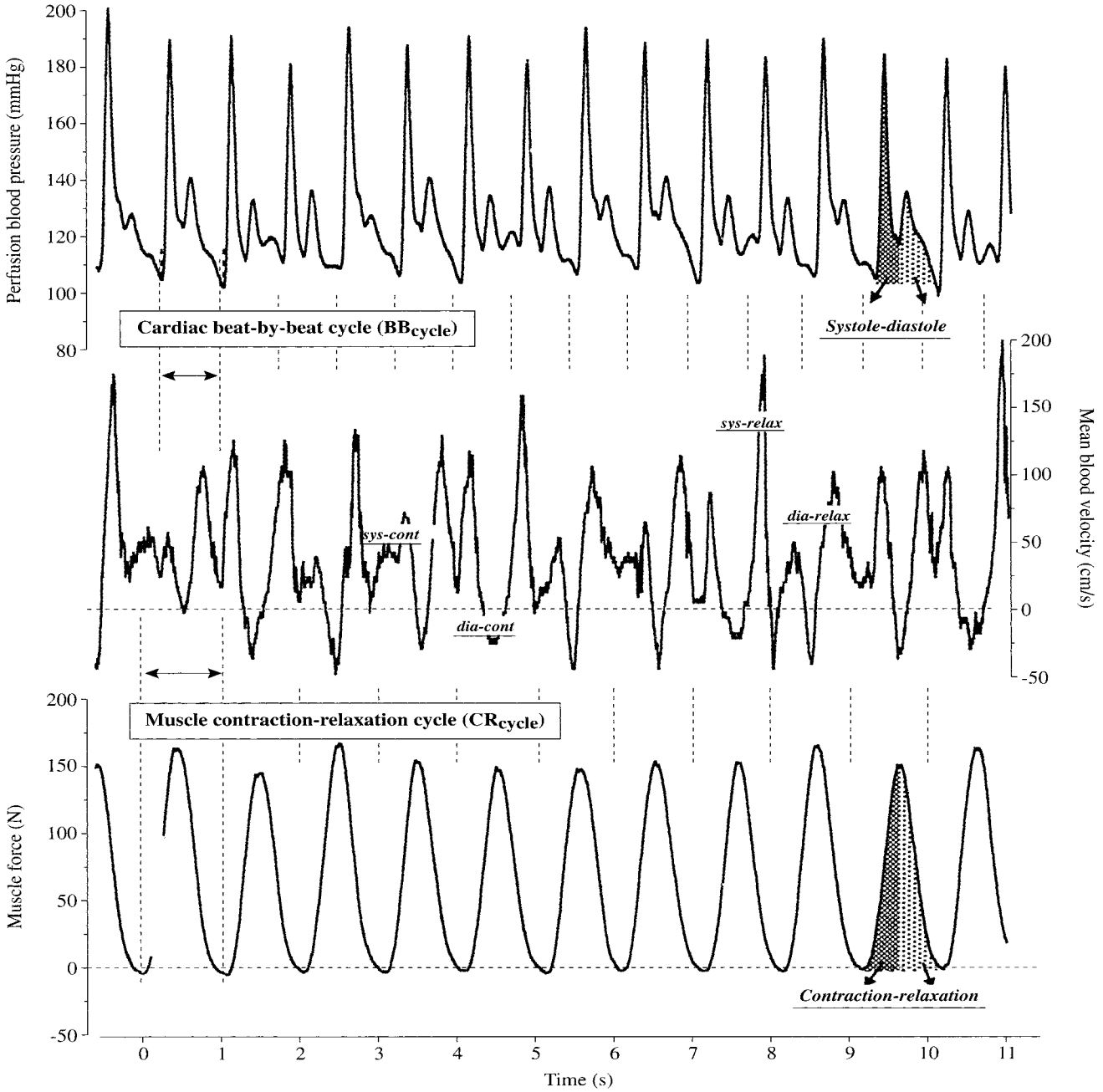

Figure 1.—Continuous recording of MBV and blood pressure in a single subject. Mean common femoral artery blood velocity (MBV), blood pressure (BP) and muscle force during steady-state DKE at 20 W and 60 cpm in one subject. At steady-state DKE, MBV was measured in relation to the cardiac beat-by-beat cycle guided by the systolic (systole) and diastolic (diastole) BP phase, as well as in relation to the muscle contraction-relaxation cycle guided by the muscle-force tracing. As previously shown by Rådegran and Saltin [10] MBV was notably increased to its highest value at the systolic BP phase during muscle relaxation, and was significantly lowered to its lowest value at the diastolic BP phase during muscle contraction. The MBV showed an intermediate value at the systolic BP phase during muscle contraction and at the diastolic BP phase during muscle relaxation. The MBV was retrograde during the diastolic BP phase during muscle contraction. The figure thus exemplifies the contribution to the magnitude of the physiological variability in blood flow by the contraction-relaxation-induced variations in muscle force, and consequently the intramuscular pressure variations, along with the superimposed influence of the BP and the tonic influence of the state of vasodilation.[10]

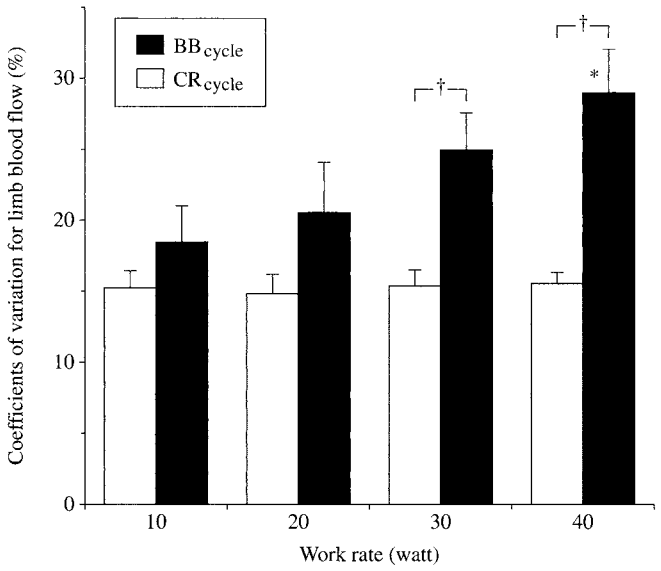

Figure 2.—LBF variability determined for 1-BB_{cycle} and 1-CR_{cycle}. The coefficients of variation (CV) for limb blood flow (CV_{LBF}) were similar (P=NS) at each work rate when determined for the muscle contraction-relaxation cycle (CR_{cycle}). The CV_{LBF} determined for the cardiac beat-by-beat cycle (BB_{cycle}) was, however, significantly (*P<0.05) higher at 40 W compared to at 10 W. A significant (†P<0.01) difference in the CV_{LBF} was furthermore seen between the BB_{cycle} and CR_{cycle} at 30 and 40 W, respectively. Values are means±SEM.

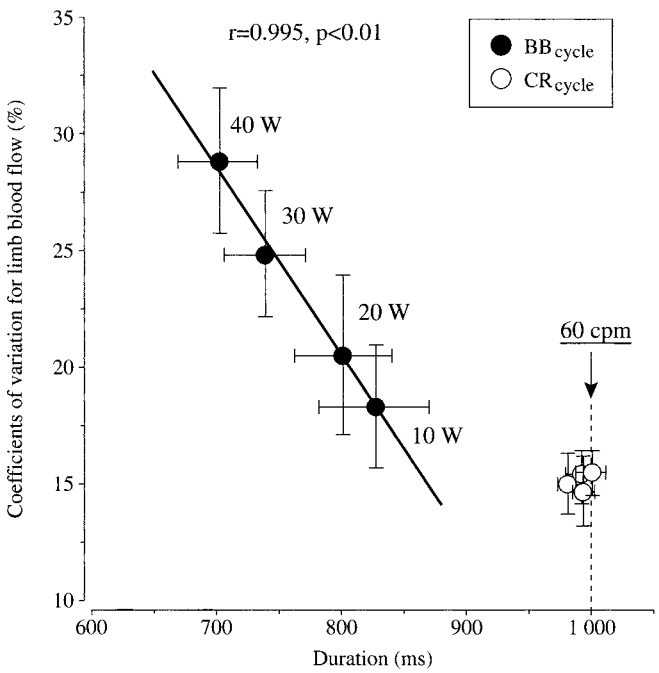

Figure 3.—Relationship between the CV_{LBF} and the duration of 1-BB_{cycle} and 1-CR_{cycle} at each work rate. There was a negative linear correlation (r=0.995, P<0.01) between the duration of the 1-BB_{cycle} and the CV_{LBF}. There was no correlation (P=NS) between the duration of the 1-CR_{cycle} and the CV_{LBF}. The duration of the 1-CR_{cycle} was constant for the incremental intensities (work rate) with a CV_{LBF} of approximately 15% which was smaller (P<0.05) compared to the range in the CV_{LBF} of 18.3-28.9% for the 1-BB_{cycle}. Values are means±SEM.

Such measurements obtained during 1-single CR_{cycle} represent predominantly the muscle contraction-relaxation-related physiological variability in LBF. The 1-single BB_{cycle} represents predominantly the cardiac cycle-related variability in LBF. The external work rates of 10, 20, 30 and 40 W at 60 cpm represented a range of exercise intensities. The CV at each work rate for the individual measurements was defined as the standard deviation (SD)/mean×100 (%). The mean CV in this study was obtained from the average CV values from the 8 subjects for each set of measurements.

Statistical analysis

Data were analyzed using multiple analysis of variance for repeated measures and Fisher's significant difference posthoc tests, when comparing more than two groups over time. A P values of <0.05 were considered as statistically significant. A P=NS indicates not statistically significant. The relationship between LBF and work rate was evaluated by using linear regression analysis. All values are means±SEM.

Results

The CV_{LBF} determined for the CR_{cycle} were similar at each work rate. The CV_{LBF} for the BB_{cycle} were higher (P<0.05) at 40 W compared to 10 W (Figure 2). The CV_{LBF} for the BB_{cycle} was furthermore higher (P<0.05) than for the CR_{cycle} at 30 and 40 W, respectively. The CV_{LBF} also showed a tendency (P=NS) to be slightly higher for the BB_{cycle} than for the CR_{cycle} at 10 and 20 W, respectively. A negative linear correlation (r=0.995, P<0.01) was found between the duration of the 1-BB_{cycle} and the CV_{LBF}. There were no correlation (P=NS) between the duration of the 1-CR_{cycle} and the CV_{LBF} (Figure 3). Heart rate at 10, 20, 30 and 40 W were 74.2±3.9, 76.2±3.7, 82.5±3.6, and 87±3.9 beats/min, respectively. The contraction rates were similar (P=NS) between 10 and 40 W with a mean range of 60.6±0.2 cpm (60.1-61.2 cpm). The mean LBF calculated from the BB_{cycle} and the CR_{cycle} were

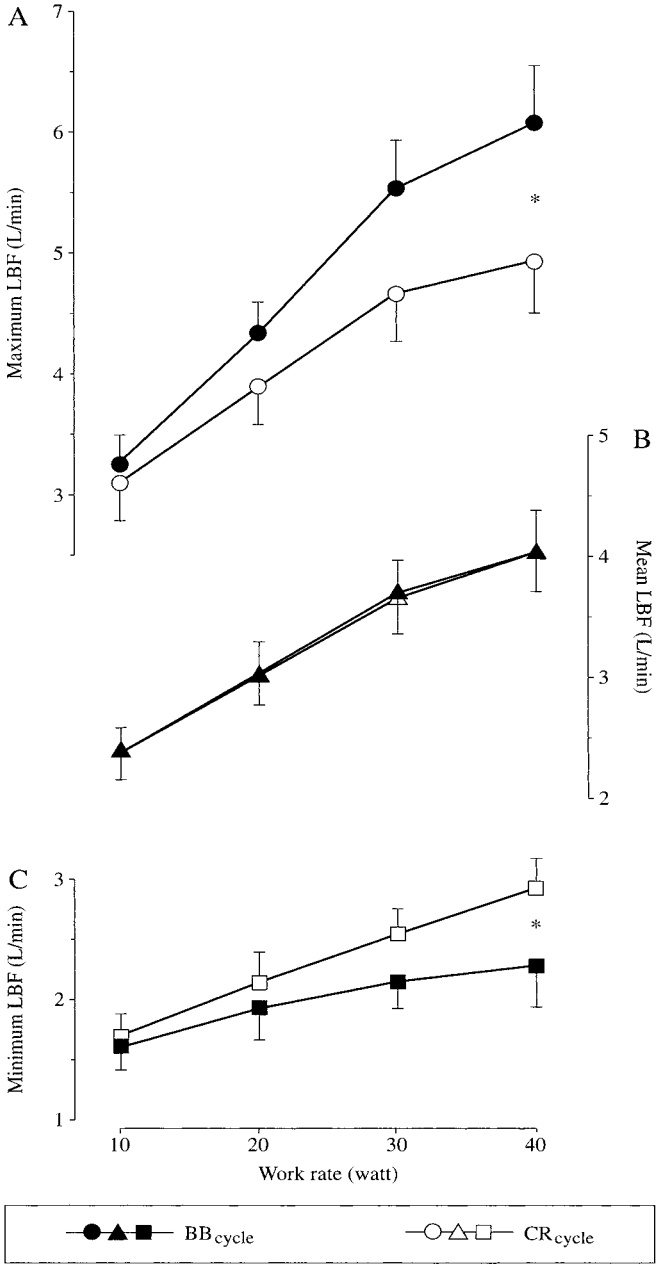

Figure 4.—Maximum, mean and minimum LBF determined for 1-BB_{cycle} and 1-CR_{cycle}. Maximum LBF (A) was significantly (*P<0.05) higher at 40 W when determined for the BB_{cycle} than the CR_{cycle}. Mean LBF (B) was similar (P=NS) for the CR_{cycle} and the BB_{cycle}. A positive linear correlation (P<0.01) between mean LBF and work rate was described for both the BB_{cycle} (r=0.991) and the CR_{cycle} (r=0.993) measurements. Minimum LBF (C) was significantly (*P<0.05) lower at 40 W when determined for the BB_{cycle} than for the CR_{cycle}. There was furthermore a tendency (P=NS) that maximum LBF was higher as well as minimum LBF was lower for the BB_{cycle} than the CR_{cycle} for the intermediate incremental intensities of 20-30 W. Values are means±SEM.

almost identical (P=NS) at each incremental exercise intensity, respectively. A positive linear correlation (P<0.01) between mean LBF and work rate was observed for both the BB_{cycle} and CR_{cycle}, in support of previous findings.[4-6, 10, 17] The maximum LBF determined for the BB_{cycle} at 40 W was approximately 1.1 L/min higher (P<0.05) compared to the value obtained for the CR_{cycle} (Figure 4). The minimum LBF determined for the BB_{cycle} at 40 W was approximately 0.6 L/min lower (P<0.05) than for the CR_{cycle}. The sampling number of measurements at 10, 20, 30, and 40 W were: 197±22, 224±19, 183±21, and 145±14, respectively, for the BB_{cycle}; and 170±18, 191±13, 144±16, and 105±12, respectively, for the CR_{cycle}.

Discussion

In the present study a slight difference in the blood flow variability was observed between the BB_{cycle}- and the CR_{cycle}-averaged blood flow measurements at incremental exercise intensities (work rates) during steady-state DKE at 60 cpm. Specifically, the LBF variability (CV_{LBF}) was larger for the BB_{cycle} than for the CR_{cycle} at higher exercise intensities such as at 30 and 40 W compared to at 10 and 20 W (Figure 2). Additionally, the BB_{cycle}-induced blood flow variability was closely related to the duration of the cardiac cycle (beat-by-beat interval). The methodological implications of these findings are covered in the following discussion.

Relationship between the CV_{LBF} and the sampling cycle

As the CV_{LBF} was closely (P<0.01) related to the duration of the 1-BB_{cycle} but not the 1-CR_{cycle}, the duration of the 1-BB_{cycle} may be assumed to influence the variations in blood flow. Larger variations in the CV_{LBF}, in the range of ~18-29%, was also observed with an increase in work rate and a shorter duration of the 1-BB_{cycle} (Figure 3). The duration of the 1-CR_{cycle} was, however, constant (≈1 000 ms corresponding to 60 cpm) for the incremental exercise intensities (work rate) resulting in a smaller (P<0.05) CV_{LBF} of approximately 15%. Such a CV_{LBF} determined for the 1-CR_{cycle} measurement has previously also been found to be closely related to the muscle force during DKE at 60 cpm.[5] The results with a higher variation in blood flow with an increase in work rate for the BB_{cycle}-measurements sup-

ports the hypothesis of the present study. A major reason for the fluctuation in blood flow for the BB_{cycle}-measurement may be that as the duration of the BB_{cycle} decrease, the relative influence of the variations in the BP and intramuscular pressure variations may increase.

Dissociated maximum and minimum LBF between BB_{cycle}- and CR_{cycle}-measurements

It is well known that Doppler ultrasound is capable of continuously recording conduit arterial blood flow velocity with a high temporal resolution during dynamic knee extensor- and handgrip exercise.[5, 8, 10] Variations in the blood flow velocity can therefore be accurately described. The normal physiological variations in the blood flow velocity have previously also been estimated during DKE [1, 4, 5, 10] and rhythmic handgrip exercise.[8] In order to minimize the fluctuation in the blood flow measurement related to the measurement procedure and not to the physiological variation *per se*, blood flow has previously been estimated by averaging over a long enough series of BB_{cycle} or CR_{cycle} samplings, resulting in approximately a 5% CV.[4, 5, 8] It has, however, been unclear why the magnitude in the LBF variability is slightly different between 1-BB_{cycle} and 1-CR_{cycle} at different exercise intensities during DKE. This is now clarified with the findings of the present study. A larger flow variability (CV_{LBF}) was found at higher exercise intensities such as 30 and 40 W for the BB_{cycle}-compared to with the CR_{cycle}-sampling procedure (Figure 2). The CV_{LBF} determined for the 1-CR_{cycle} (14.7-15.4%) was similar to previously reported data (13.3-18.1%) [5] in another set of subjects. There were notably also differences when determining LBF with either the BB_{cycle} or the CR_{cycle} at higher exercise intensities, especially when measurements were made using a small number of consecutive cycles. One explanation for the higher CV_{LBF} when using the 1-BB_{cyce} at higher exercise intensities may be due to that the maximum and minimum LBF values vary between BB_{cycle}- and CR_{cycle}-measurements (Figure 4). In other words, the magnitude of the LBF amplitude between maximum and minimum value is not the same when determined for the BB_{cycle} and the CR_{cycle} at 40 W. In specific, at 40 W maximum LBF determined for the BB_{cycle} was approximately 1.1 L/min higher than that for the CR_{cycle}. Minimum LBF was furthermore approximately 0.6 L/min lower than that obtained for the CR_{cycle} (Figure 4). The maximum and minimum LBF were determined from the amplitude in the measurements influenced by the combination of the effect of the perfusion BP and the intramuscular pressure (muscle force) variations over transient short periods in the continuous flow velocity curve during DKE (Figure 1). As previously shown the highest blood flow velocity was observed when peak systolic BP occurred during the muscle relaxation phase, in support of previous findings.[10] The lowest blood flow velocity was observed when the diastolic BP occurred during the muscle contraction phase (Figure 1). The blood flow velocity showed an intermediate value at the systolic BP phase during muscle contraction and at the diastolic BP phase during muscle relaxation. The range of the magnitude between maximum and minimum LBF furthermore increased with an increase in work rate (Figure 4A and C). Maximum and minimum LBF were also more distinct for the BB_{cycle}- than for the CR_{cycle}-measurements. These findings thus suggests that LBF determined for the 1-BB_{cycle} show a higher transient value during the muscle relaxation phase and a lower transient value during the muscle contraction phase.

Conclusions

In conclusion, the present findings may serve as a guideline for how to obtain accurate measurements of transient changes in LBF during exercise in humans; and what mechanisms that may influence the methodological and physiological variability in blood flow. The findings are furthermore helpful in how to evaluate, interpret and compare previous and future measurements of exercising blood flow measured by the BB_{cycle} and the CR_{cycle} at various exercise intensities, particularly in relation to the heart rate, perfusion BP and contraction-relaxation duty cycles *per se*.

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Light source-detector spacing of near-infrared-based tissue oximeters and the influence of skin blood flow

Marco Ferrari, Valentina Cettolo, Valentina Quaresima, Scott L. Davis, Paul J. Fadel, Jian Cui, Gail D. Thomas and Craig G. Crandall

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The following is the abstract of the article discussed in the subsequent letter:

Davis, S. L., P. J. Fadel, J. Cui, G. D. Thomas, and C. G. Crandall. Skin blood flow influences near-infrared spectroscopy-derived measurements of tissue oxygenation during heat stress. *J Appl Physiol* 100: 221–224, 2006. First published September 8, 2005; doi:10.1152/japplphysiol.00867.2005.—Near-infrared (NIR) spectroscopy is a noninvasive optical technique that is increasingly used to assess muscle oxygenation during exercise with the assumption that the contribution of skin blood flow to the NIR signal is minor or nonexistent. We tested this assumption in humans by monitoring forearm tissue oxygenation during selective cutaneous vasodilation induced by locally applied heat ($n = 6$) or indirect whole body heating (i.e., heating subject but not area surrounding NIR probes; $n = 8$). Neither perturbation has been shown to cause a measurable change in muscle blood flow or metabolism. Local heating (~41°C) caused large increases in the NIR-derived tissue oxygenation signal [before heating = 0.82 ± 0.89 optical density (OD), after heating = 18.21 ± 2.44 OD; $P < 0.001$]. Similarly, whole body heating (increase internal temperature 0.9°C) also caused large increases in the tissue oxygenation signal (before heating = −0.31 ± 1.47 OD, after heating = 12.48 ± 1.82 OD; $P < 0.001$). These increases in the tissue oxygenation signal were closely correlated with increases in skin blood flow during both local heating (mean $r = 0.95 \pm 0.02$) and whole body heating (mean $r = 0.89 \pm 0.04$). These data suggest that the contribution of skin blood flow to NIR measurements of tissue oxygenation can be significant, potentially confounding interpretation of the NIR-derived signal during conditions where both skin and muscle blood flows are elevated concomitantly (e.g., high-intensity and/or prolonged exercise).

Light source-detector spacing of near-infrared-based tissue oximeters and the influence of skin blood flow

To the Editor: In a recent article, S. L. Davis et al. (1) presented the results of a study investigating the influence of the increase in the skin blood flow on the near-infrared spectroscopy (NIRS)-based measurement of the flexor digitorum muscle oxygenation during local or whole body heating. Tissue oxygenation was measured by a continuous-wave photometer (NIRO 500; Ref. 3).

We agree with the authors on *1*) criticizing prior studies for adopting poor methodologies to increase and assess skin blood flow (5, 6); and 2) recognizing the importance to investigate the influence of skin blood flow, once adequately increased and assessed, on the measurement of muscle oxygenation by NIRS. On the other hand, we disagree with the authors on the NIRS methodology (light source-detector spacing and quantification of NIRS parameters) adopted for testing their hypothesis.

As mentioned by the authors, the light source-detector separation affects the contribution of skin; in fact, increasing this separation properly allows the improvement of the sensitivity of measurement and the increase of the probability of looking at oxygenation deep under the tissue surface (10). In addition, it is well known that the depth of light penetration also depends on the thickness of subcutaneous adipose tissue (7, 9). For these reasons, were the authors wise to have used a source-detector distance of 2 cm? This distance is very short, and to convince the readers that the reported results truly refer to the oxygenation changes occurring in the investigated muscle tissue, the authors should have reported the adipose tissue thickness values and the relationship between longer source-detector distances and skin blood flow. Therefore, their generalized conclusion "skin blood flow can contribute significantly to near-infrared-derived measurements of tissue oxygenation in humans" is not supported by adequate experimental NIRS data.

The authors expressed their results in optical density (OD; without specifying the considered wavelength) instead of reporting changes in concentration of oxy- and deoxyhemoglobin [expressed in μM*cm or ΔμM if a pathlength factor is used (2)]. In addition, we would also point out the inconsistency between the reported extremely high values of OD (up to 18) and the performance of the NIRO 500 (the system is linear over a range of ± 0.7 OD; Ref. 3).

We would like to comment that, since 1998, the investigational NIRO 500 device used in the study is no longer commercially available, and it has been replaced by other instruments (tissue oximeters) that use a fixed source-detector spacing of 4 or 5 cm and offer hemoglobin oxygen saturation values ensuring a more accurate quantitation of the oxygenation changes occurring at muscle level.

In summary, the study on the potential contribution of very high levels of skin blood flow to the muscle NIRS signal is of great interest for better understanding of the potential use of NIRS in exercise physiology. However, this issue is still open and additional studies should be carried out using more recent NIRS methodologies (4, 8), which include suitable light source-detector distances, for investigating deep regions of muscle.

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REPLY

To the Editor: We thank Dr. Ferrari and colleagues for their interest and comments regarding our recent work (3). On the basis of these comments, we identified an error in the units of the reported data. As published, near-infrared (NIR) data are expressed as optical density (OD), when in fact data should have been reported as change in oxyhemoglobin concentration expressed in micromoles per liter (μmol/l). It should be noted that this error in no way changes the interpretation of the data or alters the conclusion that skin blood flow can contribute significantly to NIR-derived measurements of tissue oxygenation.

Regarding the concern that the NIR light source-detector spacing of 2 cm might be too short for the light to penetrate both the skin and the underlying muscle, we disagree that this is a limitation of the protocol. Using this spacing, we previously confirmed that the NIR signal was responsive to changes in forearm muscle tissue oxygenation during brief bouts of graded rhythmic handgrip exercise (2, 4–6) in a setting where skin blood flow and skin metabolism are unchanged (7), suggesting that the light penetrates deeply enough to reach the active muscle. In each subject in our current study (3), we confirmed that a brief handgrip evoked forearm deoxygenation to verify the appropriate positioning of the NIR probes over the flexor digitorum profundus muscle. Because the maximal depth of penetration of NIR light is approximately one-half the distance between source and detector, the observed deoxygenation during the brief handgrip would suggest that the thickness of the skin and adipose tissue layers of the young, healthy subjects participating in our study were low. Indeed, van Beekvelt and colleagues previously reported that the average thickness of forearm skin and adipose tissue layers was <3 mm in one study of 26 subjects and <4 mm in another study of 78 subjects (8, 9). Taken together, these previous studies indicate that tissue oxygenation of forearm muscle can be assessed using a source-detector distance of 2 cm, but as our recent work demonstrates, this signal could be greatly influenced by skin blood flow (3).

Finally, we note that Buono et al. (1) recently published a study in which NIR-derived tissue oxyhemoglobin concentrations were increased by local heating-induced elevations in thigh skin blood flow and were decreased by intradermal injection of epinephrine. On the basis of our findings coupled with those of Buono and colleagues, we encourage investigators to consider the potential influence of skin blood flow in the design and interpretation of future studies involving the use of NIR-derived measurements of tissue oxygenation.

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INFLUENCE OF WHOLE-BODY VIBRATION STATIC EXERCISE ON QUADRICEPS OXYGENATION

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1. INTRODUCTION

Whole-body vibration (WBV) is a neuromuscular training method recently designed to improve muscle strength and flexibility.[1-9] More recently, WBV has been proposed to be a suitable training method as efficient as conventional resistance training to improve knee-extension strength and speed of movement and counter movement jump performance in older women.[10] The acute effects of vibration seem to be connected to the duration of the stimulation, the characteristics of the subjects (well trained vs. untrained), and the magnitude of the vibration stimulus (amplitude, frequency and acceleration). When the human body undergoes vibratory stimuli, muscle activity is necessary for damping the vibratory waves. It is assumed that vibrations evoke muscle contraction, probably via the monosynaptic stretch reflex. Although the electromyography (EMG) activity of the *vastus lateralis* (VL) muscle during WBV has been investigated,[4] there are no studies about the effects of WBV on the oxygenation (oxidative metabolism) of leg skeletal muscles.

This study aimed at investigating the oxygenation response (measured as tissue oxygenation index (TOI)) in *rectus femoris* (RF) and VL muscle groups during different frequencies of WBV.

2. METHODS

Seven volunteers (age: 23±2 years; body mass: 79±9 kg) participated in this study. Subjects were physically active although none were engaged in daily, intensive or specific training programs. All subjects gave their informed consent prior participation

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after a full oral and written explanation of the experiments. Subjects were asked to stand in half-squat (HS) position (knee angle 110°) on a vibration platform (NEMES, OMP, Italy) in the following conditions: no vibrations, and randomly 30, 40, and 50 Hz WBV. Each condition lasted 110 s, and the interval between sets was 45 min. Muscle oxygenation was monitored by a 2-channel NIRO-300 oximeter (Hamamatsu Photonics, Japan). The emission and detection probes were kept at a constant geometry and distance (4.5 cm apart) by a rigid rubber probe holder. Muscle O_2 saturation in RF and VL was measured as TOI (%). TOI reflects the balance between O_2 supply and O_2 consumption in the examined muscle volume. TOI was also measured during the standing (S) position that preceded the HS position at the beginning of each set. Concomitantly total hemoglobin volume changes (ΔtHb, μM*cm) were monitored. The sampling rate of NIRS data was 6 Hz. Adipose tissue thickness underlying the monitored VL and RF area was measured with a skinfold caliper. Adipose tissue thickness (ATT) was 4.2±0.9 mm and 4.4±1.8 mm for VL and RF, respectively. These similar ATT values allowed the correct comparison of NIRS data between the two muscle groups.

Data are reported as mean ± standard deviation of TOI and tHb changes (average over the last 5 s in every subject) for each condition. TOI and changes in tHb were compared between conditions by repeated measures analysis of variance. Significance level was set at $P<0.05$.

3. RESULTS

Oxygenation responses observed in VL and RF of one representative subject for each experimental condition are reported in Fig. 1. A significant TOI decrease was observed in RF muscle after about 40 s of WBV at 30 Hz. Concomitantly, tHb was almost stable. TOI slightly decreased in VL over the last 50 s of WBV exposure, and tHb gradually increased. TOI did not change in RF and VL in the remaining conditions, whilst tHb tended to increase. Furthermore, the pattern and the amplitude of tHb raise were different among WBV frequency conditions. Considering the averaged response over the 7 subjects (Fig. 2), WBV did not affect TOI value in VL muscle, while induced a consistent decrease of TOI in RF muscle only at a frequency of 30 Hz compared to TOI measured during baseline condition (standing). Comparing TOI of half-squat condition with TOI during WBV condition provoking the highest TOI decrease, a significant difference was found in RF (from 59.3±5.3 to 53.0±6.4%, P=0.04) and VL (57.6±2.5 to 50.3±7.9%, P=0.03).

4. DISCUSSION

Initially, WBV training was used in elite athletes to improve speed-strength performance. More recently, it is becoming extremely popular in European health and fitness clubs as an alternative training method. However, a consistent scientific support about the benefits of WBV on fitness and health is still missing. Much work has been done by Bosco et al.,[1,2] and Cardinale et al.[3-5] An increase in force-velocity, force-power and vertical-jump performance immediately after one WBV session was found.[1,2]

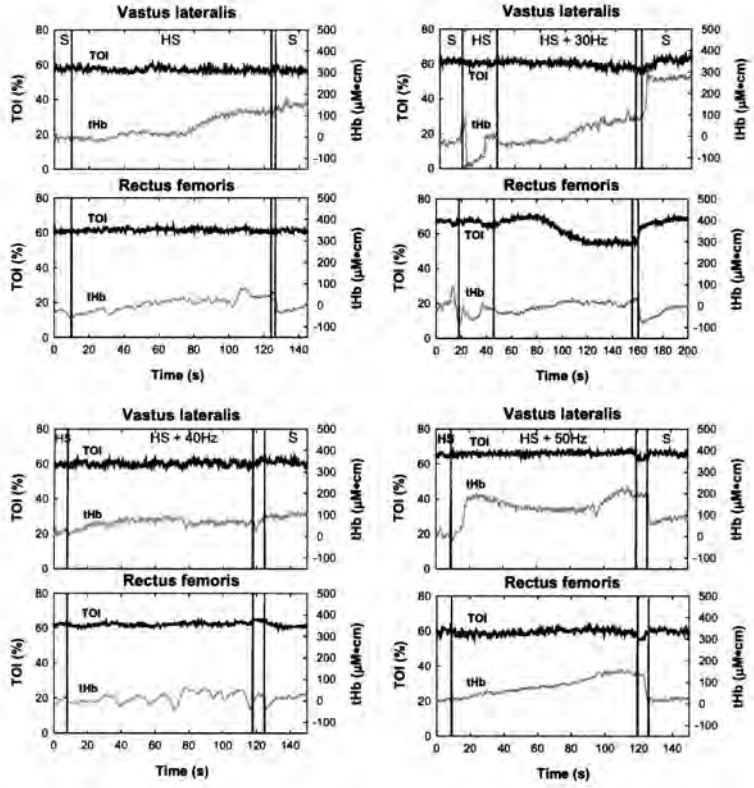

Figure 1. Time course of *vastus lateralis* and *rectus femoris* TOI and tHb changes during static HS condition only or with 30 Hz whole-body vibration (upper panels), and with 40 or 50 Hz whole-body vibration (lower panels). S: standing; HS: half-squat position (knee angle 110°).

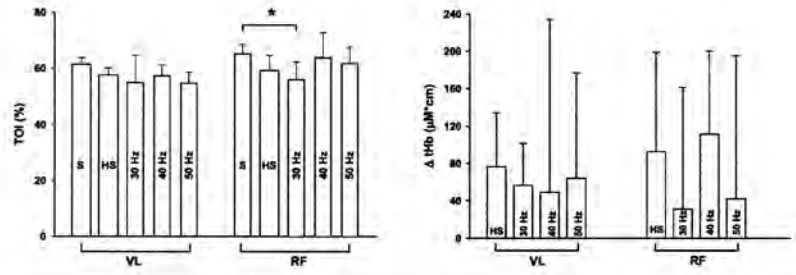

Figure 2. TOI and tHb of the *vastus lateralis* (VL) and the *rectus femoris* (RF) muscles measured at the end of 30 s standing (S), 110 s of half-squat (HS), and at the end of 110 s of the three whole-body vibrations (30, 40, and 50 Hz). *: indicates a significant difference between TOI at the end of 110 s of 30 Hz whole-body vibration and TOI measured in standing position.

The effects of WBV training on muscle performance over a longer period were also investigated.[3] It was suggested that WBV training might result in neuromuscular adaptations similar to the effects produced by explosive strength training, and that the long-term effects of WBV might depend on duration of WBV-training programs.

Recently, Delecluse et al.[6] reported that WBV (and the resulting reflexive muscle contraction) has the potential to induce strength gain in knee-extensor of previously untrained females to the same extent as resistance training at moderate intensity. Furthermore, they demonstrated that strength increases after WBV training are not attributable to a placebo effect. The EMG responses of VL muscle to different WBV were previously investigated.[4] The highest EMG root mean square was found at 30 Hz, suggesting this frequency as one eliciting the highest reflex response in VL muscle during WBV in static half-squat position.

Our study reports, for the first time, the oxygenation responses in VL and RF muscle groups during different (30, 40, 50 Hz) WBV in static half-squat position. A significant decrease of TOI was found in RF muscle during 30 Hz WBV. This suggests that the metabolic activity (as a consequence of muscle activity) in RF was higher than in VL. The oxidative metabolic activity of RF was not satisfied by the O_2 blood inflow, and the required O_2 was extracted by the local oxy-Hb with a consequent TOI decrease. Considering that, tHb is related to changes in the total volume of Hb in the muscle region of interest,[11] the observed tHb rise (Fig. 1) could reflect a local blood flow increase (vasodilatation in response to WBV). The fluctuations observed in tHb tracing of RF (Fig. 1, 50 Hz WBV panel) could be attributable to the posture changes resulting from the difficulty to maintain HS position at the highest WBV frequency used.

According to the observed inter-subjects variability of VL or RF oxidative metabolic response (different ΔTOI) to each WBV frequency, WBV training program should be individualized. However, other studies should be performed to better understand the physiological and biochemical mechanisms underlying the individual responses to WBV. This would allow the establishment of criteria to select the most effective WBV frequency and duration in planning WBV protocols for training or rehabilitation purposes.

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QUANTIFICATION OF CALF OXYGENATION IN PARAPLEGIC PATIENTS DURING PASSIVE LEG MOVEMENT

Dear Editor-in-Chief:

A recent article (4) demonstrated that passive leg movement can induce both EMG activity and alteration of calf oxygenation in a paralyzed lower limb of spinal cord–injured subjects. Although these results are interesting, the presentation of the muscle oxygenation data is inadequate. For measuring calf oxygenation, Kawashima et al. (4) used a multidistance spatially resolved tissue oximeter (NIRO-300, Hamamatsu Photonics, Japan) without exploiting the offered advantage to quantify muscle oxygenation directly as tissue oxy-hemoglobin (Hb) saturation (%). Tissue oxy-Hb saturation reflects the dynamic balance between O_2 supply and O_2 consumption and is independent on the path length of the near-infrared photons in the muscle tissue (3). Kawashima et al. (4) report the results only as changes in oxy- and deoxy-Hb values calculated relative to the resting level, and represented in micrometers. These changes should have been eventually presented at least as Δ μM*cm, because no path-length data are available for the calf of spinal cord injury patients. On the other hand, taking into account that these patients present consistent musculoskeletal degeneration (5), it would not be accurate the use of calf path-length data from healthy subjects (2).

Subcutaneous adipose tissue thickness has a substantial confounding influence on *in vivo* muscle near-infrared spectroscopy measurements, therefore it would be essential to incorporate this factor into muscle oximetry studies in order to justify comparisons between different muscle groups (7). Kawashima et al. (4) did not report the thickness of the subcutaneous adipose tissue at the measurement position in each spinal cord–injured subject. Consistent differences in the thickness of subcutaneous adipose tissue are expected among patients, and between patients and controls. The lack of this information could compromise the results of the comparison between spinal cord injury and control subjects.

Although Kawashima et al. (4) did not quantify properly muscle oxygenation, the data shown in their Figure 4 clearly suggest that the well-known postexercise hyperemic phase (evidenced as total Hb increase with respect to the pretest level) was evidenced only in the spinal cord injury patients, and it was maintained over 5 min after the end of the protocol. In addition, as previously found in walking mitochondrial disorders and muscular dystrophy patients (1,6), muscle oxygenation is not a limiting factor during passive alternate leg movement in spinal cord–injured subjects.

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Evaluation of the Skin Blood Flow Contribution to the Non-Invasive Measurement of Muscle Oxygenation by Near Infrared Spectroscopy

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Key words: oxygenation, near infrared spectroscopy, muscle.

In a recent article in the *Jpn. J. Physiol.* Buono *et al.* [1] present the results of a study investigating the influence of the changes in the skin blood flow on the near infrared spectroscopy (NIRS) based measurement of the rectus femoris muscle oxygenation during local heating or epinephrine injection. Tissue oxygenation was measured by a continuous-wave tissue oximeter (InSpectra™ Tissue Spectrometer System–Model 325, Hutchinson Technologies, Hutchinson, MN, USA).

We agree with the authors on: (i) evidencing scarce and inaccurate prior studies on this topic [2–4]; (ii) recognizing the importance to investigate the influence of high and low skin blood flow on the measurement of muscle oxygenation by NIRS. On the other hand, we disagree with the authors on the NIRS methodology (in particular, the light source–detector spacing) adopted in their study.

The light source–detector distance affects the contribution of skin; in fact increasing this distance properly allows the improvement of the sensitivity of measurement and the increase of the probability of looking at oxygenation deep under the tissue surface [5]. In addition, as already reported by the authors, it is well known that the depth of light penetration also depends on the thickness of subcutaneous adipose tissue [6, 7]. For these reasons, were the authors wise to have used a source–detector distance of 2.5 cm? This distance is very short, and to convince the readers that the reported results truly refer to the oxygenation changes occurring in the investigated muscle tissue, the authors should have explored the relationship between skin blood flow and the oxygenation measured at different source-detector distances (larger than 2.5 cm). In fact, the InSpectra™ Tissue Spectrometer optical cable distal tips are available at 25 and 35 mm spacing. Therefore, their generalized conclusion "skin blood flow can significantly affect tissue oxygenation, as measured by NIRS," is not supported by sufficient experimental NIRS data. We would like to add that a similar study has been very recently published by Davies *et al.* [8], who investigated the influence of the increase in the skin blood flow on the NIRS based measurement of the flexor digitorum muscle oxygenation during local or whole-body heating. Unfortunately also in that study, performed by using another NIRS system, the source–detector distance (2 cm) was inadequate to support their findings. We would like to comment that the other commercially available tissue oximeters, utilized also for brain oxygenation monitoring, use a fixed source–detector spacing of 4 or 5 cm, and in most cases, efficient light sources (laser diodes instead of the light-emitting diodes as in the InSpectra™ Tissue Spectrometer) to ensure an accurate quantification of the oxygenation changes in muscle tissue.

In summary, the study on the potential contribution of very high levels of skin blood flow to the muscle oxygenation is of great interest for better understanding the potentiality of NIRS in exercise patho-physiology. However, this issue is still open and further studies should be carried out using more recent NIRS methodologies [9, 10], which include suitable light source-detector distances, for investigating deep regions of muscle.

We believe that this letter adds important discussion and clarifies to the readers of *Jpn. J. Physiol.* relevant issues raised in the paper by Buono *et al.*

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Response

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We would like to thank Drs. Quaresima and Ferrari for their letter to the editor concerning our recent study that appeared in the *Japanese Journal of Physiology*. Both Dr. Quaresima and Dr. Ferrari are renowned experts in the area of NIRS and thus their concerns certainly warrant a detailed and thoughtful response.

Essentially they question whether our use of a NIRS probe with a 25 mm source–detector spacing was a wise idea. Our response is that we feel confident that the probe spacing was adequate and did not invalidate our results. We base this response on the following two points.

First, when using a 25 mm probe it has been reported that 95% of the optical signal is from a depth of 0–23 mm [1]. Since our subjects had a mean skin and subcutaneous tissue thickness of 7.7 mm, this means that at least 15 mm of superficial muscle was included in the optical signal. This statement is supported by the findings of Matsushita *et al.* [2] who reported that a source–detector distance of 20 mm was enough for detection of the NIR light passing through the muscle layer, even when the thickness of the adipose tissue was 15 mm.

Second, if the 25 mm probe spacing was not allowing NIR light to reach the underlying muscle layer, than it seems reasonable to assume that the optical signal should not respond to metabolic perturbations occurring in that tissue during exercise. However, several studies [1, 3] using the Hutchinson Technologies InSpectra Spectrometer and a 25 mm probe have reported large decreases in tissue oxygenation during exercise. In fact our laboratory routinely sees vastus lateralis StO_2 values in the 20–30% range following maximal exercise when using a 25 mm probe spacing (resting values are measured at 70–90%). We feel these findings certainly suggest that when using a 25 mm source–detector spacing a reasonable proportion of the NIRS signal is arising from the superficial muscle.

In summary, we agree with Drs. Quaresima and Ferrari that further studies examining the role of skin blood flow on the NIRS optical signal are warranted. Hopefully the concerns voiced by our two colleagues and our response will assist future investigators in designing studies to advance our collective knowledge in this important area.

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RELATIONSHIP BETWEEN HANDGRIP SUSTAINED SUBMAXIMAL EXERCISE AND PREFRONTAL CORTEX OXYGENATION

Leonardo Mottola,[1] Stefano Crisostomi,[1] Marco Ferrari,[1] and Valentina Quaresima[1]

1. INTRODUCTION

Fatigue might be defined as an exercise-induced loss of power- or force-generating capacity.[1] It has not been fully clarified what the effect is of fatiguing skeletal muscle exercise on brain, and in particular on ipsi- and contralateral prefrontal cortex (PFC). A recent functional magnetic resonance imaging (fMRI) study[2] demonstrated that during sustained muscle contractions there is a progressive involvement of the ipsilateral and contralateral PFC, whose activation may be involved in processing fatigue-related feedback and/or adjusting the descending command for the ongoing task.[3]

Functional near infrared spectroscopy (fNIRS) has been used to monitor brain oxygenation changes over the motor cortex in a wide variety of exercise modalities: finger opposition,[4] finger tapping,[5] finger flexion/extension,[6] palm squeezing,[7] plantar flexion,[8] and walking.[9] Prefrontal cortex oxygenation response upon exhaustive cycling exercise was also investigated.[10-12]

The aim of this study was to assess bilateral PFC oxygenation during a sustained submaximal handgrip isometric exercise by two-channel fNIRS.

2. METHODS

Twelve right handed volunteers (age: 28.5±4.1 yrs) participated in this study. Subjects were physically active although none were engaged in daily, intensive or specific training programs. All subjects gave their informed consent prior to participation after a full oral and written explanation of the experiments.

All subjects performed the motor task consisting of 4-min continuous isometric contraction at 30% of their maximal voluntary contraction (MVC) while their forehead

was monitored by fNIRS (Fig. 1). The study was performed in a quiet room. For oxy- and deoxyhemoglobin (O_2Hb and HHb) measurements, a 2-channel NIRS oximeter (NIRO-300, Hamamatsu, Japan) was employed. The two sets of emission and detection NIRO-300 probes were attached bilaterally to the forehead of the subjects. In each set, the emission and detection probe were kept at a constant geometry and distance (5 cm apart) by a rubber shell that in turn was attached by a double-sided adhesive sheet. The detection probes were placed in correspondence of Fp1 and Fp2 of the 10-20 system for the EEG electrode placement with the emission probes being lateral by 5 cm on both sides approximately at F7 and F8, respectively. The anterior part of the prefrontal area, including Brodmann areas 9 and 10, may be the main area of contribution to the NIRS measurements. NIRS data were collected at the frequency of 6 Hz and transferred on-line to a computer for storage and subsequent analysis. The quantification of O_2Hb and HHb concentration changes, expressed in $\Delta\mu M$, was obtained by including an age-dependent constant differential pathlength factor ($4.99 + 0.067 * age^{0.814}$).[8]

Handgrip force was measured by a system consisting of a handgrip device and a digital handgrip analyzer (MIE, Medical Research, UK) (Fig. 1). The system in turn was connected to a computer for data acquisition and analysis (Mie Cas software). The pliers were fixed in vertical position to a rigid support (Fig.1). The grip span was 2 cm, and the exact point where the subject had to grasp was marked, in order to standardize the testing conditions. Subjects exerted handgrip contractions to match the output force to the target figure on a digital display. The sampling rate for force data was 33 Hz. MVC handgrip force was measured before the experiment itself (one day before) in each subject. The MVC value was calculated by averaging the measures over 5 trials. Heart rate (HR) was measured by a pulse oximeter (Nellcor N-200, USA).

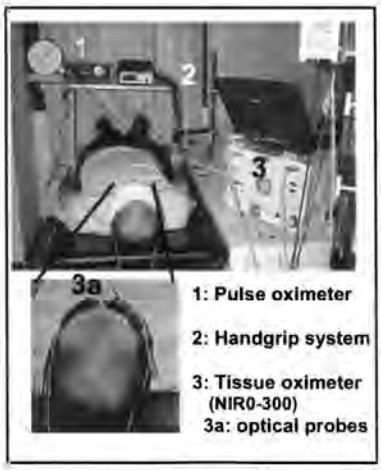

Figure 1. Experimental set-up

Data are reported as mean and standard deviation of O_2Hb, HHb, and HR and compared using repeated measures analysis of variance. Significant differences were identified using Turkey's honestly significant difference multiple comparison test. Each data point was calculated by averaging the last 5 s every 30 s of exercise. The paired *t* test

was used to compare maximal changes in O_2Hb and HHb between left and right PFC. Significance level was set at $P<0.05$.

3. RESULTS

A typical example of force profile, heart rate and concurrent changes in O_2Hb and HHb in left and right PFC (subject #4) is reported in Fig. 2. The target force was maintained constant throughout the task performance. Heart rate increased progressively during the entire duration of the exercise period, and immediately decreased after its end. In all subjects PFC oxygenation of both hemispheres was modified according to the typical tracings shown in Fig. 2. A decrease in HHb accompanied by an increase in O_2Hb was observed in both hemispheres during the course of the task. Immediately after the end of the handgrip exercise, O_2Hb and HHb showed a tendency to return gradually to pre-exercise values.

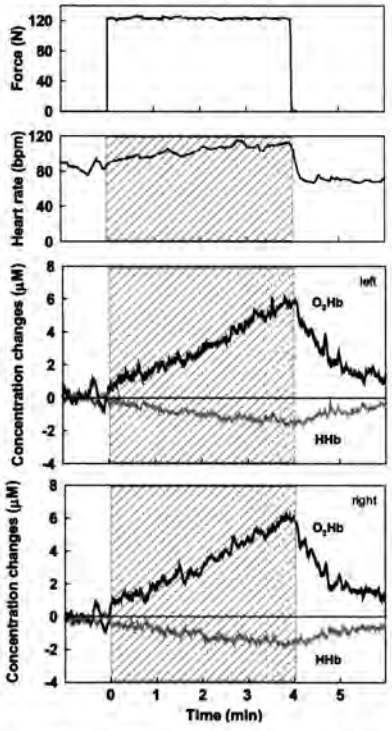

Figure 2. Time course of handgrip force, heart rate, and O_2Hb, HHb changes in left and right PFC (subject #4) before, during (■) and after isometric contraction at 30% of his maximal voluntary contraction.

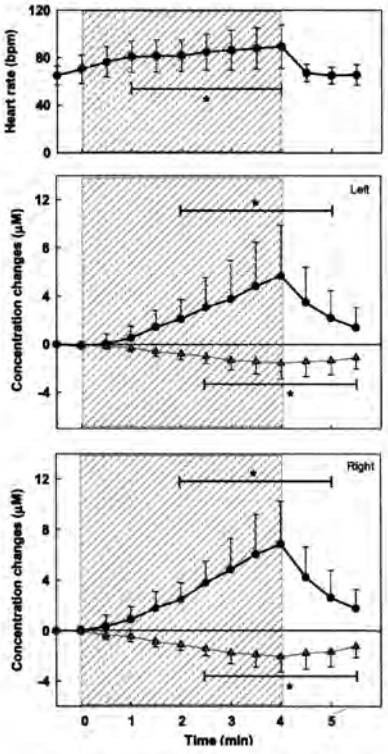

Figure 3. Mean time course of heart rate, and O_2Hb (-•-), HHb (-Δ-) changes in left and right PFC before, during (■) and after isometric contraction at 30% of their maximal voluntary contraction (n=12). Each data point represents the average over the last 30 sec every 60 sec. * significantly different from the baseline.

Figure 3 shows the time course of heart rate, O_2Hb and HHb changes in left and right

PFC over the 12 subjects. Although the inter-subject variability in the amplitude of O_2Hb and HHb changes, O_2Hb significantly increased after the first 2 min of contraction, and HHb decreased after the first 2.5 min in both PFC sides (Fig. 3). The activation was not evident anymore after the first 60 s after the end of the task performance period.

The maximal concentration changes in O_2Hb and HHb found at the end of 4-min contraction are reported in Fig. 4. Changes in HHb were found significantly higher in the ipsilateral than in the contralateral PFC.

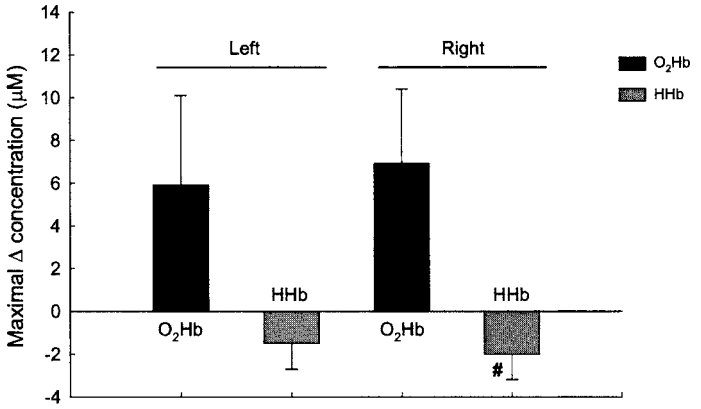

Figure 4. Maximal concentration changes at the end of 4-min continuous isometric contraction.
[#] Significantly different from contralateral PFC.

4. DISCUSSION

Since 1993, more than 80 papers have reported frontal cortex activation, measured with fNIRS as changes in concentrations of O_2Hb and HHb in healthy subjects during specific tasks, such as arithmetic calculations, speech production, spatial/visual/object working memory, semantic processing, selected attention tests, anagrams, etc.

The typical fNIRS oxygenation response over an activated cortical area consists of a decrease in HHb accompanied with an increase in O_2Hb of 2–3 fold of magnitude. The physiological significance of this response has been extensively investigated in humans[13] and in the rat brain model.[14] O_2Hb is the most sensitive indicator of the increase in cerebral blood flow (neurovascular coupling) and the direction of the changes in HHb is determined by the oxygenation and volume of the venous blood.[14]

The prefrontal cortex is involved in many processes, some of them are related to motor activity and speech. Experimental data suggest that PFC activity occurs in relation to attention, short-term memory, and complex forms of motor behavior, i.e. anticipatory preparation, motor sequences, programming of speech, etc.

Notwithstanding fNIRS has been used to monitor brain oxygenation changes over the motor cortex during a wide variety of exercise modalities,[1-9] only a few fNIRS studies about the PFC oxygenation response during motor tasks are available.[10-12] Furthermore, substantial activation in the prefrontal region in addition to expected activations

extending over the motor, premotor and supplementary motor areas was found during apple peeling by multichannel NIRS.[15]

To the best of our knowledge, this is the first time that fNIRS has been utilized to investigate PFC oxygenation during sustained submaximal handgrip exercise. In this study, the so-called cortical activation, was observed in both ipsi- and contralateral PFC sides. A potential minor contribution of skin blood flow increase to the changes in O_2Hb and HHb can be excluded during a short duration submaximal exercise, supporting the observed asymmetric HHb changes (Fig. 4). The results of this study confirm those obtained by fMRI[2] and suggest that PFC output signals drive right forearm muscles to maintain strength. The observed PFC changes are task related, as supported by the mismatched patterns of HR and O_2Hb changes (Fig. 3).

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Multichannel Time-Resolved Tissue Oximeter for Functional Imaging of the Brain

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***Abstract*—This paper reports the development and characterization of a novel multichannel time-resolved (TR) instrument for functional brain imaging studies. The instrument is based on picosecond diode lasers, fiber optics for light injection and delivery, a compact multianode photomultiplier, and a personal computer (PC) board for time-correlated single photon counting (TCSPC). The instrument has been characterized in terms of reproducibility among the nine sources and the 12 collection channels, linearity in the determination of optical properties (absorption and reduced scattering), and stability. Preliminary *in vivo* measurements were performed on volunteers to monitor the optical response to stimuli following a motor task (finger opposition, 5 Hz).**

***Index Terms*—Brain, laser biomedical applications, optical spectroscopy, optical tomography, pulsed lasers, random media, scattering, time-domain measurements.**

I. Introduction

NONINVASIVE functional human brain mapping by diffuse optical methods is a novel technique that employs near-infrared light to probe the brain for changes in parameters relating to brain function [1], [2]. Since the very first applications of near-infrared spectroscopy (NIRS) with diffusing light for functional studies, three basic approaches have been developed, namely 1) continuous wave (CW); 2) frequency domain (FD); and 3) time resolved (TR). NIRS-CW systems inject constant amplitude light power [provided by a lamp, a light-emitting diode (LED), or a laser] into tissue and monitor the amplitude decay of incident light. Thanks to relatively low cost, simplicity and overall robustness, NIRS-CW systems have been widely used not only in basic research but also in preclinical applications including tissue oximetry and functional brain imaging [3]–[5]. The key limitation of NIRS-CW is the coupling between the absorption and the scattering coefficient, causing the lack of quantitative assessment. To discriminate between absorption and scattering contribution, NIRS-FD systems use amplitude modulated light sources and record amplitude decay and phase shift of remitted light. Recently, NIRS-FD instruments have been effectively used for cerebral and muscle oximetry and breast imaging [6]–[8]. On the other hand, simultaneous estimates of both absorption and scattering can be achieved by NIRS-TR systems, which deliver ultrashort laser pulses into tissue and record the time distribution of diffusive photons. In the past, for both technological and financial constraints, NIRS-TR systems have grown on a complex laboratory scale, yet, in recent times, they have evolved towards compact and portable instruments [9]–[13]. The state of the art of NIRS-TR systems embraces several setups that differ for the characteristics of light source (repetition frequency, number of wavelengths, and geometry of injection points) and detectors (performance of electronics for signal acquisition and number and geometry of detection points). A single source and detector configuration is the very basic system, while more complex setups comprise up to 64 sources and 64 detectors [14]. To track functional changes in human tissues, by exploiting the information obtained with NIRS-TR, requires systems characterized by portability (aptness to different clinical environments and ease of use by nonqualified personnel), high acquisition frequency (acquisition time less than 1 s to follow rapid changes in human hemodynamics and oxidative metabolism), and multichannel configuration (number and geometry of sources and detectors, to get rid of local heterogeneity, which may hamper the results of measurements). Up to now, such systems have not been available either on the market or at the research and laboratory stage. In fact, on the one hand, more complex systems unavoidably have long acquisition times (from 30 s up to 30 min) [14], [15] to multiplex the optical signals to the different injection points; therefore, they are more suitable for the quasi-static monitoring of the physiological state. On the other hand, simpler systems can have very short acquisition times (less than 100 ms) but, having a single channel or a limited number of channels, they suffer from the ar tifacts that derive from the natural point-to-point variation in the physiological parameters and have poor imaging capability. With the goal to overcome these limitations, Cubeddu *et al.* have developed an eight-channel TR system for the noninvasive measurement of tissue oxygenation [16].

In this work, we focus on the development and characterization of a novel compact multichannel NIRS-TR prototype for noninvasive functional human brain mapping with a high temporal resolution and a fast image reconstruction/data analysis.

II. Materials and Methods

A. System Setup

Fig. 1 reports the scheme of the multichannel NIRS-TR system developed at the Department of Physics, Politecnico

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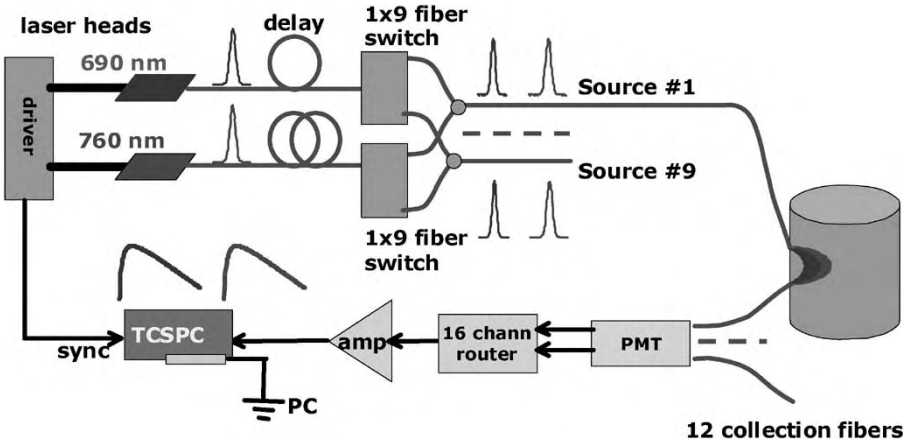

Fig. 1. Scheme of the nine-source and 12-detector TR tissue oximeter. TCSPC: time-correlated single photon counting; PMT: photomultiplier tube.

di Milano. The system is based on the following: pulsed diode lasers with 80 MHz repetition rate and 1 mW average power (Picoquant GmbH, Germany); a couple of 1 × 9 fiber optic switches (PiezoJena GmbH, Germany); a custom-made multimode graded index fiber optics combiner; a compact 16-channel photomultiplier (R5900-01, Hamamatsu Photonics, Japan); and a PC board (SPC630, Becker&Hickl, Germany) for time-correlated single photon counting (TCSPC). It is operated with two wavelengths (690 and 760 nm), up to nine injection points, and 12 independent detectors. The laser sources can be easily changed and an 818-nm laser head is also available. Using all the nine injection fibers and all the 12 collection fibers, the system can measure tissue optical properties in 30 different points over the sample surface. Using, for example, an interfiber distance of 2 cm is possible to obtain an image covering an area of 7 × 5.5 cm.

The whole system is driven by a custom-made software written in ANSI C using the LabWindows/CVI environment (National Instruments, TX). It is optimized to obtain a whole image of 30 points/s, and thus, each injection fiber emits light for 100 ms. The system flexibility enables all combinations between the nine injection fibers and the 12 collection fibers, so it is possible to obtain images with different dimension and at different sampling rates.

A robust and efficient probe was developed to hold injection and collection fibers so as to achieve good stable optical contact and sufficient light levels detected from the head. Several factors affect good optical coupling, in particular, absorption and instability due to hair and general fiber stability against the head. In a previous system [16], we used two different approaches based on fibers embedded in a neoprene rubber pad and on adhesive black Teflon fiber holders. Both systems were effectively used in preliminary *in vivo* tests and showed sufficient efficacy. The main disadvantage is the long time needed to fix the probe to the head and to precisely determine fiber positioning on the head. Many solutions have been implemented by other research groups for holding the optical fibers with a goal of rigidity, plus flexibility with respect to head shape. A few examples include fibers inserted through modified motorcycle helmets, thermoplastic molded to the contours of each subject's head, spring-loaded fibers attached to semirigid plastic forms, and fibers embedded in neoprene rubber forms [2]. The current system employs a thermoplastic pad with a custom grid of fiber positions, as shown in Fig. 2. This fiber holder can receive up to 25 fibers, more than those effectively used during the *in vivo* measurements presented in this work. In this way, it would be possible in future experiments to change the fibers' position for a better covering of the activated area without removing the holder from the patient head.

Fig. 2. Fiber holder. The white pad is a thermoplastic material used to adapt the fiber holder to the sample's surface.

B. Measurement Protocols

A protocol for standardization of diffuse optical instrument performances, developed within the framework of the European Thematic Network "Medphot" [17], was applied to determine linearity, uncertainty, and stability of the NIRS-TR setup. Solid tissue phantoms made of titanium dioxide particle (scattering agent) and toner powder (absorbing agent) embedded in a epoxy resin matrix [18] were used for system characterization. A set of 28 phantoms with optical properties typical for biological tissue in the red and near-infrared spectral range was measured: Phantoms labeled from 1 to 7 represent absorption coefficient (μ_a) changes from 0.07 to 0.49 cm^{-1} in 0.07 cm^{-1} steps, while phantoms labeled from A to D represent reduced

scattering coefficient (μ'_s) changes from 5 to 20 cm^{-1} in 5-cm^{-1} steps.

Preliminary *in vivo* measurements were performed on volunteers to monitor the optical response to stimuli, particularly to motor stimuli. The measurement protocol is composed of 20 s of baseline, 20 s of motor task, and 20 s of recovery. The protocol was repeated five times with the right (R) hand and five times with the left (L) hand. The effective motor task consists of an exercise of finger opposition at the frequency rate of 5 Hz. The optical probe was placed over the head in order to cover the underlying motor cortex, and it was centered [according to the international 10–20 system for the electroencephalogram (EEG) electrode placement] at the C_3 point. The source–detector distance was 2 cm.

C. Data Analysis

The temporal profile of the TR reflectance curve was analyzed using a solution of the radiative transport equation under the diffusion approximation for a semiinfinite homogeneous medium [19]. The extrapolated boundary condition was used to take into account the refractive index mismatch at the surface. The reflectance $R(r,t)$, i.e., the photon probability to be remitted from the tissue at a time t and a distance r from the injection point, can be expressed as

$$R(r,t) = AD^{-\frac{3}{2}}t^{-\frac{5}{2}}\exp(-\mu_a vt)\exp\left(-\frac{r^2}{4Dvt}\right) \times\left(z_o\exp\left(-\frac{z_o^2}{4Dvt}\right)-z_p\exp\left(-\frac{z_p^2}{4Dvt}\right)\right) \quad (1)$$

where A is a normalization constant, $v=c/n$ is the speed of light in the medium, $z_o=1/\mu'_s$ is the scattering mean free path, and z_p derives from the extrapolated boundary conditions and depends on the refractive index of the tissue. The diffusion coefficient $D=1/(3\mu'_s)$ was taken to be independent of the absorption properties of the medium. Simultaneous estimate of μ'_s and μ_a may be achieved by best fitting to (1), with a nonlinear least square method, the measured TR reflectance curves.

To reduce the dispersion of the fitted absorption coefficient values, we use the methods described by Nomura *et al.* [20] and known as the modified Lambert–Beer's law. First, for each wavelength λ, a reference TR reflectance curve $R_0(\rho,t,\lambda)$, at an interfiber distance ρ, is derived by averaging the curves corresponding to an initial resting period (typically 20 s). Fitting of $R_0(\rho,t,\lambda)$ yields the reference absorption value $\mu_{a0}(\lambda)$. Then, $\Delta\mu_a(\lambda)$, the variation from the reference value, is derived according to (2) and (3), taking the assumption that during the activation, the scattering coefficient do not change

$$\mu_a(\lambda)=\mu_{a0}(\lambda)+\Delta\mu_a(\lambda) \quad (2)$$

$$\Delta\mu_a(\lambda)=-\frac{1}{vt}\ln\left(\frac{R(\rho,t;\lambda)}{R_0(\rho,t;\lambda)}\right). \quad (3)$$

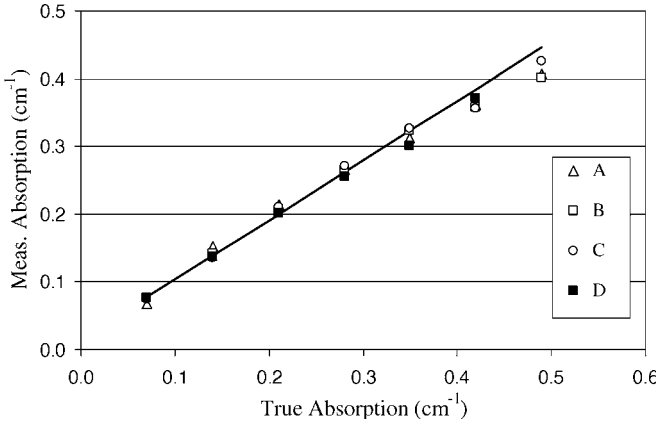

Fig. 3. Linearity of the measured absorption coefficient, at 690 nm, versus the true values of absorption coefficient. The four labels A, B, C, and D indicate four different sample series with reduced scattering coefficient between 5 and 20 cm^{-1} in 5-cm^{-1} steps.

Improvement over the standard methods is more effective when the absorption is high. In fact, in this condition, standard fitting to (1) yields high dispersion in the fitted data [21].

Taking the assumption that oxy- and deoxy-hemoglobin are the main chromophores contributing to absorption, their concentrations (O_2Hb and HHb, respectively) are easily derived by using the knowledge of the extinction coefficient [22], following the well-know Lambert–Beer's law

$$\begin{cases}\mu_a^{\lambda_1}=O_2Hb\varepsilon_{O_2Hb}^{\lambda_1}+HHb\varepsilon_{HHb}^{\lambda_1}\\ \mu_a^{\lambda_2}=O_2Hb\varepsilon_{O_2Hb}^{\lambda_2}+HHb\varepsilon_{HHb}^{\lambda_2}.\end{cases} \quad (4)$$

Since water absorption in this spectral region is much lower than haemoglobins absorption [22], a fixed amount (30%) of absorption was attributed to water and subtracted to μ_a before calculation of HHb and O_2Hb from (4). Then, total hemoglobin content (tHb = HHb + O_2Hb) and tissue oxygen saturation (SO_2 = O_2Hb/tHb) are derived.

During data analysis of *in vivo* measurements, a folding average over the five intervals associated with the left or the right hand and a 4-s moving average were applied to improve the signal to noise ratio. Furthermore, changes in O_2Hb (ΔO_2Hb) and HHb (ΔHHb) were calculated by making the difference between the concentration's value at each time and their average values during the baseline period (0–20 s).

By multiplexing the injection sources and using different collection fibers, we were able to estimate optical properties and calculate haemodynamic parameters in distinct spatial locations to create a spatial map.

III. Results and Discussion

Fig. 3 shows the results for the absorption linearity experiment at 690 nm. Similar results hold for the other wavelength. The system proved to be linear in the range of 0–0.3 cm^{-1}. An underestimation (about 20%) of absorption is found for values higher than 0.3 cm^{-1}, possibly as a result of the intrinsic limitations in the theoretical model used to analyze TR reflectance data. The estimates of the absorption coefficient is

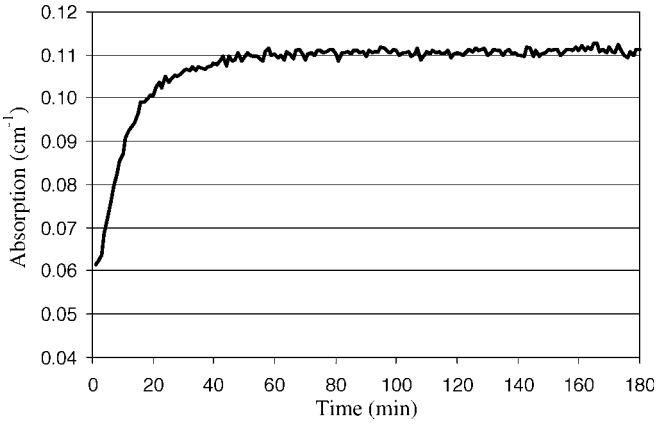

Fig. 4. Time course of the measured absorption coefficient, at 690 nm, during the warm-up stage of the system.

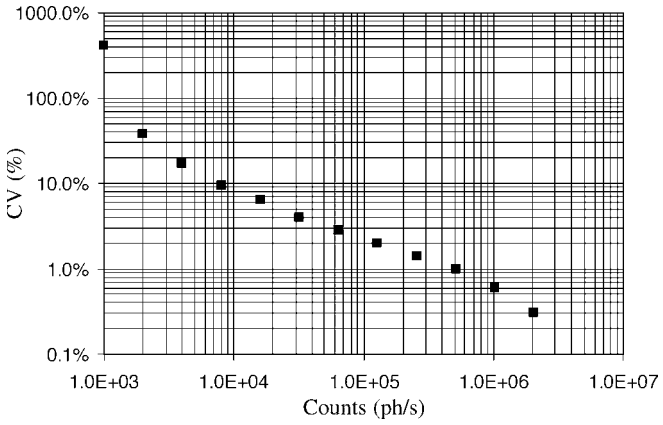

Fig. 5. Uncertainity in absorption coefficient. Plot of the measurement's CV, at 690 nm, as a function of the number of photons collected.

rather independent on the scattering properties of the probe sample.

System stability was studied over a 3-h period to analyze warm-up time and long-term drift. As it is clear in Fig. 4, a 60-min warm-up time is needed before the coefficient of variation (CV; i.e., standard deviation over average) of the absorption coefficient becomes lower than 1.6%.

A further test was performed to evaluate the noise level of the system, studying the effect of the number of counts in the TR reflectance curve on the fitted absorption coefficient. The CV for the absorption coefficient is found to be lower than 3% for 60 000 counts, while it raises up to 10% if only 8000 counts are detected (see Fig. 5). Depending on the applications (i.e., on the expected signal-to-noise ratio), these results tailor the optimization of the setup. For example, when the optical contrast is sufficient (e.g., during cuff occlusion on arm muscle), a 100-ms acquisition time can be effectively used. For brain functional imaging experiments where the changes are dramatically smaller, there is the need to improve data robustness either by increasing the acquisition time or by an off-line averaging during data analysis. To show the typical features of brain activation detected by optical noninvasive methods, we report in Fig. 6 the time course of changes in ΔO_2Hb and ΔHHb for a single detection channel. During baseline, both HHb and O^2Hb show no features, while there is a marked decrease in HHb and a corresponding increase in O_2Hb when the test is performed with the controlateral hand (R). As expected, minor changes are noticed during the task if the ipsilateral hand (L) is used. In the recovery, both HHb and O_2Hb slowly return to baseline values. Brain activation during motor task is limited to a small area in the motor cortex [2]. Therefore, we present in Fig. 7 the grey level maps of ΔO_2Hb and ΔHHb (obtained by interpolating the results from the eight collection points). Images represent the start of the measure, the middle of the motor task, when the test is performed with the controlateral hand (R), and the end of the recovery period. As expected, during the task, the activated area is revealed by an increase in O_2Hb (black area in the central image of the upper line) and by a corresponding decrease in HHb (white area in the central image of the lower line).

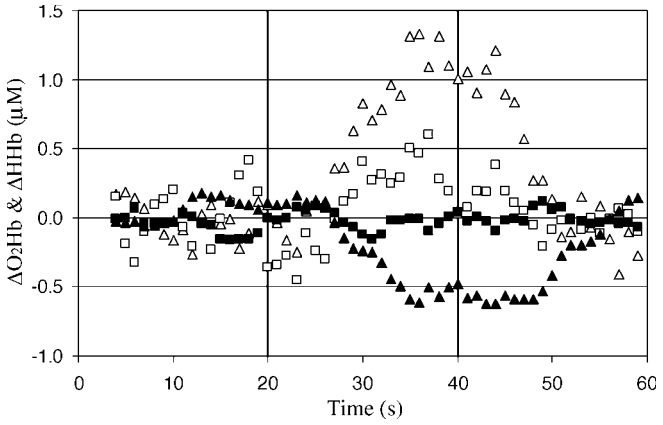

Fig. 6. Time course of ΔO_2Hb (open symbols) and ΔHHb (filled symbols) during the exercise performed with the right hand (triangle) and with the left hand (square). The vertical lines represent the task interval. Each curve is an average of the five measures performed with the same hand. A mobile average of 4 s was applied.

The spatial resolution of NIRS images is mainly determined by the scattering, which imposes severe limitation to photon propagation in diffusive media. A typical value for spatial resolution is 1 cm. Improvements can be partially obtained by a proper arrangement of source and detector fibers or by a tomographic approach [2].

IV. Conclusion

The potential advantage of NIRS-TR systems is the possibility to get a deeper insight into functional human brain mapping. Key advantages of NIRS-TR are the discrimination between absorption and scattering coefficient (not possible with NIRS-CW and difficult with NIRS-FD), the increased penetration depth and spatial resolution with respect to the other optical techniques, and the possibility to quantitatively evaluate the contribution of cerebral tissue by naturally exploiting the information encoded in time. The development of improved NIRS-TR systems and their application in functional imaging studies will serve not only to definitely set its potentiality but also as a feedback to the development of improved NIRS-CW and NIRS-FD setups for next-generation optical imaging devices.

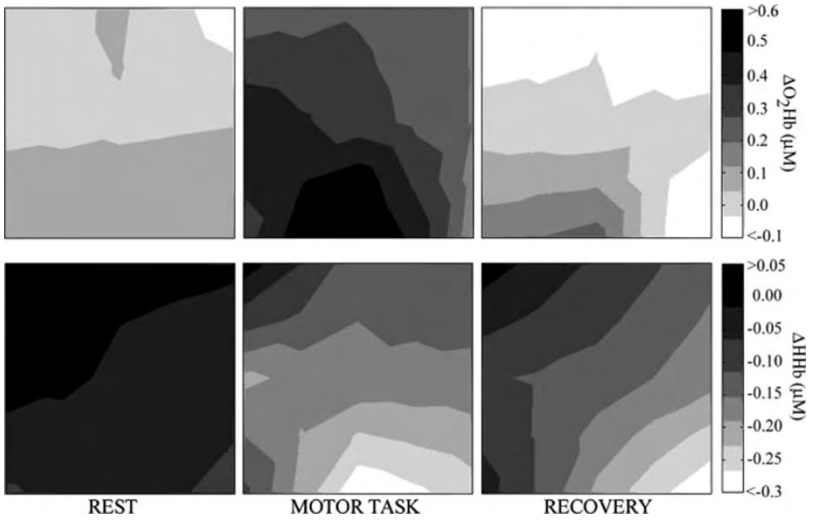

Fig. 7. Grey level maps representing changes in O_2Hb (top row) and HHb (bottom row) over the cortex region during the baseline period (left column), the motor task performed with the right hand (middle column), and the recovery period (right column).

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Biceps brachii myoelectric and oxygenation changes during static and sinusoidal isometric exercises

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Abstract

Surface myoelectric signal changes occurring during sustained isometric contractions have been extensively studied with quantitative surface electromyography (sEMG) and are described by means of some sEMG global variables in time and frequency domain (such as the median power spectral frequency). Recently, the possibility of studying local muscle O_2 saturation during exercise using non-invasive methods has been enhanced thanks to the use of near-infrared spectroscopy (NIRS). The purpose of this work was to combine NIRS and sEMG techniques to analyze the relationship between modifications of sEMG parameters and the underlying metabolic status of the exercising biceps brachii muscle. This relationship was tested under different isometric contraction modalities, namely static (ST) at 20, 40, 60 and 80%MVC and sinusoidal (SIN) at 40 ± 20 and 60 ± 20%MVC. Results clearly indicated the presence of an initial fast phase of muscle O_2 desaturation followed by a slow phase, regardless of the contraction modality. Moreover, the initial rate of muscle O_2 desaturation was related to the level of force output ($R = 0.92$), but it was independent on the contraction modality ($p < 0.05$). Similarly, changes in sEMG parameters were related to force level (Conduction Velocity-CV vs. Force: $R = 0.87$; sEMG Median Frequency-MDF vs. Force: $R = 0.86$). The high correlation found between CV-MDF and Tissue Oxygenation Index (TOI) slope ($R = 0.73$ and 0.72, respectively) suggests a strong relationship between NIRS and sEMG data. This study indicates that muscle O_2 demand during isometric contractions from low to high force levels is influenced by the type of active motor units and not from the type of isometric exercise modality.

Keywords: Surface electromyography; Near-infrared spectroscopy; Isometric exercise; Oxidative metabolism; Muscle O_2 saturation; Myoelectric fatigue

1. Introduction

The analysis of surface electromyogram (sEMG) has been extensively used to describe the early changes occurring during sustained isometric contractions (for a review see De Luca, 1997). Such changes can be evaluated by means of sEMG global variables in time and frequency domains. The root mean square value (RMS) of sEMG and the average muscle fiber conduction velocity (CV) are the most frequently used in the time domain, and the median frequency of the power density spectrum (MDF)

Abbreviations: sEMG, surface electromyography; RMS, root mean square value; MDF, median frequency of sEMG power density spectrum; MU, motor units; CV, muscle fiber action potential conduction velocity; O_2Hb, oxyhemoglobin; HHb, deoxyhemoglobin; tHb, total Hb volume; NIRS, near-infrared spectroscopy; TOI, tissue oxygenation index; SmO_2, muscle oxygen saturation; BB, biceps brachii; MVC, maximal voluntary contraction; ST, static isometric exercise; SIN, sinusoidal isometric exercise.

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in the frequency domain. Amplitude changes of sEMG are mainly affected by the number of active motor units (MU) and their mean firing rate, whereas MDF decay overtime and concomitant reduction of the CV (Farina et al., 2002b) observed during a sustained isometric contraction have been interpreted as the result of local changes in muscle fibers membrane properties (Farina et al., 2002a; Merletti et al., 1990). The sEMG power spectrum compression over time is affected by force level (Basmajan and De Luca, 1985), showing a higher rate of decrease as force increases, and this is thought to be due to the higher blood occlusion at higher contraction levels.

Moreover, MDF and CV may be jointly used to provide an indirect estimate of muscle fiber type composition (Sadoyama et al., 1988; Westbury and Shaughnessy, 1987) and MU recruitment (Farina et al., 2002b; Sbriccoli et al., 2003). To this respect, among the various possible indicators of Henneman's size principle, CV has been recently validated also under dynamic cyclic exercise (Farina et al., 2007).

The ability to study local muscle oxidative metabolism during exercise using non-invasive techniques has been enhanced thanks to the use of near-infrared spectroscopy (NIRS) (Bhambhani, 2004; Boushel et al., 2001; Neary, 2004; Quaresima et al., 2003). Different NIRS methods have been proposed (Delpy and Cope, 1997) to assess muscle O_2 saturation (SmO_2), the most widely used being the near-infrared spatially resolved spectroscopy (Delpy and Cope, 1997). This technique provides both an average tissue O_2 saturation (from small vessels, such as the capillary, arteriolar and venular bed), and the changes in oxyhemoglobin (O_2Hb), deoxyhemoglobin (HHb) concentration, as well as the changes in derived hemoglobin volume ($tHb = O_2Hb + HHb$). SmO_2 reflects the dynamic balance between O_2 supply and O_2 consumption in the investigated tissue volume.

A number of previous studies have combined sEMG data with muscle oxygenation data (by NIRS) during exercise (Burnley et al., 2002; Kouzaki et al., 2003; Miura et al., 2000; Praagman et al., 2003; Takaishi et al., 2002; Yoshitake et al., 2001). For example, Miura et al. (2000) and Yoshitake et al. (2001) reported a correlation between dynamic exercise intensity, increased neuromuscular activation and aerobic metabolism. Additionally, Praagman et al. (2003) found a linear relationship between level of isometric effort, sEMG amplitude and muscle O_2 uptake. While previous studies have indicated the feasibility and importance of coupled sEMG-NIRS measurements, further investigations are needed using more advanced techniques and methodologies. In fact, the heterogeneity in the tested muscles and exercise protocols, the somehow limited sEMG analysis technique adopted, the methodological limitations of the utilized NIRS devices (first generation) must be taken into account.

In addition, these previous study have not explored the relationship between muscle oxygen demand and quality of the active MUs. According to the size principle for ordered recruitment (Henneman et al., 1965), it can be hypothesized that during isometric static contractions any relationship between CV and O_2 desaturation (ΔTOI) will be strongly influenced by MU recruitment. At the same time, this association could be modulated by adopting a non-stationary (i.e. oscillating) isometric contraction strategy.

Thus, the present study was designed to: (1) investigate the relationship between biceps brachii (BB) MU recruitment and BB O_2 desaturation time course during sub-maximal isometric contractions; (2) additionally, examine the influence of the modality (static vs. sinusoidal) of isometric contractions on MUs behavior (namely MU recruitment). To these purposes, sEMG and NIRS measurements were taken during 30-s isometric static contractions performed at various percentages of the maximal voluntary contraction (MVC) and during isometric sinusoidal contractions. We hypothesized that different isometric constant force levels, as well as different isometric contraction modalities, would have a different impact on local blood flow, and MUs activity measured from the NIRS and sEMG.

2. Methods

2.1. Subjects

Seven healthy subjects (3 Males, 4 Females, age: 34 ± 6 years, body mass: 74 ± 6 kg, height: 173 ± 6 cm) participated in this study. None had any previous history of neuromuscular disorder and each gave written informed consent prior to the experiment. The study was approved by the University Ethics Committee and conformed to the regulations laid out in the Declaration of Helsinki on the use of human subjects in research.

All subjects attended the laboratory on two occasions. During the first visit subjects were familiarized with the experimental procedures. In the second visit subjects were asked to perform two different tasks as described below.

Subjects seated comfortably in a custom-modified chair with the dominant (right) forearm placed in a plastic shell. For each subject, the height of the shell was adjusted to obtain an elbow angle equal to 90° (Sbriccoli et al., 2003). Subjects' shoulder was secured through a strap to the modified chair back. The hand was maintained halfway between pronation and supination. Forearm shell was connected to a piezoelectric force transducer (Kistler Instrument AG, type 9311A, Winterthur, Switzerland) connected to a charge amplifier (Kistler Instrument AG, type 5001).

Before probe placement, skinfold and subcutaneous thickness was measured in correspondence of the central part of BB muscle belly using a Harpenden caliper (Gima, Milano, Italy). An experienced operator repeated the measure three times. Average skinfold thickness was 4.2 ± 1.6 mm (means $\pm$ SD).

2.2. MVC assessment

The MVC task consisted of rapidly increasing the force exerted and to follow the performance on the computer screen while being encouraged to achieve a maximum, and to maintain it for at least 5 s before relaxing.

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Subjects performed three MVC attempts spaced by a 10-min recovery time. During the second and the third attempt, a visual feedback of the previous (or best) performance attained was provided to the subject who tried to improve his performance. The MVC value was set as the maximum value obtained from the three MVC trials.

2.3. Static isometric exercise (ST)

ST exercises were performed at 20, 40, 60 and 80%MVC (indicated as ST20, ST40, ST60, ST80, respectively). A line representing the appropriate target level of force output was displayed on a computer screen along with the actual output of the force transducer, providing the subject with continuous feedback. Exercises lasted 30 s each with a 30-min interval between exercises, which was a convenient time to allow a complete recovery. The different force outputs were administered to subjects in random order to minimize the cumulative effects of fatigue. One attempt was performed at any force level.

2.4. Sinusoidal isometric exercise (SIN)

SIN exercise consisted of performing one 30-s contraction matching a sinusoidal trace displayed on a computer screen. The sinusoid frequency was set at 0.5 Hz. The sinusoidal target was set at two ranges of force: from 20 to 60%MVC (mid value 40%MVC, indicated as SIN40), and from 40 to 80%MVC (mid value 60%MVC, indicated as SIN60). SIN exercises were spaced by a 30-min recovery. The entire experimental session lasted approximately 150 min.

2.5. EMG measurements

The BB main motor point was identified by means of electrical stimulation (Farina et al., 2000). After abrasion and cleaning with ethyl alcohol, NIRS optical probe (source-detector distance: 4.5 cm) supported by a rigid rubber shell, and a four linear array sEMG electrode (silver bars, 5 mm long, 1 mm thick; 10 mm apart) were placed and fixed with an adhesive tape symmetrically on both sides of muscle belly midline. During this manoeuvre particular care was taken to prevent excessive external pressure on the muscle belly. The sEMG reference electrode was placed over the olecranon.

The sEMG signals were amplified using a portable amplifier (SATEM, Rome, Italy; mod. VD 10/4, pass band 10–1000 Hz). Three single differential sEMG signals (SD1, SD2, SD3) were recorded. From the three SD signals, two double differential signals (DD1, DD2) were then computed and used for CV calculation as described in the following paragraphs.

2.6. NIRS measurements

NIRS measurements were carried out using a tissue oximeter (NIRO-300, Hamamatsu Photonics, Japan) based on the near-infrared spatially resolved spectroscopy (collection time 6 samples/s). The design and the features of this device have been described previously (Suzuki et al., 1999). The theory behind this approach and the reliability to measure tissue O_2 saturation has been reported (Suzuki et al., 1999). The NIRO-300 provides a tissue oxygenation index (TOI, expressed in %) which has been tested either in vitro or in vivo (Boushel et al., 2001; Suzuki et al., 1999). The TOI value reflects predominantly the mean of arteriolar, capillary, and venular O_2 saturations with a minor (less than 20%) contribution from myoglobin (Quaresima et al., 2001; Ferrari et al., 2004). In addition, the NIRO-300 provides concentration changes in O_2Hb and HHb (expressed in $\Delta\mu M$ cm), and the derived changes in tHb. The tHb changes (ΔtHb), being strictly related to blood volume changes, can be considered an indirect measure of local blood flow changes. Thus, considering that the measured adipose tissue thickness was relatively low and the penetration depth of the NIRS signal is almost half of the source-detection separation (Ferrari et al., 2004), the changes in TOI (ΔTOI) and tHb reflected mainly BB metabolic and hemodynamic changes.

After the probe test on a phantom to analyse the total probe sensitivity and the sensitivity difference between the three sensors of the detection probe, the optical probe supported by a rigid rubber shell, was firmly attached to the skin overlying the muscle parallel to the major axis of the arm, by a double-side adhesive sheet. Also the sEMG electrodes was fixed over the muscle medially to the rigid rubber shell. The optical probe and the sEMG electrode array were further secured by a soft elastic band (Tensoplast, Smith + Nephew, England). Pen marks were made on the skin to check for any sliding of the rubber shell during the exercise. No downward sliding of the optical probe was observed at the end of the measurements in any subject. After fixing the probe holders on the subject, an initialization procedure was carried out. The latter sets each laser power automatically establishing the optimum measurement condition. The zero set procedure (carried out just before the beginning of each baseline condition) was adopted to return the O_2Hb, HHb and tHb parameters to the zero value. This procedure does not affect the TOI value because TOI is measured as absolute value instead of a change with respect to the arbitrary initial zero value.

After amplification, all signals from force transducer, electromyograph and tissue oximeter were sent to a personal computer via an A/D converter (DAQ Card 16X-E10, 12 bit resolution, National Instruments, Austin, Tx, USA.). These signals were sampled at 2048 samples/s and the acquisition lasted 60 s: 10 s of rest, 30 s of exercise, 20 s of rest after exercise.

2.7. EMG data analysis

The analysis of sEMG during all isometric contractions was performed in time and frequency domain. The RMS and MDF were computed over the central single differential channel signal (Sbriccoli et al., 2003) on epochs of one second. Since NIRS data were collected every 1/6 of second, sEMG data epochs were properly overlapped (i.e., 341 samples $\cong$2048/6) in order to have 6 RMS and 6 MDF values per second.

Average muscle fiber action potential CV was assessed by means of cross-correlation function (Sbriccoli et al., 2003) between the two double differential channels using the same sEMG segmentation as for RMS/MDF data and NIRS data. Estimates of CV were accepted only when the EMG cross-correlation function values were higher than 0.8 throughout the whole duration of the test. All subjects were included in CV computations. Only two CV computations (one for ST60 test and one for SIN40 test) were not included due to a poor cross-correlation value. For each contraction performed, RMS, MDF and

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CV data were normalized with respect to the corresponding maximum value obtained during the respective MVC test.

2.8. NIRS data analysis

Fig. 1 shows a typical time-course of BB ΔTOI at ST80 consisting of an initial rapid decrease (fast phase) followed by a phase with a slower decay rate. The beginning and the end of the fast phase were automatically identified by a procedure that firstly smoothed the ΔTOI time-course by a 7-degree polynomial interpolation, and then the procedure looked for a negative long plateau in the first derivative of the relative smoothed time-course. This plateau was preceded and followed by an easily detectable decreasing and increasing phase, respectively. The fast ΔTOI decreasing phase was quantified by the slope of least square regression line.

In order to take into account the subsequent slow decreasing phase of ΔTOI, ΔTOI values corresponding to the end of exercise (indicated by STOP line in Fig. 1) were defined as ΔTOI_{min}.

The same time intervals defined for the ΔTOI fast phases were used also to compute the slopes of linear regression analysis on CV and MDF data. On the contrary, considering the evident non-linearity of tHb and RMS in the same time interval, these data were not considered for regression analysis.

2.9. Statistical analyses

A two–way analysis of variance (factors: force level and contraction modality) was used to test the dependency of MDF, CV, ΔTOI slopes during fast and slow phases from the force level (ST20, ST40, ST60, ST80, SIN40, SIN60) and the contraction modality (ST and SIN). As a main effect of either factor was found, a two-tailed paired Student's *t*-test with Bonferroni correction was implemented. Statistical significance was set at $p < 0.05$ for all tests performed. Statistical computations were performed using SPSS® software (v.11, 2001, SPSS Lead Technologies Inc., Chicago, IL, USA). Data are presented as means ± standard errors (SE).

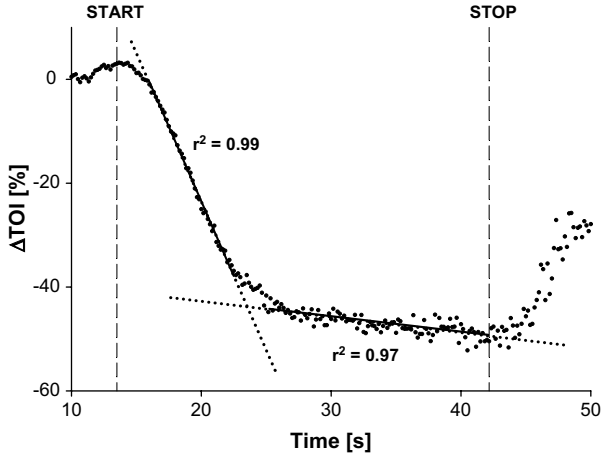

Fig. 1. Least square method used to determine the linear portion of the first fast phase of ΔTOI decrease during biceps brachii exercise. The plot refers to an isometric steady state exercise performed at 80% of the maximal voluntary contraction. Dashed vertical lines denote the beginning and the end of steady state phase of the exercise. The first and last sample of the linear interpolation defined the interval over which all the other relevant linear regressions were computed. See text for further details.

3. Results

In Figs. 2 and 3, the time course of NIRS and sEMG data at the different force levels during the ST and SIN exercises is shown (left and right panels, respectively). Fig. 4 shows ΔTOI, MDF and CV slopes computed during the fast phase in both ST and SIN exercises at any force level, while in Fig. 5 the relationship between sEMG and ΔTOI data is shown for both ST and SIN exercises. For the sake of clarity, in Figs. 2 and 3 a point every 10 is reported, and standard errors are omitted.

4. NIRS data

Force, ΔTOI and ΔtHb data are depicted in the upper, middle and lower panel of Fig. 2, respectively.

4.1. ST isometric exercise

All subjects were capable of tracking the force precisely at any ST force level but ST80, where a progressive decline in the target force was observed after the first 10-s from the beginning of the contraction (upper left panel).

At rest, absolute BB ΔTOI value (middle left panel) was 69.5 ± 6.3% (grand average over 7 subjects, 6 tests each; $N = 42$). ΔTOI started to decrease after a consistent delay from the beginning of the contraction, ranging from 5.3 s (on average) at ST20 to 2–4 s for all the other force levels.

In any condition ΔTOI_{min} was reached at the end of the exercise (see Table 1) because, at all ST force levels, ΔTOI continued to slowly decline up to the end of exercise. ST80 exercise turned out to be the most fatiguing, as demonstrated by the early drop in force output, although ΔTOI_{min} values at ST60 and ST80 were not statistically different each other. ΔTOI_{min} at ST20 was different from all the other ΔTOI_{min} values ($p < 0.025$ after Bonferroni correction), and the greatest drop in ΔTOI_{min} was obtained between ST20 and ST40.

The relationship ΔTOI slopes vs. isometric force for ST exercises had the form:

$$\text{slope } [\Delta TOI] = 0.52 - 0.082x \quad (1)$$

with x is force expressed in %MVC and $R = 0.92$.

At the beginning of the ST exercise, ΔtHb immediately decreased with force output increase (lower left panel). However, after the first abrupt drop, ΔtHb started to recover toward corresponding pre-exercise values at ST20. The same behavior was found, but less markedly, during ST40. At ST60 and ST80, ΔtHb levelled off during the first 5–6 s of exercise steady state and then slowly recovered. An evident hyperaemic phase at the end of all the contractions was present, its amplitude depending upon the level of force.

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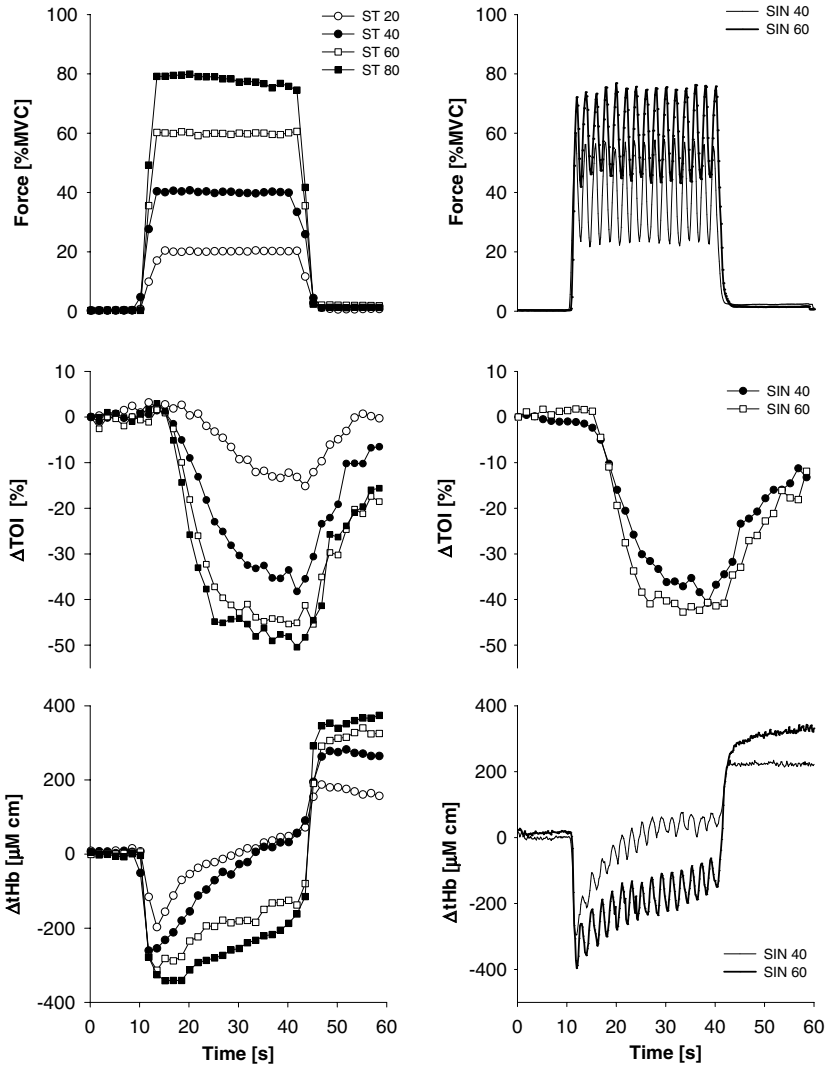

Fig. 2. Force and NIRS data during ST and SIN exercises. Left Side: ST data (ST20, ST40, ST60, ST80); Right Side: SIN data (SIN40, SIN60). Upper panel: force; Middle panel: ΔTOI; Lower panel: ΔtHb. The mean curves obtained in all trials by the 7 subjects are reported. Data are expressed as a percentage of the maximum value obtained during the MVC test. For the sake of clarity, standard errors are not reported.

4.2. SIN isometric exercise

As reported in the upper right panel of Fig. 2, on average subjects were capable of correctly tracking the force task, although in this condition the subjects' variability associated with the force matching task was much more evident.

Muscle O_2 desaturation during SIN exercises increased with force output although ΔTOI_{min} values between SIN40 and SIN60 contractions were not different each other (middle right panel).

ΔtHb oscillated in opposition of phase with force output. In particular, ΔtHb fluctuations minima were associated with the maximum force of each cycle until the end of the exercise with a time lag of ±0.17 s. During SIN40 exercises, ΔtHb crossed the rest value in correspondence of the 7th force oscillation cycle and then stabilized above the rest value. The overall ΔtHb increase was reduced during SIN60 exercises suggesting a more consistent blood flow restriction in the BB muscle. At the end of the SIN exercises, ΔtHb promptly increased.

The comparison between ΔTOI in ST and SIN exercises showed a statistical differences for ST20 vs. SIN40 and ST40 vs. SIN60 ($p < 0.05$).

ΔTOI slopes obtained during SIN contractions were different from each other ($p < 0.05$). However, there was no difference in the ΔTOI between the ST and SIN contractions. The analysis of variance failed to show any statistical dependence of ΔTOI slopes on contraction modality.

5. sEMG data

RMS, MDF and CV data are depicted in the upper, middle and lower panel of Fig. 3, respectively.

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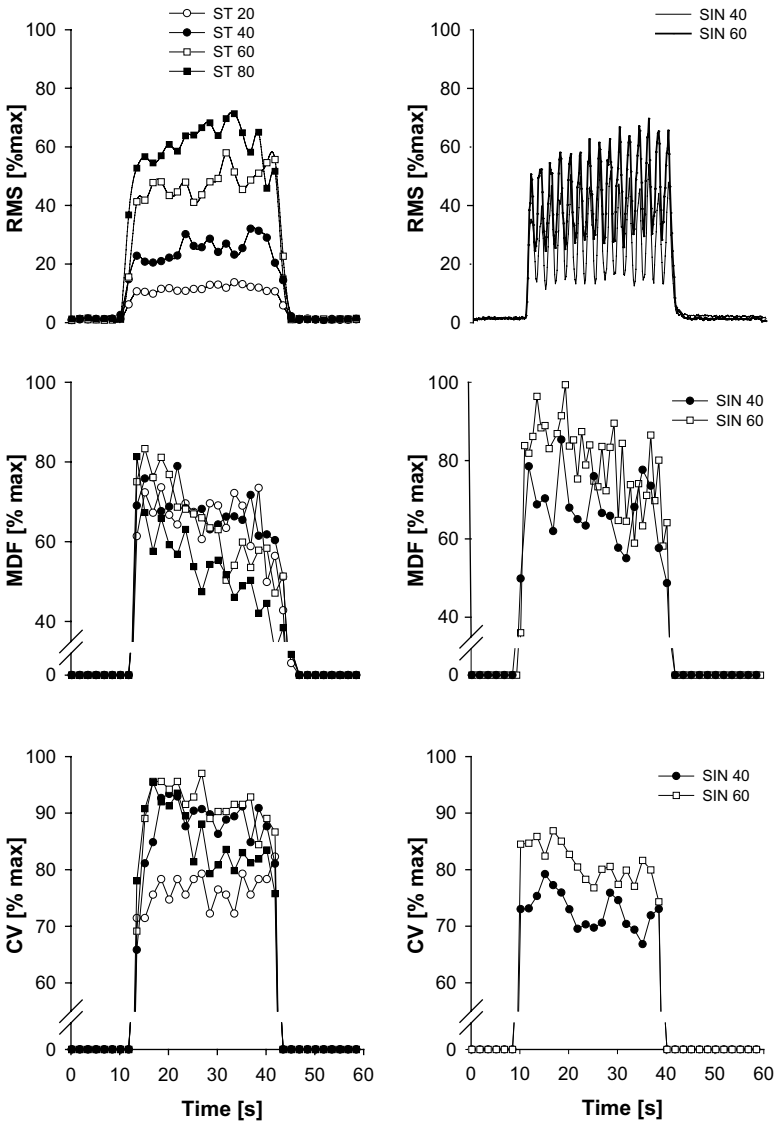

Fig. 3. sEMG data during ST and SIN exercises. Left side: ST data (ST20, ST40, ST60, ST80); Right side: SIN data (SIN40, SIN60). Upper panel: RMS; middle panel: MDF; lower panel: CV. The mean curves obtained in all trials by the seven subjects are reported. Data are expressed as a percentage of the maximum value obtained during the MVC test. For the sake of clarity, standard errors are not reported.

5.1. ST isometric exercises

The RMS for ST contraction showed dependence from the force level, being higher as a function of force increases (upper left panel of Fig. 3). In accordance with force data (see Fig. 2, upper left panel), approximately at 2/3 of ST80 contraction RMS started decreasing.

The MDF values at the start of ST contraction were in the range of 75–80% of maximum. MDF fast slopes showed dependence on the force level ($p < 0.05$) but not on the motor task. The greatest difference in MDF fast phase slope was obtained between ST60 and ST80 ($p < 0.05$; Fig. 4b).

The relationship MDF slopes vs. isometric force had the form:

$$\text{slope [MDF]} = 0.22 - 0.027x \quad (2)$$

where x is force expressed in %MVC and $R = 0.86$.

CV slopes during the fast phase were dependent on force level (Fig. 4c, $p < 0.05$), being CV values computed at ST20 lower than those obtained at the other ST force levels.

The relationship CV slopes vs. isometric force for ST experiment has the form:

$$\text{slope [CV]} = 0.064 - 0.0086x \quad (3)$$

with x is force expressed in %MVC and $R = 0.87$.

5.2. SIN isometric exercises

During SIN contractions, RMS fluctuated with force; at SIN60 an increase over time in RMS was observed attributable to ongoing myoelectric fatigue.

As observed for the ST contractions, the MDF fast phase for SIN contractions were statistically dependent

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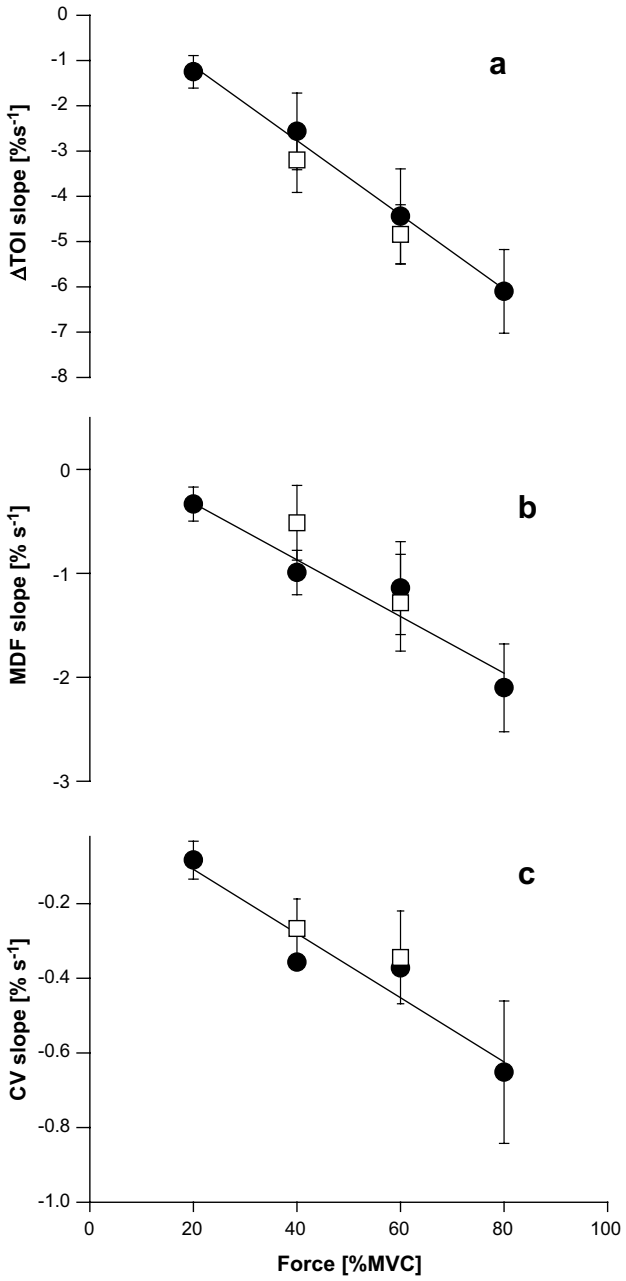

Fig. 4. ΔTOI, MDF and CV slopes for ST and SIN contractions at different force levels. The abscissa of SIN contractions was chosen in accordance to their respective force central value (i.e. 40 and 60% MVC). Statistically significant differences are omitted for the sake of clarity. See text for further details. Closed circles: ST exercises; open squares: SIN exercises. Means ± SE; $N = 7$.

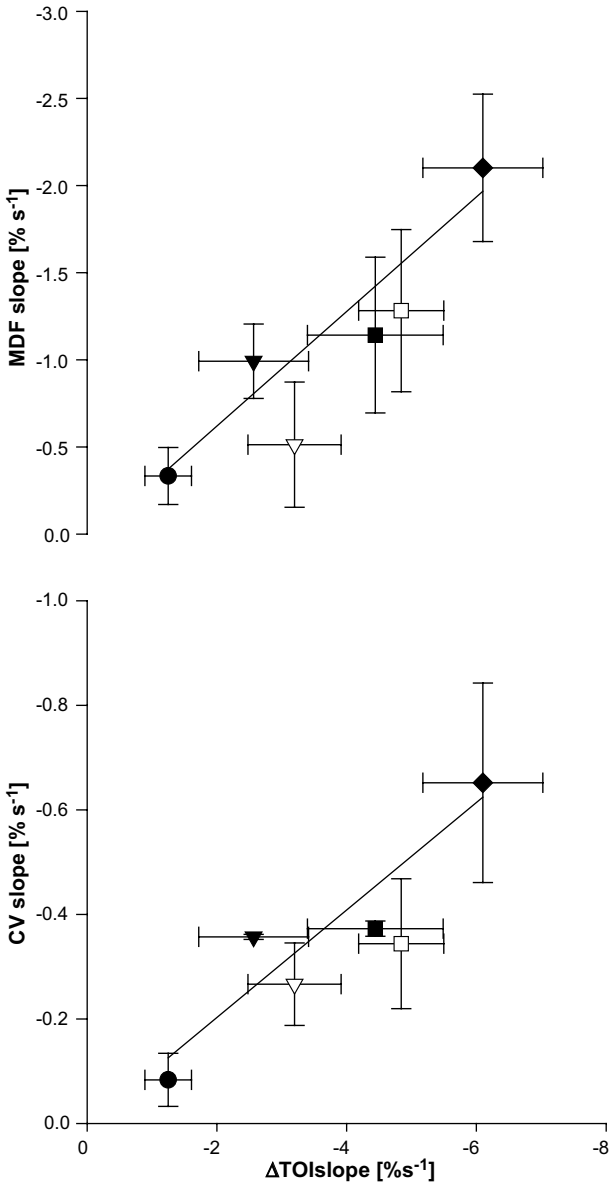

Fig. 5. Relationship between MDF/CV slopes and ΔTOI slope during ST and SIN contractions. From left to right: ST20 (●), ST40 (▼), SIN40 (▽), ST60 (■), SIN60 (□), ST80 (◆). Statistically significant differences are omitted for the sake of clarity. See text for further details. Means ± SE; $N = 7$.

on the force level but not on the motor task ($p < 0.05$; Fig. 4b).

The statistical analysis showed a significant difference between SIN40 and SIN60 MDF slopes ($p < 0.05$).

No statistically significant differences were present between SIN40 and ST20 MDF slopes; the slope of SIN40 was significantly lower than that obtained at ST40 and ST60 ($p < 0.05$). The MDF slope at SIN60 was lower than that at ST80 ($p < 0.05$).

6. NIRS and EMG data: comparisons

As mentioned above, ΔTOI, MDF and CV slopes obtained during the fast phase in both experimental conditions are reported in Fig. 4. All these three parameters were significantly correlated with force level for ST and SIN experiments ($p < 0.05$).

In Fig. 5, the relationship between MDF and CV slopes versus ΔTOI slopes is shown for the fast phase for ST and SIN experiments (filled and empty symbols). Each symbol refers to a given force level for the ST and SIN experiments. The fast phase slopes of MDF and CV computed

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Table 1
ΔTOI_{min} (%) values reached by the different subjects at the end of the isometric static (ST) and sinusoidal isometric (SIN) exercises

	ST20	ST40	ST60	ST80	SIN40	SIN60
S1	−33.8	−49.3	−60.3	−67.1	−62.3	−62.1
S2	−22.7	−35.9	−39.6	−49.2	−31.4	−43.5
S3	−14.9	−27.1	−49.7	−62.2	−27.5	−51.8
S4	−29.9	−51.8	−62.5	−71.2	−56.6	−61.5
S5	−14.2	−39.5	−63.1	−73.2	−38.9	−62.5
S6	−10.7	−41.7	−41.0	−45.6	−41.5	−44.8
S7	−16.7	−41.6	−46.7	−53.0	−41.5	−57.2
Mean	−20.4*	−40.9	−51.8	−60.2	−42.8	−54.8
SE	3.3	3.1	3.8	4.2	4.8	3.1

See text for further details. *Denotes a statistically significant difference ($p < 0.05$) of the ΔTOI_{min} 20% from the other ΔTOI_{min} values.

on ST contractions show a high degree of correlation with ΔTOI slopes, being:

$$CV = -0.07 + 0.081x \quad (4)$$

where x is ΔTOI slope and $R = 0.73$; and:

$$MDF = -0.22 + 0.26x \quad (5)$$

where x is ΔTOI slope and $R = 0.72$.

From this figure, it is evident that, in terms of ΔTOI fast phase slopes, SIN data fit well with ST data. Namely, SIN40 values fall between those at ST40 and ST60 while data from SIN60 are between ST60 and ST80. Considering the MDF and CV slopes, SIN40 is between ST20 and ST40, while SIN60 data fall between ST60 and ST80.

7. Discussion

The main finding of this study was the demonstration of a relationship between sEMG changes and O_2 desaturation (ΔTOI) of the BB muscle during static and cyclic isometric exercises. The results of the present study can be summarized as follows:

- two different phases of ΔTOI decline, namely a fast and a slow phase, were found during isometric contractions independently of the exercise intensity and modality;
- the rate of the fast phase of BB desaturation as well as ΔTOImin values reached at the end of slow phase were influenced only by the level of force, and not by the exercise modality;
- CV and ΔTOI data, from either ST and SIN exercises, clearly indicates that MU recruitment strongly influences oxygen desaturation in the active muscle;
- tHb data during ST and SIN exercises, suggest that muscle blood flow is not completely restricted even at the highest force levels (80%MVC).

As reported in Table 1, the maximal O_2 desaturation was obtained at ST80; it is to note that the larger change was observed between ST20 and ST40. In fact, the drop in de-oxygenation between these two force levels is twice as much the differences obtained between the other force levels. This result is compatible with the Henneman's size principle (Henneman et al., 1965) that dictates the orderly recruitment of individual MUs. Namely, MUs are recruited in an orderly fashion, from type I, oxidative, to type IIb, mostly anaerobic, as the force output increases as also summarized by Bottinelli and Reggiani (2000). Accordingly, the rate of muscle CV and MDF decays is dependent on the type of recruited MUs that, in turn, depends on actual force output (Merletti et al., 1990). Following our results, this seems to be the case. A possible explanation for the greater drop in ΔTOI_{min} observed between ST20 and ST40 can be that in the BB muscle the recruitment of large oxidative fibers is prevalent between 20 and 40%MVC and almost completed at 60%MVC. This is also reflected by the trend shown by MDF-CV fast phase slopes vs. ΔTOI reported in Fig. 5. In fact, between 40 and 60%MVC the increase in ΔTOI fast phase slope is not accompanied by a correspondent change in MDF and CV slopes. Besides, from 60 to 80%MVC the rate of change of sEMG parameters shows a new steep increase whereas in the same force interval changes in ΔTOI are reduced (Figs. 4 and 5). As stated in the introduction, CV is now accepted as a size principle parameter (Farina et al., 2007) also in dynamic conditions (cyclic exercises). Following the above description, these results can be explained on the basis of an increasing and prevalent recruitment of Type IIB glycolitic fibers in BB muscle after 60%MVC. Considering the fact that either MDF and CV computed over sEMG signals are average values a certain "inertia" must be taken into account. However, although a scarce capability of these parameters to promptly detect a significant recruitment of a given population of MUs, our results seem to convincingly provide evidence of the Henneman's principle.

The maximal desaturation obtained at ST80 (see Table 1) is partly in agreement with Kahn et al. (1998), who investigated brachioradialis oxygenation changes during isometric contractions by single distance continuous wave NIRS. However, those authors found a peak of muscle de-oxygenation at 50%MVC, whilst at higher force levels muscle de-oxygenation was lower. For the purposes of the present study, these differences have to be considered marginal, since they can simply come out from the different muscles explored (although having a similar functional role) and from the diverse NIR apparatus employed.

On the other hand, SIN contractions provide an indirect indication about the possible influence of MUs recruitment on aerobic metabolism: it is to note, in this particular case, that the oxygen initial utilization is almost identical to that of ST contractions, whilst the MDF and CV changes are reduced, at least during the SIN40 exercise. This is possibly due to the fact that this low contraction regimen is as such to promote a marginal – intermittent – recruitment of fast twitch, mostly anaerobic, MUs.

After the initial fast phase, BB desaturation rate slows down. It has been well documented (Lippold et al., 1960;

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Sbriccoli et al., 2003; West et al., 1995), for several muscle groups, that the amplitude of the sEMG during an isometric contraction increases with both the duration and intensity of an isometric steady state effort. There is less agreement on the relationship between changes of sEMG spectral parameters and recruitment and or modulation of MUs firing rate (Farina et al., 2002b). However, it is accepted that for a muscle to produce more force, it is necessary to increase the excitatory drive to its MUs, either in terms of newly recruited MUs or of increasing the firing rate of the already active. This is reflected, in the present work by BB desaturation rate, MDF decay and CV decay that all increase when the isometric force output increases. To this respect, we should consider the unbalance between O_2 supply and muscle O_2 demand. From data presented in Fig. 3, it is evident that the RMS increases with force and a certain degree of change in muscle blood volume, namely of ΔtHb, is always present. At low force levels (ST20 and ST40) the ΔtHb behavior seems to indicate that even during the contraction the muscle blood volume reaches values greater than those obtained at rest. This result cannot be explained only on the basis of a blood displacement from the inner portion of the muscle toward muscle surface region, at least for the ST20 exercise. In accordance with (Kahn et al., 1998) the ΔTOI stabilizes only during the final part of ST20 exercise, indicating that a new equilibrium point between O_2 supply and consumption is possible, whilst at ST40 this seems not to be the case. Moreover, ΔtHb is not stationary neither at ST60 and ST80 being more likely, in this particular case, a redistribution of forces between muscle units and namely of those attributable to viscoelastic tissues. On the other hand, an internal pressure unbalance between deep and superficial part of the muscle and a rotation of the MUs could not be the sole causes of the instability of muscle blood volume as suggested in previous works (Sejersted et al., 1984; Sjögaard et al., 1986; Søgaard, 1995). The RMS results presented in this work are not compatible with the hypothesis of MU rotation other than at ST80. In fact, the RMS is either stable (ST20) or increases overtime at ST40 and ST60. Only in the last third of ST80, a dip in RMS amplitude is present and this is timed in accordance with the decrease in average force. However, it is noteworthy that in this phase the slope of ΔtHb recovery remains unchanged, thus the effect of MUs rotation and/or internal pressure unbalance, if present, should be non-significant. Furthermore, at ST60 and mostly at ST80, ΔtHb starts to change few seconds after the mechanical steady state is reached. With a fair approximation, this time corresponds to the beginning of the slow phase of muscle desaturation. The scenario could be as follows: the reduction of internal muscle pressure allows for a minimal blood supply that, however, is not enough to match muscle metabolic demand. A "contamination" of the muscle oxygenation signal by an increased volume of oxygenated blood in the skin, as suggested by Grassi et al. (2003), is still possible but, under the present experimental conditions (isometric), a thermoregulatory mechanism cannot be invoked.

7.1. Limitations

The two probes, metabolic and electromyographic (NIRS and sEMG), were as close as possible each other but not exactly on the same muscle portion. In substance, they explored adjacent muscle portions on the two sides of an ideal muscle mid line. This choice may raise some criticism, however, this configuration was chosen for the following reason. The BB muscle offers, in its middle portion, space enough to accommodate the two probes. Muscle deformations in the middle part are minimal with respect to the distal portion as shown by cine phase contrast magnetic resonance imaging (Pappas et al., 2002). On the other hand, an "in-series" arrangement of the probes offers the drawback of large muscle deformation also during isometric contraction. Thus, since a relative stability of muscle geometry is a main requisite for the optimal working of either probe, the middle portion of muscle belly is the best choice for probes positioning. Besides, it has been recently shown that BB metabolic demand during exercise is much more homogeneous in correspondence of the central part of muscle belly (Pappas et al., 2002).

The major advantage of the NIRS measurements is the possibility to be performed repeatedly. The main NIRS results in sports science have been reported and discussed in several recent reviews (Neary, 2004; Bhambhani, 2004). Despite the advantages of NIRS, there are limitations of this study that warrant discussion. Some of the limitations are related to the assumptions made in NIRS in general. (1) Absorbing compounds. Haemoglobin is considered the main absorbing component in the tissue volume interrogated. (2) Sample volume. The use of NIRS allows the investigation of only a few cubic centimetres of superficial BB muscle. Therefore, it is assumed that the investigated portion of a given muscle is recruited in proportion to the work performed. (3) The accuracy of TOI measurement relies on the assumption that muscle tissue is macroscopically homogeneous. This is not certainly true for *in vivo* measurement due to the skin-fat layer separating the NIRS probe from the muscle. However, the multi-distance method (Suzuki et al., 1999) strongly reduces the effect of superficial layer on the determination of TOI because the light intensity is measured at several different source–detector distances allowing the measurement of the slope of light attenuation versus distance. This method provides a high signal-to-noise ratio without being so sensitive to the optical coupling and to the presence of superficial tissue layers such as the fat layer. The superficial layers of tissue affect all the light bundles similarly and therefore their influence cancels out. Only deeper tissue layers have an effect on the TOI values. (4) The lack of muscle biopsies or alternative non-invasive methods to substantiate metabolic claims. In the present study it was

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not possible to take muscle biopsy samples. Given the above mentioned considerations, we have been careful not to extend our finding beyond the limitations of the NIRS technology that we utilized.

Another methodological issue, relevant to sEMG signal analysis, is represented by motor point location with respect to recording electrodes. The procedure we adopted for localizing the motor point is well-tested (Farina et al., 2000). In addition, an electrodes array offers the advantage, over the conventional two-electrode technique, that visual inspection of the raw sEMG signal allows an easy identification of electrode misplacement and, thus, its prompt repositioning in a more reliable portion of muscle.

Finally, it can be argued that MUs population below the probes was not uniform or largely different from subject to subject. Muscle fiber distribution within individual human skeletal muscles is far from being precisely defined. However, high threshold MUs have been claimed to be superficially located in the human BB muscle (Clamann, 1970; Manta et al., 1996). In support of this view, more recent studies that used fluorodeoxyglucose positron emission tomography indicated: (a) a decreased metabolic efficiency in the most peripheral part of the BB muscle, and (b) a regionalization of slow twitch muscle fiber in the medial and superficial portion of BB muscle (Pappas et al., 2001).

This combined study suggests that muscle aerobic demand during isometric contractions from low to high force levels is influenced by the kind of active MUs and not by the isometric exercise modality thus confirming the relationship between ongoing changes of myoelectric signal and changes in local muscle oxidative metabolism. The combined NIRS-sEMG approach offers the opportunity for a deeper non-invasive investigation of muscle function not only in sedentary healthy subjects but also in special populations, from athletes to neuromuscular patients.

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QUANTIFICATION OF QUADRICEPS O_2 DESATURATION IN RESPONSE TO SHORT SPRINT CYCLING

Dear Editor-in-Chief:

A recent article (8) investigated vastus lateralis O_2 desaturation in response to 10 very short (6 s) sprint cycling bouts. Although the results are interesting, the presentation of the muscle oxygenation data is inadequate. For measuring muscle oxygenation, Racinais et al. (8) used a multidistance spatially resolved tissue oximeter (NIRO-300, Hamamatsu Photonics, Japan) without exploiting the offered advantage to quantify muscle oxygenation directly as tissue oxyhemoglobin (O_2Hb) saturation (%). Tissue O_2Hb saturation reflects the dynamic balance between O_2 supply and O_2 consumption and is independent of the pathlength of the near-infrared photons in the muscle tissue (1,3). Near-infrared spatially resolved spectroscopy implies that the light intensity is measured at several different source–detector distances (1,3). Then, this noninvasive technique allows the measurement of the slope of light attenuation versus distance and provides a high signal-to-noise ratio, without being so sensitive to the optical coupling and to the presence of superficial tissue layers.

Racinais et al. (8) drew their physiological conclusions on the basis of the interpretation of the following data: 1) percent changes of the deoxyhemoglobin (HHb) values calculated relative to the rest level in their Figure 1, and 2) HHb changes ($\Delta\mu$M) in the Results section using the differential pathlength factor (2). Unfortunately, Racinais et al. (8) did not report changes in total Hb (ΔtHb = ΔO_2Hb + ΔHHb) and O_2Hb saturation that are necessary for a correct interpretation of muscle oxygenation changes. HHb changes might represent tissue oxygenation changes only when tHb is stable. Therefore, the speculations on the muscle oxygenation changes based only on the increase and decrease of HHb during the sprint exercise are not fully reliable. On the other hand, at the onset of the sprint cycling bout, it would be expected that:

1. blood volume drops as a consequence of venous compression (blood volume is measurable as relative decrease in tHb), and
2. the utilization of the aerobic oxidative metabolic system (evaluated from the kinetics of muscle O_2Hb desaturation) is delayed (4,5).

Although Racinais et al. (8) did not accurately quantify muscle oxygenation, the data shown in their Figure 1 would suggest that the 30-s interval between bouts was not sufficient for glycolytic and oxidative ATP synthesis necessary for PCr resynthesis following intense short exercise (6). The results of previous studies (3,7) support that muscle oxygenation, measurable by near-infrared spectroscopy, can be utilized also for following the effects of specific aerobic or anaerobic training programs.

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Vastus Lateralis O_2 Desaturation in Response to Fast and Short Maximal Contraction

VALENTINA CETTOLO[1], MARCO FERRARI[1], VINCENZO BIASINI[2], and VALENTINA QUARESIMA[1]

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ABSTRACT

CETTOLO, V., M. FERRARI, V. BIASINI, and V. QUARESIMA. Vastus Lateralis O_2 Desaturation in Response to Fast and Short Maximal Contraction. *Med. Sci. Sports Exerc.*, Vol. 39, No. 11, pp. 1949–1959, 2007. **Purpose:** The purpose of this study was to investigate, in heavy-resistance strength-trained ($N = 10$) and untrained ($N = 10$) subjects, the vastus lateralis muscle oxyhemoglobin (O_2Hb) desaturation time course in response to a brief, maximal, voluntary isometric contraction. **Methods:** The two groups were not statistically different physically. Mean (± SD) age, height, and body mass of all the subjects were 28.0 ± 6.3 yr, 1.8 ± 0.1 m, and 77.8 ± 9.9 kg, respectively. Each subject performed five trials. Every trial consisted of 1) a 1-min rest period, 2) a leg press exercise of 2–4 s, and 3) a 5-min recovery period. Leg press exercise consisted of a static maximal voluntary contraction performed using the dominant leg only. Leg press strength was recorded using a load cell. Muscle O_2Hb saturation (SmO_2) was measured noninvasively by near-infrared spectroscopy (0.17-s sampling time). **Results:** Rate of force development was higher in the trained subjects than in the untrained ones (6897 ± 1654 vs 5515 ± 1434 $N \cdot s^{-1}$; $P < 0.05$). Once the exercise began, the time to the onset of SmO_2 decrease was consistently shorter in the untrained than in the trained subjects (2.81 ± 0.40 vs 3.91 ± 0.67 s, $P < 0.01$). In all the trained subjects and in two of the untrained ones, SmO_2 started to decrease once the exercise was stopped. After the end of the exercise, SmO_2 transiently decreased and reached its minimum value in 15.0 ± 3.8 and 10.1 ± 1.3 s in the trained and untrained subjects, respectively ($P < 0.01$). **Conclusion:** These data suggest that the vastus lateralis muscle of heavy-resistance strength-trained subjects could have a late activation of the oxidative metabolic system, or greater stored oxygen available, during a very fast, short, isometric maximal contraction. **Key Words:** NEAR-INFRARED SPECTROSCOPY, TISSUE OXYGENATION, SKELETAL MUSCLE, OXIDATIVE METABOLISM, MUSCLE EXERCISE, MAXIMAL VOLUNTARY CONTRACTION

BASIC SCIENCES

The three main metabolic systems providing ATP either at rest or in muscle exercise (phosphocreatine (PCr) hydrolysis, anaerobic glycolysis, and aerobic oxidative metabolism) are recruited differently according to the muscle characteristics, the exercise modality, and the training status (29). It is well established that human skeletal muscle is a heterogeneous tissue and can adapt to the variable functional requirements through mechanisms based on changes in muscle mass, fiber size, fiber type distribution, metabolic enzyme activities, and substrate supply. Human muscles are mixed muscles expressing three main fiber types: type I, IIA, and IIX, in variable proportions (7). They exhibit increasing shortening velocities in this rank order. The relative importance of the two main metabolic pathways of ATP production, that is, anaerobic glycolysis and aerobic oxidative metabolism, varies between muscle types. The slow type I fibers can sustain prolonged low-power work in association with a well-developed oxidative metabolism. The fast type IIX fibers are adapted to brief and intense contractions fueled by the anaerobic glycolytic pathway and immediate availability of PCr; type IIX fibers are much better used for fast and powerful movements (7). Type IIA fibers are fast oxidative–glycolytic and exhibit intermediate contractile function. Because short-duration, maximal-intensity exercise involves the recruitment of all the fiber types (10), the resultant metabolic response needs to be investigated in more detail, particularly in subjects whose responses may be affected by training adaptations.

Currently, the available evidence indicates that metabolic diversity involves many different aspects of muscle fiber metabolism, from substrate availability to the rate of enzymatic process of energy production and use (7). Glycogen content at rest is higher in fast than in slow fibers, and it was demonstrated that endurance training increases glycogen content and the glycolytic enzyme activities (37). Within the skeletal muscle cell at the onset of muscular contraction, PCr represents the most immediate reserve for the rephosphorylation of ATP. Nevertheless, muscle fibers differ in the availability of PCr. Several studies consistently indicate that in human muscles, resting

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PCr content is greater in fast than in slow fibers (7,26) and that sprint training increases the muscle PCr content (17). On exercise, the PCr content decreases to reach similar values in both fast and slow fibers. In contrast, resting ATP is similar in slow and fast fibers. Glycolytic and oxidative ATP synthesis allows PCr recovery. The factors affecting the rate of PCr resynthesis after intense exercise have recently been reviewed (26). The recovery is faster in slow than in fast fibers in the first minute after maximal exercise. The information currently available for strength exercise *in vivo* is limited to the postexercise phase.

So far, there is no reliable method for quantifying the instantaneous contribution of different fiber types on muscle recruitment and the resulting overall metabolic responses *in vivo*. The most useful techniques capable of measuring muscle metabolism noninvasively are ^{31}P magnetic resonance spectroscopy (^{31}P-MRS), ^{1}H magnetic resonance imaging (^{1}H-MRI), proton magnetic resonance spectroscopy (^{1}H-MRS), and near-infrared spectroscopy (NIRS). However, these techniques do not allow direct discrimination of metabolic changes at the level of type I or type II fibers *in vivo*. The ^{31}P-MRS measures muscular intracellular pH and the concentrations of the main phosphorylated compounds with a poor time resolution (longer than 1–2 s) (13). In addition, the compounds can only be quantified if the specific saturation factors remain constant during the exercise. The ^{1}H-MRI provides anatomic information (and also microvascular density) as well as muscle perfusion/oxygenation. However, being sensitive to motion artifacts, ^{1}H-MRI can be used only to investigate the postexercise recovery with a time resolution of about 0.03 s (13,38). The ^{1}H-MRS measures muscle deoxymyoglobin signal, allowing the assessment of intracellular O_2 availability at rest (33) and during exercise with a poor time resolution (longer than 12 s) (9). NIRS measures muscle oxyhemoglobin (O_2Hb) saturation (SmO_2), concentration changes of O_2Hb, deoxyhemoglobin (HHb), and total hemoglobin volume (tHb = O_2Hb + HHb), and, indirectly, blood flow and O_2 consumption (12,28,31). Therefore, NIRS has largely been used in muscle exercise pathophysiology (5,8,12,30). NIRS is a relatively low-cost technique, and it is less sensitive to motion artifacts than are ^{31}P-MRS/^{1}H-MRI/^{1}H-MRS. Moreover, NIRS can reach a time resolution of about 0.1 s, allowing the measurement of SmO_2 kinetics during the natural execution of whole-limb or whole-body exercise (not feasible inside the magnet by ^{31}P-MRS, ^{1}H-MRI, and ^{1}H-MRS), including very short exercises.

It is well established that skeletal muscle can adapt to variable functional requirements, even through changes in fiber-type characteristics and in contractile function. In particular, high-intensity exercise training increases the ability to develop force rapidly (7), the maximal integrated electromyography activity, and the cross-sectional area of the muscle (by 12% after 12 wk) (34). For example, it has recently been reported that the vastus lateralis (VL) muscle of bodybuilders was markedly adapted to hypertrophic heavy resistance exercise through 1) an extreme hypertrophy, 2) a shift towards the stronger and more powerful fiber types (IIX), and 3) an increase in specific force of muscle fibers (11). One-leg, heavy-resistance strength training provoked hypertrophy of VL muscle fibers after 9 wk of training; the cross-section area of type I, IIA, and IIX fibers increased by 18, 21, and 41%, respectively, with no significant changes in fiber-type distribution (25). Resistance training induced an increase in the VL muscle capillarization (16) and leg myoglobin (Mb) concentration (9). So far, the effects of training on muscle metabolism during intense exercise remain controversial (17,21). During cycling, the anaerobic ATP production was found to be reduced in subjects after sprint training (17). In contrast, during maximal isometric contractions, the anaerobic ATP production was found to be two- to threefold higher in sprint-trained subjects compared with endurance-trained or untrained subjects (21).

The metabolic changes induced by heavy-resistance, systematic strength training have mainly been investigated by ^{31}P-MRS using tests of prolonged duration (from about 30 s up to several minutes) (21,36). Towse et al. (38) have found, by ^{1}H-MRI and NIRS in sedentary and active subjects, a similar postexercise muscle O_2Hb desaturation after 1 s of ankle dorsiflexion of the anterior tibialis muscle. The postexercise transient hyperemia measured by ^{1}H-MRI was more than threefold greater in active compared with sedentary subjects. To the best of our knowledge, there are no studies on the recruitment of the diverse skeletal muscle metabolic systems during very short, maximal, voluntary contractions.

The main purpose of this study was to investigate the effects of a brief and fast maximal isometric voluntary contraction on VL SmO_2 (measured by NIRS) in heavy-resistance strength-trained and untrained subjects. On the basis of the literature, we assumed that the heavy-resistance strength-trained subjects would have, with respect to the untrained subjects, 1) an increased ability to use nonoxidative resources and/or an increased supply of substrate to be used nonoxidatively; 2) a higher PCr concentration on average; 3) a hypertrophy of type I, IIA, and IIX fibers; 4) a higher capillarization; and 5) a higher myoglobin content. Therefore, we hypothesized that we would find a delayed beginning of the use of the aerobic oxidative metabolic system (evaluated as muscle O_2Hb desaturation) in the VL muscle of the heavy-resistance strength-trained subjects during a very short maximal contraction that would provoke a complete occlusion of the blood flow.

MATERIALS AND METHODS

Subjects. Two groups of healthy male volunteers (trained and untrained) took part in this study. The 10 trained subjects were involved in heavy-resistance strength-training programs for more than 1 yr (> 2 h·d^{-1}; 3–7× wk^{-1}). The

10 untrained subjects were university students who did not spend any time on specific physical exercise. The two groups were not statistically different by unpaired *t*-test for age ($P = 0.97$), height ($P = 0.30$), or weight ($P = 0.07$). Mean (± SD) age, height, and body mass of all the subjects were 28.0 ± 6.3 yr, 1.8 ± 0.1 m, and 77.8 ± 9.9 kg, respectively. After receiving a complete explanation of the purpose and the procedures of the study, subjects gave their written consent; none of them reported recent thigh injuries. The study was approved by the university ethics committee and conformed to the regulations laid out in the Declaration of Helsinki on the use of human subjects in research.

Experimental design. All subjects performed five trials on a modified leg press machine (Leg Press, TechnoGym, Italy). Every trial consisted of 1) a 1-min rest period, 2) a leg press exercise of approximately 2–4 s, and 3) a 2-min recovery period. The leg press exercise consisted of a static maximal voluntary contraction (MVC), for which the subjects were instructed, on verbal command, to act against the footplate "as forcefully and as fast as possible" using only their dominant leg, and to maintain the MVC for a time period of approximately 2–4 s while the other leg was resting. The dominant leg was determined by the Edinburgh dominance test (32), to which specific items were added regarding foot preference. During the trial duration, volunteers were positioned on the seat of the leg press with a knee angle of 110° (full extension being 180°). Knee joint angle was determined with a handheld goniometer. The subject waist was fixed in position by bands; during the exercise, the subjects were allowed to stabilize their upper body by holding the handles of the leg press machine. NIRS recording was interrupted at the end of the 2-min postexercise recovery period of each trial. Subjects then remained seated, moving freely and relaxing their legs, for the next 2 min. The fifth minute of recovery corresponded to the rest period of the subsequent trial. During the intertrial periods, cardiac frequency was monitored by a pulse oximeter (N-200; Nellcor, Pleasanton, CA), with the sensor attached on the forehead. Cardiac frequency returned back to baseline values at the end of the rest period (data not shown). Neuromuscular and metabolic fatigue was considered to be minimal because of 1) the small number of repetitions performed, 2) the sufficient rest interval between trials, and 3) the good health of all the subjects. The sufficient rest interval between trials was confirmed by *post hoc* analysis, which demonstrated that the mean tissue oxygenation index (TOI) values, evaluated from −4 to −1 s before each MVC, returned to the baseline values (data not shown). Subjects were familiarized with the protocol before the beginning of the study. The first trial was preceded by a 10-min warm-up performed on an electronically braked cycle ergometer (Ergocard II, OTE Biomedica, Italy; 50 W, 50–60 rpm).

Force instrumentation. Leg press strength was recorded using a calibrated load cell (UU-K300, Dacell, Korea) inserted into the mechanical vinculum that fixed the seat to the foot board of the leg press machine. The force signal was monitored and recorded (at a rate of 100 Hz) by means of a digital oscilloscope (TDS 210, Tektronix Inc, Beaverton, OR); the data were stored on a personal computer for offline analysis. Force transducer calibration was performed according to the manufacturers' specifications. In particular, the electrical signal, produced by the transducer when 100-, 500-, 900-, 1500-, 2100-, and 3300-N loads were placed on the load cell, was recorded to determine the relationship between the force applied and the transducer's output. Before every testing session, the reproducibility of the measure was verified by applying a 1500-N load. The measured linearity and repeatability were better than 0.3% and 0.2%, respectively. For each trial, the force was continuously measured at least 5 s before, during, and 5 s after the exercise.

NIRS instrumentation. The NIRS measurements were performed with a NIRO-300 oximeter (Hamamatsu Photonics K.K., Japan) (35). After the probe testing on a phantom to analyze the total probe sensitivity and the sensitivity difference between the three sensors of the detection probe, the optical probe (consisting of one emitter and one detector, 4.5 cm apart), supported by a rigid rubber shell, was firmly attached to the skin overlying the belly of the VL muscle, parallel to the major axis of the thigh and at 14–20 cm from the knee, by a double-sided adhesive sheet. The rigid rubber shell, in turn, was secured by a soft and elastic bandage (Tensoplast, BSN Medical, South Africa). For identification of the VL muscle belly, on the day before the measurements, each subject was asked to perform a preliminary leg press isometric contraction. The identified area was carefully shaven before the experimentation. A pen mark was used to indicate the correct position of the probe holder shape for the next day. Pen marks were also made on the skin to check for any sliding of the rubber shell during the exercise. No sliding of the probe was observed at the end of the measurements in any subject. The NIRS data were recorded with a sampling rate of 6 Hz. Events were marked on the NIRO-300 to indicate the start/stop of each trial and the onset/end of each exercise. The measured NIRS data by the NIRO-300 were 1) SmO_2 as TOI (expressed as a percentage), 2) concentration changes in O_2Hb and HHb (expressed in micromoles per liter per centimeter), and 3) the derived changes in tHb (expressed in micromoles per liter per centimeter). These measurements can be affected by the contribution of Mb oxygenation changes (9,12). TOI reflects the local balance between O_2 supply and O_2 consumption. The tHb volume changes, being strictly related to blood volume changes, can be considered an indirect measure of changes in local blood flow. After fixing the probe holders on the subjects, an initialization procedure was carried out. The latter sets each laser power automatically, establishing the optimum measurement condition. The zero-set procedure (carried out just before the beginning of each baseline condition) was adopted to return the O_2Hb, HHb, and tHb parameters

to the zero value. This procedure does not affect the TOI value, because TOI is measured as an absolute value instead of a change with respect to the arbitrary initial zero value. The adipose tissue thickness overlaying the VL muscle was measured with a skinfold caliper (British Indicators Harpenden, UK). An unpaired *t*-test established that there was no difference between the two groups ($P = 0.11$). The adipose tissue thickness was 3.1 ± 0.8 mm (mean ± SD). Considering that the adipose tissue thickness was relatively low, and the penetration depth of the NIRS signal is almost half of the source-detector separation (4.5 cm in the optical probe of the NIRO-300), the changes in TOI and tHb reflected mainly muscle metabolic and hemodynamic changes of VL (12).

Data analysis. Strength and NIRS data were exported in text format without filtration. Analysis was performed with custom software developed in Matlab (version 5.3, The MathWorks Inc.).

Force data analysis. Each force dataset was expressed in newtons (by the measured calibration factors) and smoothed (Savitzky–Golay filter, polynomial order 2, frame size 41). The resting mean and SD force values were determined in the time interval from 1 to 4 s after the start of the recording of the force signals (Figs. 1 and 2A). This interval terminated around 1 s before the MVC onset. The MVC onset was identified as the force value higher than the threshold and maintained for at least 1 s. The threshold was considered the rest mean force value plus two times the rest SD value. The rest 2-SD value range was 170–269 and 100–243 N for trained and untrained subjects, respectively. The mean and SD of the force expressed during each exercise were calculated for 1.5 s of the exercise in the time interval from 0.5 to 2.0 s after the MVC onset. The exercise end was identified as the time when the force value became lower than the mean, minus 2 SD of the force expressed during the exercise. For each trial, the following force parameters were considered: 1) mean force output (F_m), 2) force duration (T_F), and 3) maximum rate of force development (RFD). F_m was the mean force expressed during the specified 1.5 s of exercise minus the rest mean force. T_F was the difference between the end and the onset of exercise according to the force data. RFD was the first

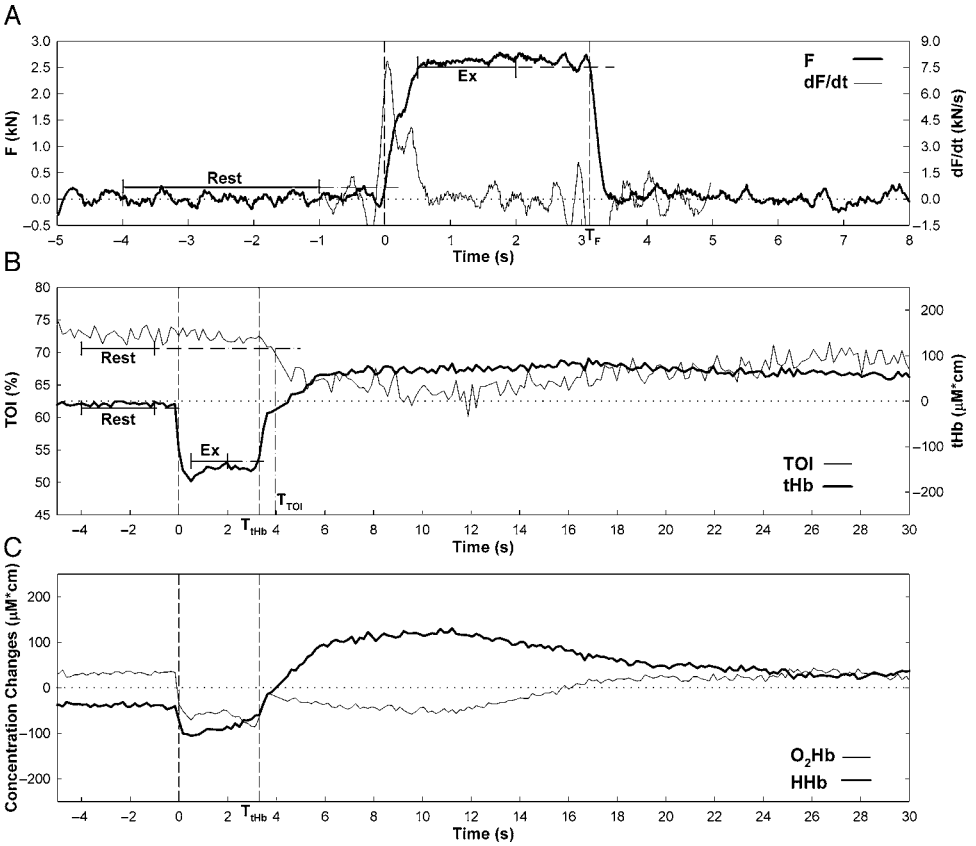

FIGURE 1—Changes before, during, and after a 3-s static maximal voluntary leg press exercise of a trained subject. *A*) Leg force output (*thick line*) and the corresponding first derivative (*thin line*); *B*) tissue oxygenation index (TOI, *thin line*) and total hemoglobin concentration changes (tHb, *thick line*); *C*) oxyhemoglobin (O_2Hb, *thin line*) and deoxyhemoglobin changes (HHb, *thick line*). The two *vertical dashed lines* in *panel A* indicate the onset/end of the exercise calculated by the force duration (T_F = 3.13 s). The two *vertical dashed lines* in *panels B and C* indicate the onset/end of the exercise calculated by the tHb concentration changes provoked by exercise (T_{tHb} = 3.30 s). The *dash-dotted vertical line* in *panel B* indicates the time to the onset of TOI decrease (T_{TOI} = 3.96 s). The *rest* and *ex* segments indicate the time intervals used for calculating the average and the SD of *F*, TOI, and tHb before and during the exercise. These segments are extended up to the threshold values used to identify the onset/end of the exercise and the T_{TOI} (see Methods).

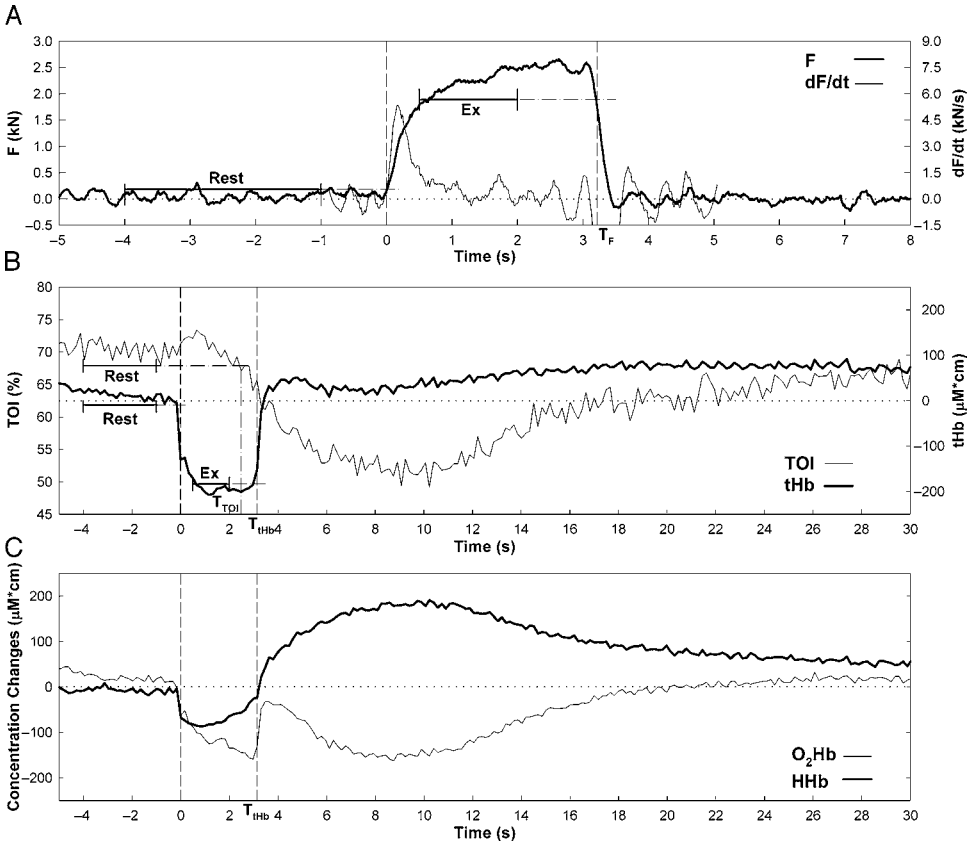

FIGURE 2—Changes before, during, and after a 3-s static maximal voluntary leg press exercise of a untrained subject. *A*) Leg force output (*thick line*) and the corresponding first derivative (*thin line*); *B*) tissue oxygenation index (TOI, *thin line*) and total hemoglobin concentration changes (tHb, *thick line*); *C*) oxyhemoglobin (O_2Hb, *thin line*) and deoxyhemoglobin changes (HHb, *thick line*). The two *vertical dashed lines* in *panel A* indicate the onset/end of the exercise calculated by the force duration (T_F = 3.21 s). The two *vertical dashed lines* in *panels B and C* indicate the onset/end of the exercise calculated by the tHb concentration changes provoked by exercise (T_{tHb} = 3.14 s). The *dash-dotted vertical line* in *panel B* indicates the time to the onset of TOI decrease (T_{TOI} = 2.48 s). The *rest* and *ex* segments indicate the time intervals used for calculating the average and the SD of *F*, TOI, and tHb before and during the exercise. These segments are extended up to the threshold values used to identify the onset/end of the exercise and the T_{TOI} (see Methods).

derivative maximum of the force–time dataset. For each subject, the reported force and NIRS data are referred to the best performance trial with regard to the maximal RFD value.

NIRS data analysis. The mean and SD values of resting tHb and TOI were calculated for the time interval from −4 to −1 s (Figs. 1 and 2B and C) before the exercise-onset event marker. This rest interval terminated around 1 s before the MVC onset. The onset of the exercise was identified as the time at which the tHb values became, for at least 1 s, lower than the mean minus two times the SD of the resting tHb. The rest 2-SD value range was 9–46 and 8–37 μM·cm for trained and untrained subjects, respectively. The mean and SD values of tHb and TOI occurring during each MVC were calculated for the time interval from 0.5 to 2.0 s after the identified onset of the exercise. The exercise end was identified as the time at which the tHb values became, for at least 1 s, higher than mean plus two times the SD value of the tHb expressed during the exercise. The onset of TOI decrease was identified as the time at which the TOI values became, for at least 1 s, lower than the mean minus two times the SD of the resting TOI. The rest 2-SD value range was 1.2–2.4% and 1.9–2.5% for trained and untrained subjects, respectively. For each analyzed trial, the following NIRS parameters were considered: 1) mean tHb and TOI changes during exercise (ΔtHb_{mean} and ΔTOI_{mean}, respectively), 2) contraction duration based on NIRS data (T_{tHb}), 3) time to the onset of TOI decrease (T_{TOI}), 4) maximum postexercise TOI decrease (ΔTOI_{min}), 5) time to maximum postexercise TOI decrease (T_{TOImin}), 6) half-recovery time of TOI ($T_{1/2TOI}$), 7) maximum postexercise tHb increase (ΔtHb_{max}), and 8) time to maximum postexercise tHb increase (T_{tHbmax}). ΔtHb_{mean} and ΔTOI_{mean} were the tHb and the TOI values, respectively, calculated as means for the specified 1.5 s of exercise minus the corresponding mean rest values. T_{tHb} was the difference between the end and the onset of the exercise based on tHb signal. T_{TOI} was the onset of TOI decrease minus the onset of the exercise for NIRS data. The ΔTOI_{min} was the difference between the minimum TOI value reached during the postexercise phase and the corresponding mean resting value. T_{TOImin} was the time at which TOI reached its minimum

value during the postexercise phase. The $T_{1/2TOI}$ was the time at which TOI recovered 50% of ΔTOI_{min} from minimum TOI. The ΔtHb_{max} was the difference between the maximum tHb value reached during the recovery phase and the corresponding mean resting value. T_{tHbmax} was the time at which tHb reached its maximum value during the recovery. T_{TOImin}, $T_{1/2TOI}$, and T_{tHbmax} were counted from the onset of the exercise as identified by using the tHb values.

Statistics. Statistical analyses were performed using the SigmaStat 3.5 package (Systat Software Inc., Richmond, CA). The average values were expressed as means ± SD. A one-way analysis of variance (ANOVA) was used to compare the data between the two groups of subjects (training effect). A two-way ANOVA was used to compare the data between groups and the order trial selected (trial effect). A two-way repeated-measures ANOVA was used for comparisons within subjects (signal or exercise effect) and groups, followed by the Student's *t*-test when appropriate. Results were considered statistically different at $P < 0.05$. Bland and Altman's limits-of-agreement plot (6) was employed to assess the level of agreement between the exercise duration determined using the force–time curve and the tHb–time curve.

RESULTS

Figures 1 and 2 show a typical time course of leg force and TOI, as well as O_2Hb, and HHb changes (used to calculate tHb changes) measured on a trained subject (Fig. 1) and an untrained subject (Fig. 2). These subjects were chosen as representative of the difference between the two groups. The diverse force performance between the trained and untrained subjects is shown by the dissimilar RFD values (about 7800 and 5000 $N \cdot s^{-1}$ in the trained and untrained subject, respectively). The onset of the exercise clearly provoked an abrupt drop of tHb, which could be attributable mainly to venous compression. tHb was almost stable for the exercise duration and promptly started to increase after the exercise end; then, a transient tHb overshoot was observed. tHb returned slowly to its preexercise level within 1–3 min (data not shown). On the other hand, in the trained subject TOI was almost stable during the exercise period (force duration, 3.13 s) and started to decrease 3.96 s after the beginning of the exercise, whereas in the untrained subject (force duration, 3.21 s) TOI started to decrease at 2.48 s. After the end of the short exercise bout, in both subjects TOI consistently and progressively decreased, reaching actual minimum values of 63.4 and 51.6% in 11.39 and 9.74 s in the trained and untrained subject, respectively; then, TOI progressively returned to the preexercise level in about 1–1.5 min.

Table 1 reports the leg force and VL muscle oxygenation/hemodynamic parameters for the best performed trial with regard to the highest RFD value. No relationship between the two groups was found regarding the chronological order of the trial associated with the highest RFD value ($P = 0.73$). The analysis of variance revealed a significant difference in RFD between the exercises performed by the trained and untrained subjects ($P < 0.05$). In contrast, F_m and T_F were not significantly different between the two groups ($P = 0.28$ and 0.14 for F_m and T_F, respectively). The duration of the exercise, according to tHb changes, was not significantly different between the two groups ($P = 0.25$). Moreover, T_{tHb} was significantly higher than T_F within each group ($P < 0.001$). However, the Bland–Altman plot between T_{tHb} and T_F (Fig. 3) shows 1) no trend in the data as the mean time duration increases, 2) a 95% confidence interval from −0.14 to + 0.42 s, and 3) a bias of +0.14 s. The latter can be explained by the different sampling times of the NIRO-300 and the force transducer (0.16 s and 0.01 s, respectively).

At rest condition, a significant interindividual variation in the TOI percentage was found in both groups (73.5 ± 5.1 and 71.4 ± 4.4% in the trained and untrained groups, respectively). The maximum TOI achieved during exercise with respect to the rest condition was not different between the two groups (2.5 ± 1.3 and 2.8 ± 1.3% in the trained and untrained groups, respectively; $P = 0.60$). During the exercise, tHb and TOI values changed significantly with respect to the rest condition ($P < 0.001$ and $P < 0.01$ for tHb and TOI, respectively). The amplitude of these changes was similar in both groups ($P = 0.95$ and 0.35 for tHb and TOI,

TABLE 1. Leg force and vastus lateralis muscle oxygenation/hemodynamic parameters.

	Trained ($N = 10$)	Untrained ($N = 10$)
Force duration (s)	2.75 ± 0.39 (1.93 to 3.34)##	2.94 ± 0.45 (1.89 to 3.51)#
Mean force output (N)	2086 ± 497 (1735 to 3232)##	1983 ± 455 (1272 to 3032)#
Maximum rate force development ($N \cdot s^{-1}$)	6897 ± 1654 (5020 to 10137)##	5515 ± 1434 (2951 to 8258)*#
Contraction duration calculated by tHb changes (s)	2.94 ± 0.44 (1.98 to 347)##	3.04 ± 0.42 (2.14 to 3.63)#
Mean tHb changes during exercise ($\mu M \cdot cm$)	−229 ± 103 (−325 to −33)##	−261 ± 198 (−594 to −19)
Mean TOI changes during exercise (%)	+1.1 ± 0.9 (+0.0 to +2.7)##	+0.8 ± 1.5 (−1.1 to +3.6)
Time to the onset of TOI decrease (s)	3.91 ± 0.67 (3.13 to 4.95)##	2.81 ± 0.40 (2.31 to 3.30)**#
Maximum postexercise TOI decrease (%)	−15.4 ± 6.9 (−29.0 to −7.4)	−22.1 ± 7.4 (−39 to −14)*
Time to maximum postexercise TOI decrease (s)	15.0 ± 3.8 (9.6 to 21.1)	10.1 ± 1.3 (8.8 to 12.9)**
Half-recovery time of TOI (s)	29.6 ± 8.5 (21.8 to 51.8)	21.8 ± 5.1 (15.7 to 32.7)
Maximum postexercise tHb increase ($\mu M \cdot cm$)	+94.0 ± 39.2 (+39 to +175)	+72.6 ± 32.3 (+15.8 to +115.6)
Time to maximum postexercise tHb increase (s)	26.8 ± 7.1 (13.5 to 34.8)	32.6 ± 12.5 (13.0 to 54.6)

Values are means ± SD with range (minimum to maximum).
tHb, total hemoglobin volume; TOI, tissue oxygenation index.
Significant difference between groups (two-way ANOVA, training effect): * $P < 0.05$; ** $P < 0.01$. Significant difference within groups for T_F vs T_{tHb} and for T_{tHb} vs T_{TOI} (paired Student's *t*-test): # $P < 0.05$; ## $P < 0.01$.

respectively). The time to the onset of TOI decrease was consistently shorter in the untrained subjects than in the trained ones (Table 1; $P < 0.01$). This difference is better illustrated by Figure 4, which shows the time to the onset of the TOI decrease versus the exercise duration measured in all the subjects. Nine measurements collected on trained subjects are above the identity line (with two data points overlapping), and one is coincident with the identity line. Six measurements collected on untrained subjects are below the identity line, two are coincident with the identity line, and two are above, though very close, to the identity line.

Maximum postexercise TOI decrease was consistently greater in the untrained subjects, and the time to maximum postexercise TOI decrease was consistently longer in the trained subjects (Table 1; $P < 0.05$ and $P < 0.01$ for ΔTOI_{min} and T_{TOImin}, respectively). Half-recovery time of TOI was similar in both groups ($P = 0.06$). Figure 5 reports the maximum postexercise TOI decrease (ΔTOI_{min}, %) versus half-recovery time of TOI ($T_{1/2TOI}$, s) for trained and untrained subjects. Maximum postexercise tHb increase and time to maximum postexercise tHb increase were not significantly different between trained and untrained subjects ($P = 0.96$ and 0.37 for ΔtHb_{max} and T_{tHbmax}, respectively).

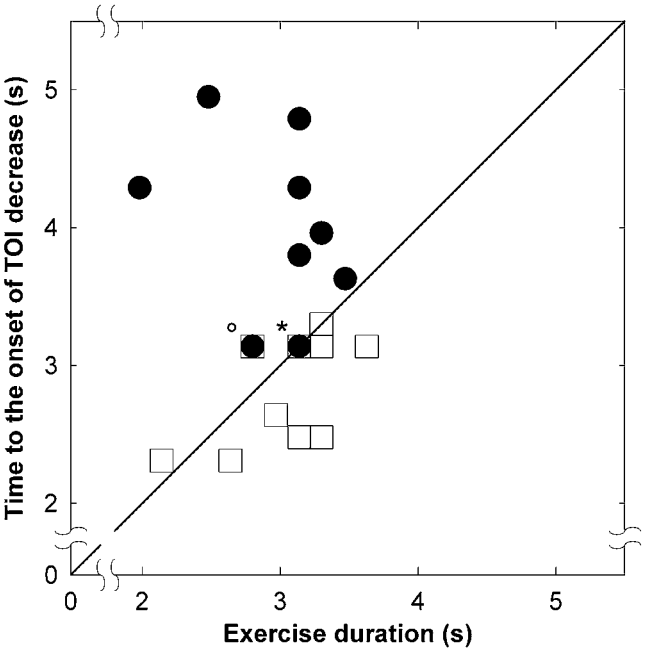

FIGURE 4—Time to the onset of TOI decrease vs the exercise duration (identified on tHb changes) for trained (*full dots*, $N = 10$) and untrained subjects (*open squares*, $N = 10$). The symbol size corresponds to the NIRO-300 sampling time (0.16 s). *Solid line*, identity line. Five data points are overlapped. ○ Three overlapping data points (two trained and one untrained); * two overlapping data points (one trained and one untrained).

DISCUSSION

These results are consistent with our hypothesis that, on a brief and fast maximal isometric voluntary contraction, VL muscle of heavy-resistance strength-trained subjects would have, with respect to the VL muscle of untrained subjects, a delayed beginning of the use of the aerobic oxidative metabolic system (evaluated as muscle O_2Hb desaturation). In particular, the SmO_2 of the VL muscle of the trained group started to decrease only after the end of the exercise in 9 of 10 subjects, and just at the end of the MVC in the remaining subject (Fig. 4). In the case of the untrained group, SmO_2 started to decrease before the end of the exercise in 8 of 10 subjects only. To the best of our knowledge, this is the first time that the characteristics of NIRS of high temporal resolution and low sensitivity to motion artifacts have been exploited to investigate the time course of SmO_2 during an explosive intense exercise.

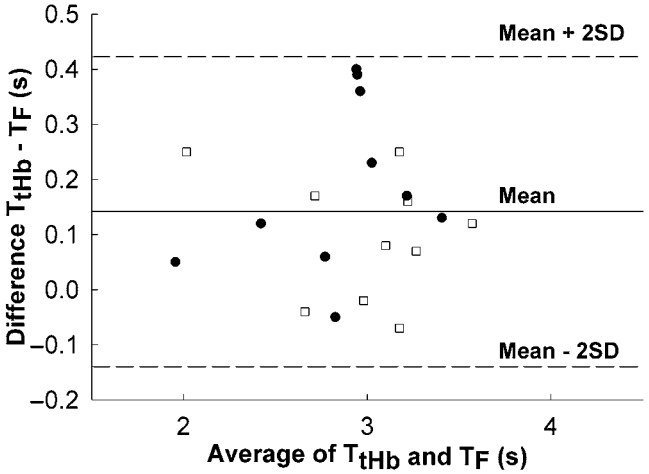

FIGURE 3—Bland–Altman representation of exercise duration determined by using the force–time curve (as T_F) and tHb–time curve (as T_{tHb}). *Full dots*, trained subjects; *open squares*, untrained subjects.

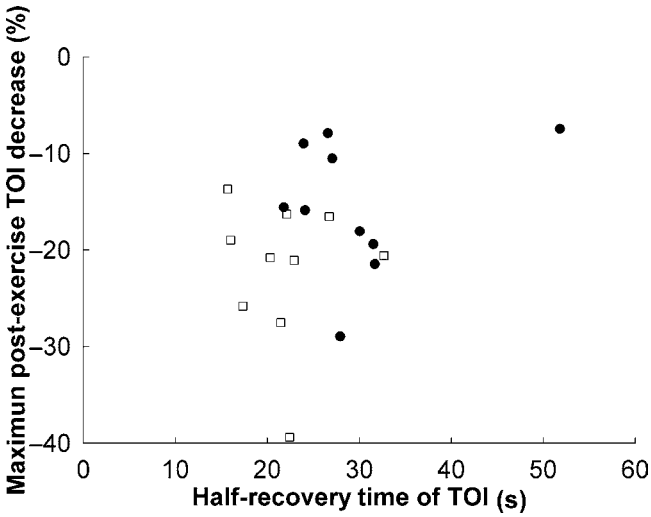

FIGURE 5—Maximum postexercise TOI decrease (as ΔTOI_{min}) vs the half-recovery time of TOI (as $T_{1/2TOI}$) for trained (*full dots*, $N = 10$) and untrained (*open squares*, $N = 10$) subjects.

The maximum rate of force development is an important strength parameter because it incorporates the aspect of contraction time, which is neglected using the F_m (1). RFD describes the ability to rapidly develop muscular force and reflects the ability of a subject to realize the contraction "as forcefully and as fast as possible." So, the maximum RFD value can be considered one of the most reliable muscle force–dependent tests of explosive force production (27). According to previous studies (2,27), in the present study all five trials were used for the assessment of the RFD reliability, whereas the trial associated with the highest RFD value served for the data analysis. The relatively large SD of the RFD values found in the present study (Table 1) is in agreement with values reported in recent similar studies (2,27,38). Although the rapid exertion of maximum force requires more practice than exerting force *per se*, this intersubject variability of RFD values could be explained by the diversity of one or more of the following physiological factors: muscle fiber type and myosin heavy-chain composition, muscle cross-sectional area, viscoelastic properties of the muscle–tendon complex, and neural drive to the muscle (2). Strength and endurance training produce widely diversified adaptations, with little overlap between them (29). Strength training typically results in increases of muscle mass and muscle strength. In contrast, endurance training induces increases in maximal O_2 uptake and metabolic adaptations that lead to an increased exercise capacity. Training induces gains in RFD (1,34), so, as would be expected, in the present study the heavy-resistance strength-trained subjects developed an RFD higher than that produced by the untrained subjects.

The mean force output was not significantly greater in the trained versus untrained subjects (Table 1) and was highly correlated with the maximum force achieved during MVC ($P < 0.001$, $R = 0.97$; data not shown). Similar results were found by others when the force output was collected from different groups of subjects (active vs sedentary) (38). Therefore, because the F_m of the two groups was similar (at least for the time period between 0.5 and 2 s of MVC), and assuming that the exercise energetic cost was not substantially different between the two groups (21), the delayed time to onset of TOI decrease in the trained group suggests that the VL muscle of the trained subjects, during a very short and fast high-intensity isometric contraction, uses other metabolic systems rather than the aerobic oxidative one. The delayed activation of the aerobic oxidative metabolic system (evaluated as muscle O_2Hb desaturation) in the trained subjects could be a consequence of a larger proportion of type II fibers and a higher PCr concentration on the average, or greater PCr breakdown and anaerobic glycolytic ATP provision in trained than in untrained subjects.

Our results are also in agreement with a recent ^{31}P-NMR study (21) that demonstrates marked differences in force production, aerobic as well as anaerobic gastrocnemious muscle metabolism, between endurance-trained, sprint-trained, and untrained subjects during four maximal isometric contractions of 30-s duration each. No difference was found in resting PCr/ATP among the three groups. The groups differed with respect to PCr breakdown; sprinters demonstrated about 75% breakdown in each contraction compared with about 60 and 40% for untrained and endurance-trained subjects, respectively. In particular, during the first 5 s of MVC, PCr decreased by about 10% and pH increased by about 0.1 units in sprint-trained subjects. Conversely, PCr and pH were unchanged during MVC in the untrained subjects, suggesting that the aerobic system started to be used.

A delayed VL muscle desaturation has also been observed at the onset of cycling exercise by Grassi et al. (14). The authors consider PCr hydrolysis and anaerobic glycolysis responsible for the delay or the attenuation of the increase in ADP concentration within the cell after rapid increase in ATP demand, thereby "buffering" a more rapid activation of oxidative phosphorylation. In isolated single-frog myocytes, it was found that at the contraction onset, a monoexponential decrease in intracellular PO_2 was preceded by about 10 s in which PO_2 remained constant (23,39). The results of those studies suggest that there was plenty of O_2 available at the mitochondrial level in these cells during the first seconds of contraction (39). Therefore, in the subjects of the present study, the exploitation of the aerobic oxidative metabolism, which uses O_2 available in the mitochondrial matrix, could not be excluded during the very short exercise. If stored oxygen is greater in the trained subjects, this may partly explain a later onset of TOI decrease.

In human skeletal muscle, the role of Mb and its relationship with factors such as muscle perfusion and metabolic capacity are not yet well understood (40). Unfortunately, NIRS is unable to differentiate between the signal attenuation attributable to Hb and Mb, because the absorbency signals of these two chromophores overlap in the near-infrared range. Mb is a confounding factor at 10% of the whole NIRS signal (12). Considering the poor temporal resolution of ^{1}H-MRS, no data are available on Mb desaturation during very short MVC (9). The present NIRS results collected on trained subjects suggest that although VL muscle blood flow was interrupted, Hb and Mb did not desaturate during the 2–4 s of high-intensity exercise. During the recovery of high-energy phosphate levels after exercise, Mb is expected to be fully saturated and does not affect the whole NIRS signal. Recently, leg Mb concentrations, measured by NMR, were shown to be 25% greater in endurance-trained athletes as compared with sprinters, and to correlate with mitochondrial oxidative production of ATP (9). We could speculate that in our study the heavy-resistance strength-trained subjects might also have higher Mb concentration compared with untrained subjects. Combined ^{1}H-MRS and NIRS studies are needed to clarify not only the issue of the contribution of Mb to the NIRS signal, but also the kinetics and the amount of Mb desaturation during exercises with different workloads (9).

An accurate determination of the beginning/end of the MVC as well as the stability of the blood volume (measured as tHb changes) during the exercise are both necessary to claim the validity of our results. It is well known that the muscle contraction pinches the arteries/arterioles and veins/venules along the fascicular lines, whereas the capillaries are relatively uncompressed (15). A VL muscle maximal isometric voluntary contraction provokes a complete obstruction of muscle blood flow (3,4). This is witnessed by the fact that tHb, after an immediate initial drop, was stable during the exercise period. The exercise duration was determined either on force or tHb time courses (Figs. 1 and 2). The beginning of the exercise evaluated on the basis of both force and tHb tracings was coincident for the immediate effect of the muscle contraction pinch on the muscle blood volume. Although T_{tHb} was higher than T_F, the Bland–Altman plot shows a small bias attributable to the different sampling times of the NIRS instrumentation and the force transducer (Fig. 3).

A diverse postexercise TOI decrease (less intense in the trained subjects) was found (Table 1 and Fig. 5). Figure 5 clearly illustrates the large data-point dispersion in ΔTOI_{min}, which is also confirmed by the high SD reported in Table 1. The half-recovery time of TOI was not different between trained and untrained subjects. The presence of a data point with a prolonged recovery time (about 50 s) might be explained by the subject's difficulty to relax the VL muscle immediately after the exercise. A similar SmO_2 time course was also found in the finger flexor muscle after a 10-s MVC (22). In that study, a significant positive correlation between postexercise SmO_2 recovery rate (measured by NIRS) and the time constant for PCr resynthesis (measured by ^{31}P-MRS) was found. The postexercise SmO_2 recovery rate closely correlated with muscle O_2 consumption, but not with forearm blood flow. A delayed SmO_2 recovery has recently been reported in the tibialis anterior muscle after a 3-s MVC (24).

Glycolytic and oxidative ATP synthesis allows PCr recovery after MVC. The recovery is faster in slow than in fast fibers for the first minute after maximal exercise (7). The factors affecting the rate of PCr resynthesis after intense exercise have been recently reviewed (26). In our study, the O_2 supply is limited during the early phase of post-MVC metabolic recovery in the VL muscle of trained and untrained subjects, because TOI transiently decreased after the MVC. On the other hand, it has been reported that PCr recovery is limited by O_2 availability in trained subjects (18) and by mitochondrial oxidative capacity in untrained subjects (19). In fact, it has been demonstrated in exercise-trained subjects that PCr recovery occurred more rapidly when inspired oxygen fraction was 1.0 than when it was 0.21 (18).

The time course of the TOI recovery depends also on the post-MVC muscle blood-flow increase. It is generally accepted that tHb changes are related to blood-flow changes (12). Taking into account that no differences were found in the increase of the maximum postexercise tHb and its corresponding time between trained and untrained subjects (Table 1), the differences in postexercise TOI decrease cannot be attributable to differences in postexercise muscle blood flow. The differences in the VL muscle oxygenation recovery after maximal cycling exercise found between sedentary and active subjects (20) could be explained by differences in postexercise muscle blood flow on prolonged exercise and/or muscle capillarization. In our study, the very short duration of the VL muscle isometric exercise (3 s vs several minutes) was not capable of generating significant postexercise muscle blood-flow differences, as indirectly indicated by the tHb changes. Conversely, Towse et al. (38) have recently found, by ^{1}H-MRI, a postexercise transient hyperemia more than threefold greater in active compared with sedentary subjects after a 1-s ankle dorsiflexion of the anterior tibialis muscle. Nevertheless, any assumptions done concerning the training-induced adaptations that would have influenced the results between the two groups remain to be verified in future studies by invasive or other measurements.

The major advantage of NIRS is represented by the possibility to perform tissue oxygenation measurement repeatedly. The main NIRS results in sports science have been reported and discussed in several recent reviews (5,30). Despite the advantages of NIRS, there are limitations of this study that warrant discussion. Some of the limitations are related to the general assumptions made in NIRS. 1) *Absorbing compounds*: Hemoglobin is considered the main absorbing component in the tissue volume interrogated. 2) *Sample volume*: The use of NIRS allows the investigation of only a few cubic centimeters of superficial VL muscle. Therefore, it is assumed that the investigated portion of a given muscle is recruited in proportion to the work performed. 3) *The accuracy of TOI measurement relies on the assumption that muscle tissue is macroscopically homogeneous*: This is not certainly true for *in vivo* measurement, because of the skin-fat layer separating the NIRS probe from the muscle. However, the multidistance method strongly reduces the effect of the superficial layer on the determination of TOI (35). 4) *The difference in the time intervals of the force and the NIRS recordings*: In this study, the force and the NIRS data were recorded at 100 and 6 Hz, respectively. Although other NIRS instruments have a higher time resolution (up to 50 Hz) than that of the NIRO-300, they measure concentration changes in O_2Hb and HHb only (12). 5) *The range in contraction duration between subjects and between trials*: It was quite difficult to standardize the duration of a very short MVC. Future studies should be designed to include a variable duration of MVC and intertrial interval. 6) *The lack of muscle biopsies or alternative, noninvasive methods to substantiate either metabolic claims or inferences regarding fiber type and recruitment*: In the present study, it was not possible to take muscle biopsy samples. 7) *Other methods for measuring muscle activity such as*

EMG would have been beneficial. However, the simultaneous measurement of EMG and NIRS would have been very difficult in the measured muscle because of the size of the optical probe, and it would have required extra trials to be performed by the subjects, to collect EMG information separately. Given the above-mentioned considerations, we are careful to not extend our finding beyond the limitations of the NIRS technology that has been used.

In conclusion, the data from this study suggest that the VL muscle of heavy-resistance strength-trained subjects could have a late activation of the oxidative metabolic system, or greater availability of stored oxygen, during a very fast and short isometric maximal contraction. Considering that leg press exercise 1) is a common exercise used by athletes to enhance performance in sport, 2) is responsible for development of the largest and most powerful muscles of the body, and 3) mimics, from the neuromuscular point of view, many athletic movements, the results of this study could give a valuable contribution to exercise science. For instance, NIRS and leg press exercise could be used to identify, noninvasively, in single muscle groups, the contribution of the aerobic energy system during very short and fast intense exercise, and, secondly, to observe the effects of specific aerobic or anaerobic training programs on the starting time of the aerobic energy system activation.

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Gastrocnemius Medialis and Vastus Lateralis Oxygenation during Whole-Body Vibration Exercise

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[1]Olympic Medical Institute, Northwick Park Hospital, Harrow, UNITED KINGDOM; [2]University of Aberdeen, College of Life Sciences and Medicine, Aberdeen, UNITED KINGDOM; and [3]University of L'Aquila, Department of Sciences and Biomedical Technologies, L'Aquila, ITALY

ABSTRACT

CARDINALE, M., M. FERRARI, and V. QUARESIMA. Gastrocnemius Medialis and Vastus Lateralis Oxygenation during Whole-Body Vibration Exercise. *Med. Sci. Sports Exerc*., Vol. 39, No. 4, pp. 694–700, 2007. **Purpose:** The aim of this study was to investigate the effects of different whole-body vibration (WBV) frequencies on oxygenation of vastus lateralis (VL) and gastrocnemius medialis (GM) muscles during static squatting in sedentary and physically active healthy males. **Methods:** Twenty volunteers (age: 24.6 ± 2.9 yr; body mass: 80.6 ± 11.8 kg; height: 178.1 ± 7.6 cm) participated in this study. Ten subjects were sedentary individuals and 10 were athletes practicing different sports. All subjects completed four trials (control, and 30-, 40-, and 50-Hz WBV) in a randomized controlled crossover design. The trials consisted of static squatting on a vibrating platform for a total duration of 110 s. Muscle-oxygenation status was recorded with near-infrared spectroscopy. **Results:** The data analysis revealed no significant treatment-by-time interactions in tissue-oxygenation index (TOI) or Δ total hemoglobin volume (tHb) in VL and GM muscles. A significant main effect of time in TOI of both VL and GM muscles was identified ($P < 0.001$). VL TOI significantly decreased by 2.8% at 90 s in the control condition and by 3.3% at 110 s in the 30-Hz condition; VL TOI significantly increased by 2.1 and 3.0% at 30 s in the 40- and 50-Hz conditions, respectively. GM TOI significantly decreased by 3.2% at 60 s, by 4.1% at 90 s, and by 4.3% at 110 s in the control condition, and by 5.5% at 110 s in the 30-Hz condition. **Conclusion:** This study showed that WBV exercise with frequencies of 30, 40, and 50 Hz and small amplitudes does not affect muscle oxygenation of VL and GM muscles to a higher degree than a nonvibration condition. **Key Words:** VIBRATION EXERCISE, MUSCLE OXYGENATION, NEAR-INFRARED SPECTROSCOPY, OXIDATIVE METABOLISM

Whole-body vibration (WBV) has been promoted as an alternative exercise intervention able to affect neuromuscular performance (4,6) in young and old individuals. This new neuromuscular training method consists of squatting on specially designed plates producing sinusoidal oscillations of different frequencies and amplitudes (6). It has been suggested that the sinusoidal vibration generated by the plate oscillations elicits reflex muscle activity in the lower limbs (5,9,26), mainly via monosynaptic pathways.

Muscle activation during squat exercise on vibrating surfaces is still a controversial topic. In fact, although recent work from De Ruiter et al. (8) indicates that vibration elicits only low levels of muscle activation in leg extensor muscles, Rittweger et al. (25,24) have shown that both frequency and amplitude of vibration increase specific oxygen uptake and thus muscle activity. Very recently, Yamada et al. (34) have reported that squatting exercise with low-frequency, small-amplitude vibration performed on a tilting vibrating plate reduced muscle-oxygenation levels of vastus lateralis (VL) more than squatting without vibration as measured by near-infrared spectroscopy (NIRS). An increase in oxygen use was reported as the most likely cause.

Vibration exercise intensity can be determined by manipulating two parameters: amplitude and frequency (4,6). In most of the vibrating plates currently available on

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the market, vibration frequency is the only parameter that can be changed, and notwithstanding manufacturers' instructions, there is no real evidence to suggest the optimal training frequency to be adopted. Therefore, the determination of the effects of different WBV frequencies on muscle oxidative metabolism represents an important aspect to be analyzed to provide guidelines for WBV training programs.

The possibility of noninvasively studying local muscle oxidative metabolism during exercise has been enhanced in the last few years, thanks to the use of NIRS (2,10,12,15, 21,31). For the quantification of muscle O_2 saturation, different NIRS methods are available; so far, one of the most largely used in muscle studies is represented by near-infrared, spatially resolved spectroscopy (NIR_{SRS}). NIR_{SRS} provides an average (from small vessels, such as the capillary, arteriolar, and venular bed) tissue O_2 saturation and concentration changes in oxyhemoglobin (O_2Hb), deoxyhemoglobin (HHb), and total hemoglobin (tHb = O_2Hb + HHb). Tissue O_2 saturation represents a dynamic balance between O_2 supply and consumption in the investigated tissue volume.

During exercise, both blood flow and oxidative metabolism in skeletal muscle respond to meet increased oxygen demand. For this reason, NIRS measurements can provide an indication of localized muscle activities (21). Few studies have been conducted using NIRS during WBV exposure. In particular, recent work from Maikala et al. (16) shows a decrease in lumbar erector spinae oxygenation and blood volume in healthy males during seated WBV, independently of vibration dose. The authors show that prolonged exposure to such a form of WBV could lead to fatigue in erector spinae, and they suggest this as a possible underlying factor for low-back pain. Considering the lack of information regarding muscle oxygenation during WBV exercise, we aimed to investigate the effects of different WBV frequencies on oxygenation of VL and gastrocnemius medialis (GM) muscles during static squatting in sedentary and physically active healthy males. We hypothesized that vibration would determine a decrease in muscle oxygenation in GM and VL greater than in the control condition, because of an increase in muscle activation. Furthermore, we hypothesized that the oxygenation of GM muscle, because of its proximity to the vibration source, would be more affected than the oxygenation of VL during WBV.

METHODS

Subjects

Twenty volunteers (age: 24.6 ± 2.9 yr; body mass: 80.6 ± 11.8 kg; height: 178.1 ± 7.6 cm) participated in this study. Ten subjects were sedentary individuals (body mass: 78.6 ± 7.1 kg; height: 177.1 ± 6.9 cm), and 10 were athletes (body mass: 83.6 ± 16.7 kg; height: 179.4 ± 9.0 cm) practicing different sports: road cycling (1), weight lifting (2), mountain biking (2), rugby (1), volleyball (2), full contact (1), and triathlon (1). All subjects gave their written informed consent before participation. The study was approved by the ethics committee of the University of L'Aquila.

Muscle-Oxygenation Measurements

Muscle oxygenation was assessed by NIR_{SRS} using a two-channel tissue oximeter (NIRO-300, Hamamatsu Photonics, Japan). The design and the features of this device have been previously described (28). The theory behind the NIR_{SRS} approach and the reliability to measure tissue O_2 saturation has been reported (28). The NIRO-300 provides tissue O_2-saturation data as tissue-oxygenation index (TOI, expressed in percentage), which has been tested both *in vitro* and *in vivo* (3,28). The TOI value reflects predominantly the mean of arteriolar, capillary, and venular O_2 saturations, with a minor (less than 20%) contribution from myoglobin (23). In addition, the NIRO-300 provides, independently of TOI, changes in O_2Hb and HHb (expressed in $\Delta\mu M \cdot cm$) and the derived changes in total hemoglobin volume ($\Delta tHb = \Delta[O_2Hb] + \Delta[HHb]$). The tHb changes, being strictly related to blood volume changes, can be considered an indirect measure of local blood flow changes. After the probe test on a phantom to analyze the total probe sensitivity and the sensitivity difference between the three sensors of the detection probe, the two optical probes (each consisting of an emitter and a detector kept at a constant geometry and distance of 4.5 cm by a rigid rubber probe holder) were firmly attached to the skin overlying the belly of the GM and VL muscle groups of the right leg. In the case of hairy skin, the skin was carefully shaven before the experimentation. The optical probes were further secured by an elastic band. No downward sliding of the optical probes was observed at the end of the measurements in any subject. After fixing the probe holders on the subjects, an initialization procedure was carried out. The latter sets each laser power, automatically establishing the optimum measurement condition. The zero-set procedure (carried out just before the beginning of each baseline condition) was adopted to return the O_2Hb, HHb, and tHb parameters to the zero value. This procedure does not affect the TOI value, because TOI is measured as absolute value instead of a change with respect to the arbitrary initial zero value. The NIR_{SRS} data were recorded with a sampling rate of 6 Hz.

Adipose tissue thickness underlying the monitored VL and GM area was measured with a Harpenden skinfold caliper. Adipose tissue thickness of sedentary subjects was 4.6 ± 1.2 and 3.4 ± 0.7 mm for VL and GM, respectively. Adipose tissue thickness of athletes was 3.6 ± 0.9 and 2.9 ± 0.9 mm for VL and GM, respectively.

For each subject, TOI and tHb data are reported as mean values for the last 5 s (30 data points) in each considered

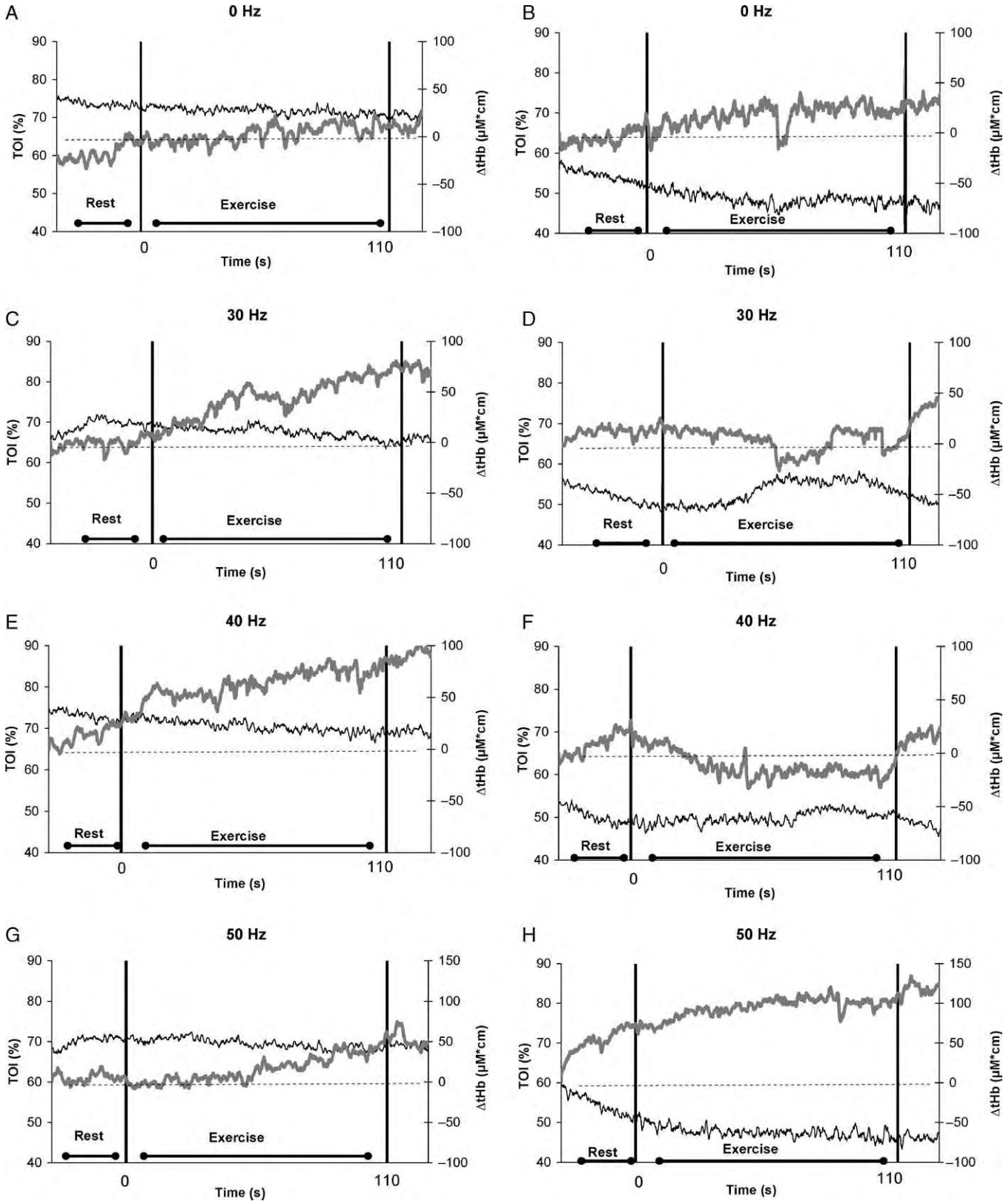

FIGURE 1—Typical time course of vastus lateralis (*left panels*) and gastrocnemius medialis (*right panels*) muscle TOI (%) (*thick black line*) and tHb concentration (*gray thick line*) changes measured on an athlete during the control condition (*A*, *B*), 30-Hz WBV (*C*, *D*), 40-Hz WBV (*E*, *F*), and 50-Hz WBV (*G*, *H*). The *vertical bars* indicate the beginning and the end of the treatment.

condition (vibration and control) and time (baseline and at 30, 60, 90, and 110 s).

Experimental Procedures

Subjects were asked to attend the experimental session after 24 h of complete rest from any physical activity. The subjects were familiarized with the protocol 1 d before the study. After the skinfold measurement, the two optical probes were positioned. Before each treatment, the subjects performed a 10-min warm-up, cycling at 50 W on an electronically braked cycle ergometer (QTE Biomedica Ergocard II, Esaote Biomedica, Italy).

The subjects (wearing their socks) were then asked to stand in half-squat position (knee angle 110°) on a vibration platform (Fitwave, Medisport, Italy), with their arms on the front handlebar, their feet parallel, and their foot stance similar to the distance between shoulders. A custom-made goniometer, fixed by velcro straps to the contralateral leg, was used to maintain the joint angle. The subjects were asked to maintain the squat position for 110 s (the maximum duration allowed by the vibrating platform) on the balls of their feet in the following randomized conditions: no vibrations, and 30-, 40-, and 50-Hz WBV.

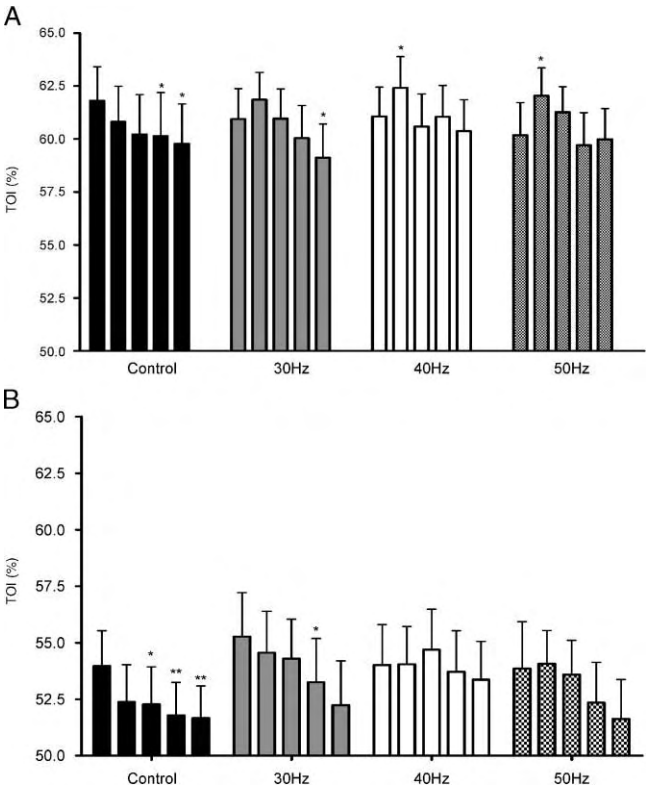

FIGURE 2—TOI (%) of vastus lateralis (*A*) and gastrocnemius medialis (*B*) in different conditions over time. Data represent measurements at baseline (*first bar*), 30 s (*second bar*), 60 s (*third bar*), 90 s (*fourth bar*), and 110 s (*fifth bar*) after the beginning of the exercise bout. No significant difference was identified between baseline values. Means ± SEM (N = 20). * P < 0.05 from baseline; ** P < 0.01 from baseline.

Each condition was preceded by a 60-s baseline in half-squat position. All subjects were able to hold the required position for the duration of the condition throughout the protocol. The vibration amplitude in all conditions was ± 4 mm (peak-to-peak displacement of the platform). Twenty minutes of rest were observed between conditions to allow for full recovery and to avoid the occurrence of fatigue. The NIRO-300 recordings were interrupted 30 s after the end of the randomized condition. Then, the subjects were allowed to move freely and, eventually, to sit on a chair. During the interval between the different conditions (rest period), the optical probes were not removed. During the 20 min of rest, the cardiac frequency was monitored by a pulse oximeter (N-200; Nellcor, Puritan Bennet, St. Louis, MO), with the sensor attached to the forehead. The cardiac frequency was completely recovered to the baseline values at the end of the rest period (data not shown).

Statistical Analysis

Data are reported as mean ± standard error of measurement of TOI and changes in tHb. A four-way analysis of variance (treatment (4) × time (5) × groups (2) × muscle (2)) was used to compare changes in TOI and in tHb. When a significant interaction was found, a repeated-measures ANOVA with Dunnet comparisons was used. Significance level was set at $P < 0.05$. The statistical analyses were performed with SPSS (Chicago, IL).

RESULTS

Some typical tracings of TOI and ΔtHb are shown in Figure 1. The statistical analysis revealed no differences between treatments in the baseline values of TOI, indicating that full recovery occurred between the treatments (Fig. 2). The statistical analysis revealed no significant differences in changes of TOI and tHb between groups (athletes and sedentary), suggesting that a short exposure to vibration in isometric squat position affects muscle oxygenation independently of the training level of the individual. Because no significant difference was identified between trained and sedentary individuals, all data were pooled and statistical analyses were performed on all 20 subjects participating in the study.

The data analysis revealed no significant treatment-by-time interactions in TOI or ΔtHb in VL and GM muscles. A significant main effect of time in TOI of VL as well as GM muscles was identified ($P < 0.001$; Fig. 2). The repeated-measures ANOVA with Dunnet comparisons revealed a significant decrease from baseline in TOI of VL in control conditions after 90 and 110 s ($P < 0.05$ and $P < 0.05$, respectively), a significant decrease from baseline in TOI in the 30-Hz condition after 110 s ($P < 0.01$), a significant increase in TOI after 30 s ($P < 0.05$) in the 40-Hz condition, and a significant increase in TOI after 30 s in the 50-Hz condition.

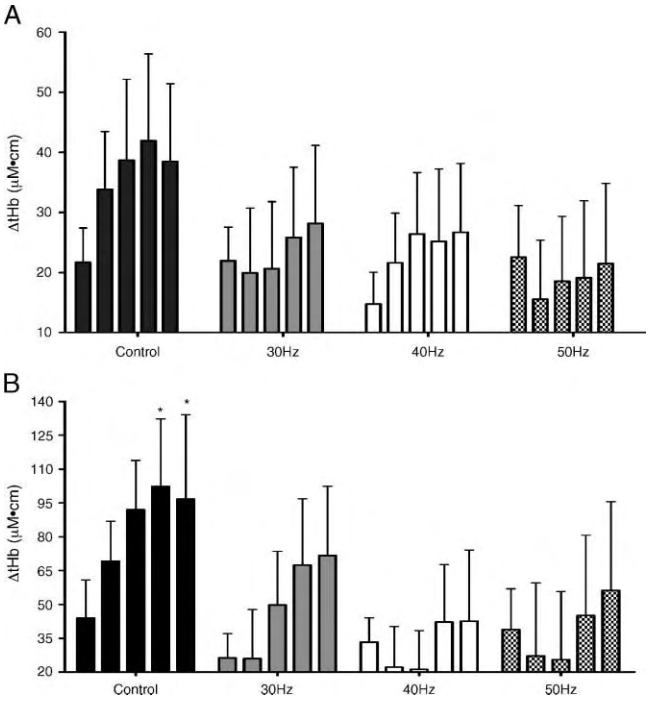

FIGURE 3—Concentration changes of tHb (μM·cm) of vastus lateralis (*A*) and gastrocnemius medialis (*B*) in different conditions over time. Data represent measurements at baseline (*first bar*), 30 s (*second bar*), 60 s (*third bar*), 90 s (*fourth bar*), and 110 s (*fifth bar*) after the beginning of the exercise bout. No significant difference was identified between baseline values. Means ± SEM (N = 20). * $P < 0.05$ from baseline.

GM TOI was found to be significantly lower than baseline at 60 s ($P < 0.05$), 90 s ($P < 0.01$), and 110 s ($P < 0.01$) in the control condition, and at 110 s ($P < 0.05$) in the 30-Hz condition. The results suggest, again, that vibration does not determine the same level of desaturation observed in the control condition. A significant main effect when comparing VL and GM TOI was identified ($P < 0.001$). The repeated measure revealed significant differences at all time points between GM and VL, suggesting different desaturation between plantar flexors and leg extensors during the task.

No significant difference was identified in ΔtHb over time in VL muscle. A significant increase for ΔtHb over time was identified in GM ($P < 0.001$; Fig. 3). The repeated-measures ANOVA with Dunnet comparisons revealed a significant increase in ΔtHb after 90 and 110 s only in the control conditions.

DISCUSSION

WBV training is becoming a popular form of exercise because it is relatively user friendly and does not require advanced instructions or complicated movements. However, few studies have been conducted on this novel exercise modality, and they all have shown contradicting results, particularly when acute responses were identified (7,8,29,30). Recent technological developments have made it possible to noninvasively study local muscle oxidative metabolism by means of NIRS (2,10,21). To the best of our knowledge, only one study thus far has been conducted using NIRS to investigate the oxygenation of lower-limb muscles during squatting exercise on a vibrating plate (34).

In the study by Yamada et al. (34), subjects performed 3 min of continuous dynamic squatting in the control and vibration conditions (15 Hz, ± 2.5-mm amplitude). The results of their study show that muscle-oxygenation levels of VL were significantly reduced after 90 s. Our results did not show any significant difference between the diverse vibration conditions and the control condition. Differences in exercise modality and vibration magnitude between the two studies could explain the disparity. In fact, Yamada et al. (34) exercised their subjects on a vibrating plate while performing dynamic squatting with a relatively large range of motion (from full extension to 60°), whereas our subjects performed a static squatting exercise. Different studies have shown that dynamic muscle contraction generated by electrical stimulation causes greater energy turnover and fatigue than static contractions performed at equal force levels (1,33). The same can hold true for WBV exercise. Furthermore, they used a similar amplitude (± 5 vs ± 4 mm in our study), a completely different frequency (15 vs 30 Hz in our study), and a different vibration device (alternating vibration side to side vs whole-plate oscillation). This suggests that WBV performed on a platform oscillating side to side can be more demanding for the lower limbs, because for brief periods during the oscillations, the body is almost entirely supported on one leg. It is also possible that the static position used in our study produced a very low level of muscle tension, and for this reason, significant differences probably would have been identified only after a much longer duration than 110 s. Furthermore, considering that Yamada et al. (34) used an incorrect statistical procedure (repeated Student's *t*-tests with no Bonferroni adjustment), it is possible that, even during dynamic squatting on a vibrating plate for short periods of time, there is no significant alteration of local oxidative metabolism, because of the low level of muscle stimulation generated by low-amplitude vibration.

As supportive evidence, recent work from Mileva et al. (20) has shown that even after four sets of eight repetitions with a load equal to 35 or 70% of the one-repetition maximum of leg extension on a vibrating leg-extension device (10-Hz vibration frequency; total duration approximately 80 s), no significant muscle-deoxygenation rate could be observed. Muscle-oxygenation level is affected by the balance between oxygen use and oxygen supply in human skeletal muscle. The lack of difference in muscle-oxygenation response between WBV exposure for 110 s and the control condition observed in our study seems to suggest that when low-amplitude vibration is applied for a

short duration, it is unlikely to alter local muscle metabolism significantly.

However, it is interesting to remark on the different effects of vibration on GM and VL over time. The results of our study show a significant desaturation in both GM and VL after 60 and 90 s of static exercise in the control condition. WBV exposure determined a significant desaturation only after 110 s in VL and GM. Considering also the significant increase in VL TOI% after 30 s at 40 and 50 Hz, and the lack of significant changes over time in GM, it seems that when vibration is superimposed to mild levels of muscle activation, some alterations in muscle metabolism and blood flow occur, delaying the hypothesized desaturation.

Previous studies have reported that muscular blood circulation in the calf and thigh was significantly increased after one bout of a 9-min WBV exercise on a tilting plate (26 Hz, 3-mm amplitude; (14)). The authors attributed the peripheral changes they observed to an exercise-induced widening of small vessels. Because TOI patterns reflect the balance between oxygen supply and demand in the target muscles, it seems feasible to suggest that the increased blood flow caused by vibration could provide an adequate oxygen supply, delaying the desaturation observed when no vibration is applied. Furthermore, considering that plantar vibration has been shown to increase supine blood flow in the calf measured by strain-gauge plethysmography by 20% (27), and that similar increases were observed by the same authors in peripheral lymphatic flow and venous drainage, it is possible that the relatively short duration of our vibration protocol might have actually delayed muscle desaturation through an improvement in muscle perfusion.

WBV exposure previously has been shown to determine higher levels of muscle activation by EMG in VL and GM muscles as compared with standing on the vibrating plate with no vibration delivered to the body (5,9). Many authors have suggested that this neuromuscular response is similar to the tonic vibration reflex (11) previously observed with direct applications of vibration to either muscles or tendons (5,6,9,13,26). The increased muscle activation observed in previous studies was hypothesized as able to produce a larger muscle desaturation. Furthermore, Rittweger et al. (25) have reported a higher oxygen uptake while performing dynamic squatting in vibration conditions as compared with nonvibration conditions, and a shorter time to exhaustion. Local muscle oxidative metabolism with vibration exercise may be sustained despite an increase in EMG activity that is possibly attributable to changes in blood flow and intramuscular pressure, and this may change with dynamic and static WBV exercise. In this light, a recent study from Vedsted et al. (32) shows no differences in the reduction of muscle-oxygenation tension between dynamic and static muscle contraction despite a marked difference in EMG and mechanomyography. The authors suggest that the lower intramuscular pressure measured during dynamic exercise was responsible for the discrepancy between muscle activation and oxygenation. No study has been conducted so far on intramuscular pressure during vibration exercise, but other mechanisms such as a reduction in blood viscosity (14), an increase in total peripheral resistance and opening of more capillaries (19), and an enhanced peripheral blood and lymphatic flow (27) could be responsible for maintaining oxygen supply despite an increase in motor unit recruitment.

The results of our study seem to suggest that short-duration WBV performed in static conditions with small amplitudes does not cause the same level of muscle desaturation that is observed from squatting without vibration, and could also delay the desaturation observed in similar conditions without vibration. Considering the lack of desaturation observed in our study and the possibility for vibration to increase blood flow in the exercising muscles, we suggest that WBV exercises with a total duration shorter than 2 min could be used as a warm-up procedure in athletes. Needless to say, more studies are needed to elucidate the vascular mechanisms and to evaluate what happens when long-duration vibration exercise is performed, and also whether there is any value to using vibration to increase muscle perfusion.

At the moment, it is not clear whether WBV represents a training stimulus strong enough to influence force-generating capacity and/or muscle metabolism (6). However, because many manufacturers are advertising the use of vibration as an exercise tool capable of positively influencing the overall fitness of an individual, it is clear that more well-controlled studies are needed to provide safe and effective guidelines for its use. Considering that our study and few other previous studies have shown that there are no potential limitations of using NIRS to analyze muscle and cerebral oxygenation in WBV research (16–18), and considering the successful application of NIRS to sports science research (21,22), future studies might be carried out employing this technique to improve the understanding of muscle oxidative metabolism in response to different vibration protocols.

In conclusion, this study has shown that WBV exercise with frequencies of 30, 40, and 50 Hz and small amplitudes does not affect muscle oxygenation of VL and GM muscles to a higher degree than a nonvibration condition. More studies are needed to elucidate the physiological responses to WBV exercise, with particular reference to the interactions between neuromuscular and metabolic demands of this novel and promising exercise intervention.

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Near-infrared spectroscopy/imaging for monitoring muscle oxygenation and oxidative metabolism in healthy and diseased humans

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Abstract. Near-infrared spectroscopy (NIRS) was initiated in 1977 by Jobsis as a simple, noninvasive method for measuring the presence of oxygen in muscle and other tissues *in vivo*. This review honoring Jobsis highlights the progress that has been made in developing and adapting NIRS and NIR imaging (NIRI) technologies for evaluating skeletal muscle O_2 dynamics and oxidative energy metabolism. Development of NIRS/NIRI technologies has included novel approaches to quantification of the signal, as well as the addition of multiple source detector pairs for imaging. Adaptation of NIRS technology has focused on the validity and reliability of NIRS measurements. NIRS measurements have been extended to resting, ischemic, localized exercise, and whole body exercise conditions. In addition, NIRS technology has been applied to the study of a number of chronic health conditions, including patients with chronic heart failure, peripheral vascular disease, chronic obstructive pulmonary disease, varying muscle diseases, spinal cord injury, and renal failure. As NIRS technology continues to evolve, the study of skeletal muscle function with NIRS first illuminated by Jobsis continues to be bright. [DOI: 10.1117/1.2805437]

Keywords: muscle; near-infrared spectroscopy; near-infrared imaging; oximetry; muscle oxygenation; muscle metabolism; exercise.

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1 Introduction

The purpose of this review article is to highlight the most recent noninvasive near-infrared spectroscopy (NIRS) and NIR imaging (NIRI) studies aimed at evaluating skeletal muscle O_2 dynamics and oxidative energy metabolism, in light of historical studies that initiated this important and still developing technology. A brief background on the methodologies and approaches are presented, along with examples of how these methodologies and approaches have been used to better understand muscle function in both health and disease. A number of detailed review articles have previously described some aspects of the use of NIRS in muscle exercise pathophysiology.[1–6] A number of recent detailed review articles describing the principles, limitations, and applications of NIRS have appeared in the literature.[7–13]

The primary reason NIRS technology is so valuable for the study of skeletal muscle is the strong dependence of skeletal muscle on oxidative metabolism. During exercise, skeletal muscle O_2 consumption (VO_2) can rise 50 fold with subsequent increases in O_2 delivery (DO_2) of up to 10 fold. Because of this, pathological impairments of either VO_2 or DO_2 will severely limit exercise and thus functional capacity. The net oxidative energy pathway in muscles can be described by the following equation:

$$3ADP + 3Pi + NADH + H^+ + 1/2O_2 = 3ATP + NAD^+ + H_2O,$$

where ADP is the adenosine diphosphate, Pi is the inorganic phosphate, NADH is the reduced nicotinamide adenine dinucleotide, ATP is the adenosine triphosphate, and NAD^+ is the nicotinamide adenine dinucleotide.

Early developments of dual wavelength spectrophotometers set the stage for the development of NIRS *in vivo*.

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In-vitro studies by Chance[14] and Chance and Connelly[14,15] showed that the newly discovered mitochondrial signal of NADH responded to electrical muscle stimulation in a fraction of a second, even at less than 10 °C, coupling muscle contraction to mitochondrial function. Jobsis,[16] together with Ramirez, Weber, and others, followed up with *in-vitro* optical studies of the bioenergetics of organs, heart, liver, brain, and adrenal and salt glands. Jobsis focused especially on skeletal muscle and greatly improved the technique when he moved to Duke University, where he performed a series of outstanding muscle physiology studies. These studies bridged the gap between bioenergetics and physiology and exploiting the relationship of the previous equation, that DO_2 in combination with the provision of other chemical substances, are the major key players for mitochondrial VO_2 or muscle oxidative metabolism.

Prior to the development of NIRS, skeletal muscle oxygenation (a balance between DO_2 and VO_2) and metabolism were evaluated in humans by conventional analytical biochemistry invasive methods after obtaining biopsy specimens. The strength of the biopsy approach is that a wide array of metabolites can be measured for studying specific metabolic pathways. The disadvantage of the biopsy technique is that biopsies cannot be easily performed during muscle contractions and have limited repeatability, thus limiting the ability to obtain time course data. To overcome these disadvantages, magnetic resonance spectroscopy (MRS)[17] was developed to measure *in-vivo* free (active) forms of phosphate compounds and intracellular pH, as well as intramyocelluar myoglobin (Mb) levels. MRS remains a valuable technology for the measurement of *in-vivo* energy status, oxygen saturations, and blood flow, but its high cost, large size, and limited availability reduce the usefulness of this method.

The continuing development of NIRS technology eventually leads to the study of intact organisms. The extension of the optical technology to wider spectral and time regions was epitomized by the elegant instrument of Lubbers and Thiefs (rapid spectroscopy) and by the work of Kramer and others who explored the NIR region, noting that the NIR light penetrated the hand, setting the stage for Jobsis' brilliant discovery[18] that the skull is not a barrier to NIR light, as recounted in his own words as follows.[19] Very briefly, on 28 December 1976 his family enjoyed a grilled chuck roast with a part of the shoulder blade of the steer—a flat piece of bone 3 or 4 mm thick. When his son Paul held the object up against the light, Jobsis noticed that the shadow of a finger could easily be seen in the diffused red light coming through the bone. Then he speculated that NIR light at longer wavelengths would penetrate the human skull and provide access to the tissue. His extraordinary scientific exploration started at a table with his family over a dinner with a very American cut of beef (he used this expression himself). In fact, the properties of the skull to enhance the NIR signals was later quantified in studies of the cat brain, where the removal of the skull shortened the NIR photon migration pathlength. Thus Jobsis' discovery opened the very active field of NIR studies of brain and stimulated the studies of skeletal muscle in human subjects, a tradition carried on elegantly by his son, Paul Jobsis.

In the intervening years, numerous studies have developed and refined the NIRS approach of studying skeletal muscle *in vivo*. They have experimented with the wavelengths and arrangement of light sources and detectors, as well as the portability of the devices.[20–26] Equally variable have been the experimental approaches and subject populations used to take advantage of NIRS technologies.

2 Methodological Issues Related to the Noninvasive Evaluation of Muscle Oxygenation and Metabolism Using Near-Infrared Spectroscopy

The first issue related to the use of optics to study skeletal muscle *in vivo* is the choice of wavelengths. Wavelengths ranging from 700 to 3000 nm show much less scattering and thus better penetration into biological tissue than visible light. However, light absorption by water limits the tissue penetration above 900-nm wavelength, leaving the 650- to 900-nm range. The major absorbing compounds of this wavelength region are intravascular hemoglobin (Hb), intramuscular Mb, skin melanin, and mitochondrial cytochrome c oxidase.[18] NIRS measurements rely on O_2 dependent absorption changes that occur in the theme, and copper containing compounds.

The most common, commercially available NIRS devices use single-distance continuous-wave light (NIR_{SDCWS}). To calculate the changes in oxy-Hb/Mb, deoxy-Hb/Mb, or total-Hb/Mb, the equation of a two- or multiple-wavelength method can be applied according to the following Beer-Lambert law.

$$\Delta OD = -\log_c(I/I_0) = \varepsilon PL\Delta[C], \tag{1}$$

$$\Delta[C] = \Delta OD/\varepsilon PL, \tag{2}$$

where ε is the extinction coefficient $(OD/\mathrm{cm/mM})$ (=constant), PL is the pathlength, $[C]$ is the concentration of absorber (mM), I is the detected light intensity, I_0 is the incident light intensity, and OD is the optical density.

The major advantage of NIR_{SDCWS} devices is in their simple design. The invention of laser diodes and LED light sources in the NIR region, and of Si diode integrated chip detectors, has made possible inexpensive and wearable NIR detectors of muscle function.[23,27] A major limitation to the NIR_{SDCWS} devices is that they currently provide only the relative values of tissue oxygenation. The main reason for a lack of quantification by NIR_{SDCWS} is the unknown path of NIR light through biological tissues. The pathlength of light will vary due to variations in tissue composition (adipose tissue versus muscle, discussed later), blood volume (can increase or decrease heme concentrations over time), and muscle shape (altered during muscle contractions).

The pathlength of NIR light can be measured using other optical approaches, including time-resolved spectroscopy (NIR_{TRS})[20,24,28] and phase modulation spectroscopy (NIR_{PMS}).[29–31] NIR_{TRS} uses expensive single photon detectors to measure the time the light spends in the tissue, while NIR_{PMS} uses the change in phase of coherent light to determine the time the light spends in the tissue. These approaches provide absolute values of oxygenated and deoxygenated Hb/Mb and Hb/Mb O_2 saturation (SO_2) in the skeletal muscle. Spatially resolved NIR_{SRCWS} (NIR_{SRCWS})[32,33] provides relative changes in Hb/Mb and absolute values of SO_2. NIR_{SRCWS} using multiple light sources coupled to one detec-

tor solves multiple equations for pathlength. These approaches have been used in the study for skeletal muscle oxygenation and metabolism, and technological improvements will make these approaches more practical in the future.

What is known about the pattern of the light path from the light source to the detector is that it follows a banana-shaped curve, in which the penetration depth into the tissue is approximately equal to half the distance between the light source and the detector.[23] If light source-detector separation was set to be 3 cm, penetration depth would be 1 to 2 cm and the measured volume would be approximately 4 cm^3.[20] Usually, light source-detector distance ranges from 12 to 50 mm.[34–37] Subcutaneous adipose tissue thickness greatly influences the light pathlength and makes it difficult to quantify tissue oxygenation, especially in the measurements of muscle oxygenation from the skin surface.[11,32,38–40] The influence of adipose tissue thickness on the NIR spectra of human muscle was studied by Monte Carlo simulations of a two-layer structure and with phantom experiments.[41] The study suggested that subject-to-subject variation in the fat optical coefficients and thickness can be ignored if the fat thickness is less than 5 mm when the source-detector separation is 40 mm. Other studies indicated that for a fat thickness of 5 mm, the signal intensity reduces approximately by 0.2 (80% signal of zero fat thickness) with a light source-detector separation being 30 to 40 mm, and further reduces by 0.3 to 0.6 with a separation of 15 to 20 mm, respectively.[39,42] The correction curve is presented for the influence of an adipose tissue thickness ranging from 0 to 15 mm with a source-detector separation being 15 to 40 mm.[39,42,43] The curve was obtained from the results of both Monte Carlo simulation and *in-vivo* experiments.[39,42]

$$S = \exp[-(h/A_1)^2] - A_2 G(\alpha,\beta), \tag{3}$$

where S is normalized measurement sensitivity, h is adipose tissue thickness, $G(\alpha,\beta)$ is a gamma distribution, and the constants A_1, A_2, α, and β at a light source-detector separation of 15 mm are 6.9, 1.15, 7.86, and 0.80, respectively. Considering that the value of S is determined in practice only by h, then the corrected values are obtained by dividing the measured values by S. A qualitative description of reduced NIRS signal intensity by a larger adipose tissue thickness was illustrated in a previous review.[11]

In NIR_{SDCWS} measurements, there is the assumption that pathlength does not show any significant change during exercise, recovery, and other intervention periods, otherwise the values obtained are either underestimated or overestimated, as is shown in Eqs. (1) and (2). During and after the end of arterial occlusion, the changes in pathlength of the forearm muscle ranged from −8.3 to −2.1% at 780 nm, and from −2.2 to 0.74% at 830 nm.[28] Changes in pathlength were less than 10% during arterial occlusion with maximum voluntary contraction (MVC).[24] Differential pathlength factor (DPF) in the thigh muscle decreased slightly, but significantly from baseline (DPF at 690 nm=5.22; DPF at 830 nm=4.49 on average) to peak cycle exercise (DPF at 690 nm=4.88; DPF at 830 nm=4.27 on average) (−6.5% at 690 nm and −4.9% at 830 nm).[44] For an accurate evaluation of muscle oxygenation during arterial occlusion, exercise, and recovery, changes in pathlength should be extensively examined in a wide range of exercise mode/intensity and among varying subjects.

A technological limitation to the use of NIRS is the similar absorption spectra for Hb and Mb. This makes it difficult to distinguish between the two by the optical properties alone. A number of studies have taken advantage of ^{1}H-magnetic resonance spectroscopy (^{1}H-MRS) measurements of Mb[45–47] to estimate the relative contributions of Hb and Mb to the total NIR signal. Combined ^{1}H-MRS and NIRS studies of canine muscle during exercise in normoxic and hypoxic conditions concluded that the NIR signal came 65% from Hb and 35% from Mb.[48] As canine muscle contains more Mb than human muscle, this suggests more than 65% of the signal from human muscle comes from Hb during normoxic conditions. During ischemia, MbO_2 levels appear to decline only after 4 min,[49] while NIRS measured oxygen signals decline almost immediately and reach near maximal levels at 4 min.[50,51] From this, Ferrari, Mottola, and Quaresima suggested that NIRS-measured SO_2 values would reflect predominantly (at least 80%) HbO_2 saturation during exercise in humans.[2] A simulation experiment based on combined measurements of ^{1}H-MRS and NIRS concluded that the overall NIR signal would be greater than ~50% Hb.[52] In contrast, Tran et al. reported a greater contribution of Mb signal than Hb to the overall NIR signals in a study using ^{1}H-MRS.[53] The differing conclusions from these studies highlight the need for additional studies to clarify not only the issue of the contribution of Mb to the NIR signal, but also the kinetics and the amount of Mb desaturation during exercises under different conditions.[54] To acknowledge this concern, many studies present NIRS-measured oxygen saturation as HbO_2/MbO_2. For simplicity, this work presents oxygenated Hb/Mb expressed as O_2Hb, deoxygenated Hb/Mb as HHb, and total Hb/Mb as tHb.

Recent advances in NIRS technology have included the addition of multiple-source detector pairs to "image" skeletal muscle. This has been done to take advantage of classical studies that have shown regional differences in skeletal muscle oxygenation and metabolism in different locations within a muscle.[55] Several multiple-channel NIR imaging systems have been developed to detect regional differences in muscle oxygenation.[43,56–62] By simultaneously collecting data from multiple muscle regions, these devices avoid the variability caused by position dependent differences in muscle oxygenation that plague all single location measurements. Imaging devices also allow the study of regional differences in how skeletal muscle responds to exercise. The challenge of NIR imaging systems is how to evaluate the much greater amounts of information that are collected. The application of NIR imaging technology to the study of exercising muscles is illustrated in Fig. 1.

3 Types of Measurements Made on Skeletal Muscle Using Near-Infrared Spectroscopy

3.1 *Muscle Oxygenation*

The most common measurement made with NIRS is muscle oxygenation, or the fraction of Hb that is bound to oxygen. Relative changes in O_2Hb, HHb, and tHb are also reported. Because of the difficulty in quantifying NIR_{SDCWS}, muscle

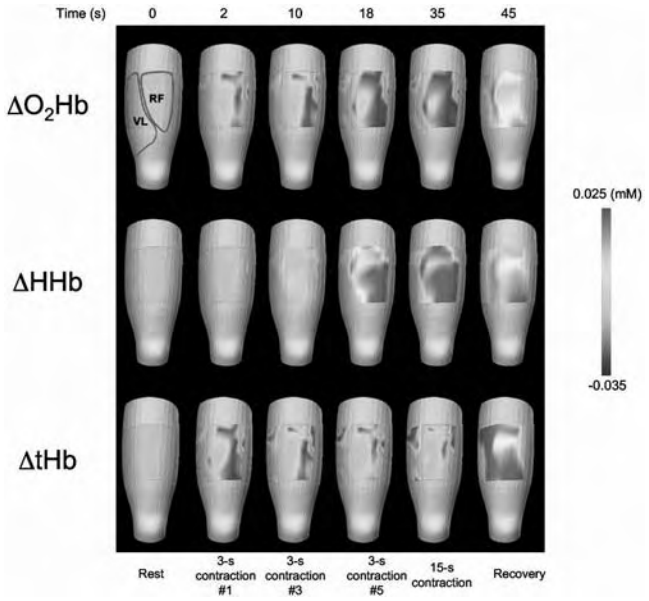

Fig. 1 Near-infrared (NIR) images from the quadriceps muscles before, during, and after intermittent isometric knee-extension exercise (IKEx). The NIR imaging system had 200 channels that covered a 45 cm×15 cm^2 area. The top left image indicates the approximate location of specific muscles. Contractions 1, 3, and 5 indicate images obtained during a series of 3-s duration contractions at 50% of maximum voluntary contraction (MVC), with one second rest in between. The 15-s contraction shows data at the end of a continuous 15-s MVC. The recovery image was obtained 10 s after the last contraction. These images demonstrate the spatial differences seen within muscles during exercise and recovery. The detailed description of the system and the source-detector arrangement are described in a previous paper.[42] O_2Hb is oxygenated hemoglobin and myoglobin; HHb is deoxygenated hemoglobin and myoglobin; and tHb is total hemoglobin and myoglobin.

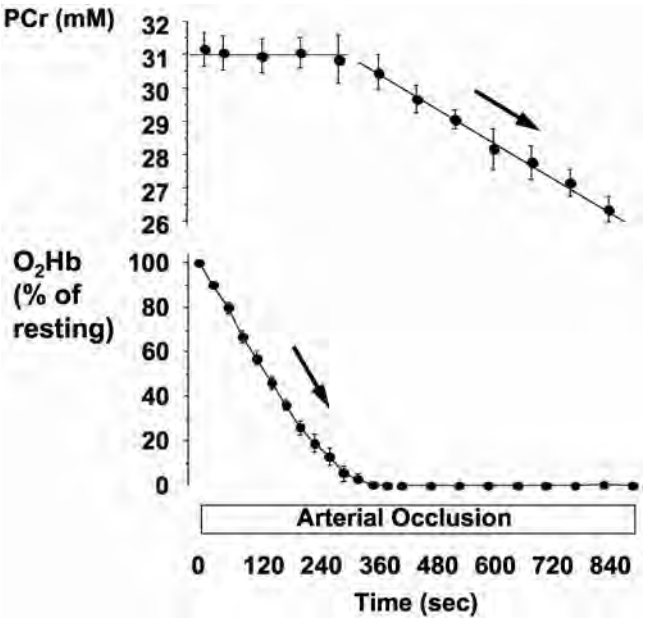

Fig. 2 An example of how to quantitatively calibrate the NIRS signal. Changes in phosphocreatine (PCr) and oxygenated hemoglobin and myoglobin (O_2Hb) in the forearm muscle were measured during 15 min of arterial occlusion by magnetic resonance spectroscopy and near-infrared spectroscopy. The detailed description of the methods is described in a previous paper.[50] Copyright (c) The American Physiological Society. Reproduced by permission of the publisher.

oxygenation is usually expressed in arbitrary units [optical density (OD)], μM×cm or μM (using DPF×source-detector spacing) for O_2Hb, HHb, and tHb. A wide variety of skeletal muscles have been evaluated using this approach, including the back extensor muscles,[63–66] gluteus maximus,[67,68] vastus lateralis,[44,69–72] vastus medialis,[70] rectus femoris,[70,71] biceps femoris,[68] calf,[72–76] dorsiflexors,[77,78] respiratory muscles,[79] trapezius,[34,80,81] deltoid,[82] triceps,[83,84] biceps brachii,[85,86] extensor carpi radialis brevis,[87] forearm flexors,[88] thenar muscles,[89] brachioradialis,[90] and masseter muscle.[91] Some researchers have used NIRS at multiple sites, such as vastus lateralis versus serratus anterior[92] and vastus lateralis versus rectus femoris,[73,93] to obtain a clearer understanding of physiological changes in the various tissues during exercise. Most studies have evaluated muscle oxygenation changes during aerobic types of exercise, but several studies have also examined high intensity[94,95] or resistance types of exercise.[96,97] While most of the information obtained pertains to muscle oxygenation, there are several studies that have documented the changes in tHb during exercise.[98,99] While most studies have evaluated muscle oxygenation changes of the exercising limb some researchers have studied inactive limb muscle oxygenation during dynamic exercise of the other limb.[83,100]

A simple and common method of calibrating NIR_{SDCWS} signals is to use the range of muscle oxygenation caused by arterial occlusion followed by reactive hyperemia.[23] The arterial occlusion method is based on the assumptions that 5 to 6 min of ischemia will result in the complete disappearance of O_2Hb, and that the reactive hyperemia after occlusion will almost completely eliminate HHb. So while O_2Hb and HHb in arbitrary units may vary between measurement sites and individuals, the occlusion calibration will account for these changes. Quantitative calibration of NIR_{SDCWS} signal is possible in a combination with MRS measurement by applying a 15-min ischemia to the muscles (Fig. 2).[50] The rate of decline of muscle O_2Hb during ischemia can be compared with that of muscle PCr in mM per second or a conversion to mMO_2 per second. As a result, this method provides quantitative values of both muscle oxygen store and muscle VO_2 (mVO_2).

Several studies reported the validity of NIRS-measured O_2Hb and HHb signals in animals and humans under steady-state conditions. Wilson et al. demonstrated a linear relationship between NIRS measurements and venous SO_2 (SvO_2) using an *in-situ* canine muscle preparation.[101] Shiga et al. found a strong linear relationship ($r=0.934$; $P=0.01$) between the change in the HHb signal and arterial SO_2 (SaO_2) in a hypoxic-dog model.[27] Mancini et al. found muscle oxygenation and SvO_2 of human forearm muscles to be closely related during exercise.[102] They also demonstrated that muscle oxygenation level decreased with an intravascular norepinephrine administration, and increased with a vasodilator (nitroprusside) administration. Muscle deoxygenation was quantified during resting arterial occlusion in human skeletal

muscles using NIR_{TRS}. In a study using NIR_{TRS}, muscle deoxygenation (SO_2-TRS) during arterial occlusion was compared to SvO_2 and interstitial partial pressure ($PintO_2$).[28] At the end of occlusion, SO_2-TRS (24.1±5.6%) agreed with SvO_2 (26.2±6.4); and $PintO_2$ (14.7±1.0 Torr) agreed with PvO_2 (17.3±2.2 Torr). Thus, there are several studies that have validated NIRS measurements relative to established invasive methods.

However, there have been a number of studies that have failed to validate NIRS measurements. Both Costes et al. and MacDonald et al. reported discrepancies between the NIR signal of the vastus lateralis and the femoral SvO_2 during a cycling exercise under normoxic conditions, while a correlation between the two parameters was reported under hypoxic conditions.[103,104] A possible explanation for the discrepancies is that the NIRS signal contains information of arterioles, capillaries, venules, and intracellular Mb, and that the O_2 gradient from an arteriole to venule is large in normoxic conditions, such that variations in blood volume from arteriole to venule could alter the NIRS signal without change in venous oxygen signals.[11] The lower oxygen levels during hypoxic conditions would reduce this effect. However, further research is needed to clarify NIRS signal contribution from arterioles, capillaries, venules, and Mb under varying oxygenation status and in varying measurement protocols.

Recently, good association was found between regional quadriceps oxygenation at three different measurement sites and SvO_2 during one-legged dynamic knee extension exercise, even under normoxic conditions.[93] It may be that by using multiple measuring locations, the NIRS signal shows better agreement with the entire extremities SvO_2. A good relationship was also found between vastus lateralis oxygenation and femoral arterio-venous O_2 difference (a-vO_2D) during one-legged dynamic knee extension exercise under normoxic as well as hypoxic and hyperoxic conditions.[7] Thus, it is broadly accepted that the NIRS-oxygenation/deoxygenation signal has considerable agreement with the changes in SvO_2 and/or a-vO_2D under varying oxygenation status of the human muscles.

In nonsteady-state conditions, such as at the onset of exercise and in recovery after exercise, changes in muscle oxygenation determined by NIRS provide relevant information on muscle oxidative function. The rate of deoxygenation at the onset of exercise,[105] recovery time of muscle reoxygenation after submaximal to maximal exercise,[23,106–110] and the rate of reoxygenation after brief high intensity MVC exercise[111] are among indicators for evaluating muscle oxidative capacity. These studies have reported good agreement between faster PCr recovery kinetics and faster oxygenation kinetics measured with NIRS. A different outcome was obtained after maximal short-duration isometric exercise, where higher oxidative capacity muscle (faster PCr kinetics) was inversely related to the rate of muscle reoxygenation after the exercise.[111] The result of this study was attributed to the hypothesis that muscle reoxygenation rate after this type of short high intensity exercise may be influenced more by VO_2 than by DO_2, when O_2 demand is still high and O_2 supply is not fully activated.

3.2 *Muscle Oxygen Consumption and Muscle Blood Flow*

3.2.1 *Transient arterial occlusion method*

Evaluation of muscle energy metabolism using NIRS is difficult, because the measured oxygenation levels do not specifically reflect mVO_2; rather, they reflect the balance between muscle DO_2 in relation to mVO_2. To dissociate mVO_2 from DO_2 using NIRS, two approaches have been used; the transient arterial occlusion method and the venous occlusion method. The transient arterial occlusion uses 10 to 30 s of arterial occlusion provided by a pneumatic tourniquet to interrupt DO_2 to the monitored muscle.[26,50,112–116] Measurements of resting mVO_2 using this approach in the forearm muscles of young health males was found to have a small amount of variability (23.0±1.2%/min),[50] and to be consistent between studies by different investigators.[51] NIR_{TRS} has also been used to measure resting mVO_2, providing results in absolute units (0.82 $\mu M\,s^{-1}$).[28] The transient arterial occlusion method has also been used to measure forearm muscle metabolism during exercise.[50] Varying moderate intensities were used to provide a range of mVO_2 levels, and resulting mVO_2 values were compared to simultaneous MRS measurements of phosphorus metabolities. A significant correlation was found between NIRS measured mVO_2 and MRS measured PCr ($r^2=0.99$, $p<0.01$), and ADP ($r^2=0.98$, $p<0.01$) concentrations. The linear relationships between exercise intensity and the NIRS and MRS measured indicators of mVO_2 supports both the thermodynamic[117,118] and kinetic[119] regulation models of mitochondrial respiration in skeletal muscle.

Validation of NIRS measurements of mVO_2 have been performed using MRS measurements of PCr kinetics, as well as measurements of whole body VO_2 performed by measuring expired gas concentrations. NIRS measured mVO_2 using the transient arterial occlusion method was significantly related to the rate of PCr recovery, a biochemical process of ATP resynthesis via oxidative phosphorylation after muscle contractions ($r=0.965$).[115] Repeated transient arterial occlusions after exercise can provide successive mVO_2 values, information that is basically similar to that determined from PCr recovery kinetics,[117,120–123] an indicator for muscle oxidative capacity. Thus, the time constant for mVO_2 recovery is an indicator for evaluating muscle oxidative capacity (Fig. 3).[124]

NIRS measured muscle oxygenation was also compared to pulmonary O_2 consumption (pVO_2) in 16 healthy males during an exercise tolerance test on a cycle ergometer.[125] A significant positive correlation was observed between HHb and pVO_2 ($r=0.893$ to 0.986), and a negative correlation between pVO_2 and O_2Hb ($r=0.726$ to 0.978). There are several reports indicating that: 1. oxygenation of forearm flexor muscles closely reflected the exercise intensity and the metabolic rate determined by MRS during exercise[112,126,127] and during recovery,[112,126] and 2. that muscle oxygenation level (percent of arterial occlusion) showed a linear relationship with mVO_2, though in a limited range ($3.2<mVO_2<13.3$ fold of resting), during exercise (Fig. 4)[128] and recovery. These studies suggest that the initial rate of muscle deoxygenation during transient arterial occlusion is a direct measure of mVO_2, and that muscle oxygenation level itself is a reflection of mVO_2.

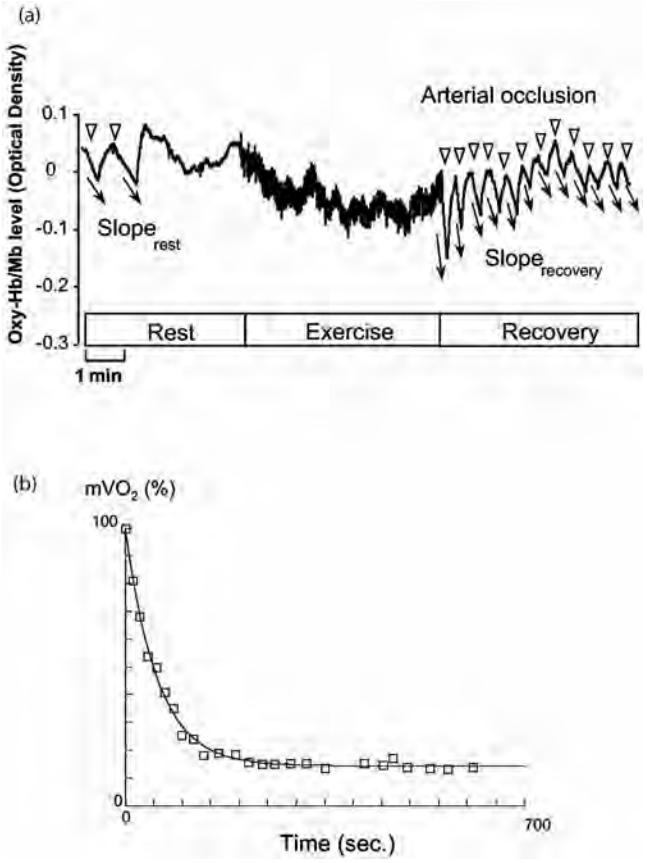

Fig. 3 An example of the repeated transient arterial occlusion method of measuring muscle oxygen consumption (mVO_2). (a) Transient arterial occlusion was applied at rest and then at various times after exercise. As highlighted by the arrows, the slope of desaturation of the O_2Hb signal was less rapid during rest than after exercise, consistent with the higher rates of mVO_2 after exercise. (b) Calculated mVO_2 values after exercise show an exponential decline consistent with changes in phosphocreatine levels from magnetic resonance spectroscopy.

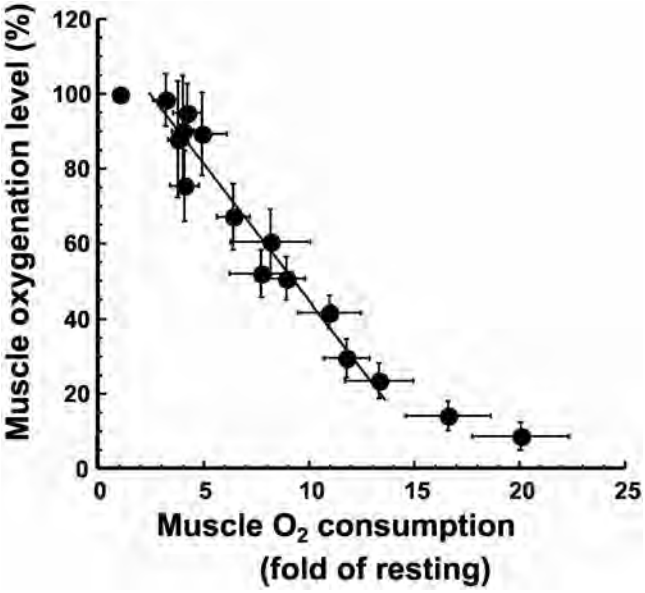

Fig. 4 Relationship between muscle oxygenation level and muscle oxygen consumption (mVO_2) in the calf muscle during incremental intermittent isometric plantar flexion exercise (IPFx). Changes in muscle oxygenation level and mVO_2 in the calf muscle were measured during IPFx (6-s contraction/4-s relaxation). The subjects performed IPFx, starting at 10% of maximum contraction (MVC) until exhaustion. The value of mVO_2 was measured by transient arterial occlusion method. Muscle oxygenation level was normalized to the overall changes during ischemia. The fall in oxygenation level reflected increases in exercise intensity, and the NIRS measurements demonstrate the increased muscle oxygen consumption results from increased exercise intensity. There is a linear relationship between muscle oxygenation level and mVO_2 in a certain range ($3.2 < mVO_2 < 13.3$, determined by the best fit by a piece-wise linear regression model) during this type of exercise.

3.2.2 *Venous occlusion method*

The venous occlusion method can be used to determine mVO_2 and muscle blood flow (mBF) by applying the same technique used in conventional venous plethysmography.[114,129] Briefly, transiently applied low cuff pressures (typically 60 mm Hg) occlude venous outflow while minimally obstructing arterial inflow. The increase in deoxygenated blood is then used to calculate mVO_2 and mBF. NIRS-determined measures of mBF and mVO_2 by the venous occlusion method have been shown to agree with traditional measurements using plethysmography[114,129] and the Fick method.[114,116,129] The advantage of NIRS is that it is capable of providing information about mVO_2 and mBF in a local area of a muscle. One of the difficulties in validating NIRS studies are that conventional methods such as plethysmograpy, Doppler sonography, and the Fick method cannot provide localized measurements. The disadvantage of using the venous occlusion method as well as the transient arterial occlusion method is that exercise must be interrupted to make the measurements. The assumption is that both mVO_2 and the mBF measured immediately after the end of the exercise reflect the mVO_2 and mBF values during exercise.

3.2.3 *Other methods for measuring muscle oxygen consumption and blood flow with near-infrared spectroscopy*

A variation of the transient arterial occlusion method is to take advantage of the ischemia produced during high intensity isometric muscle contractions. Contraction-induced compression and crimping of blood vessels produces ischemia without the need for externally applied arterial occlusion. Using the ischemic exercise method, the rate of deoxygenation measured at the onset of intermittent (5-s contraction/5-s relaxation) isometric exercise at 50% MVC followed an exponential time course with a time constant of 42.0 ± 12.5 s (mean ±SD).[126] The NIRS measurements were in good agreement with the time constant of the decrease in PCr measured simultaneously (48.2 ± 10.2 s). Muscle blood flow can be quantitatively, though invasively, measured using NIRS with an indocyanine green (ICG) dye infusion.[130] More recently, NIR diffuse correlation spectroscopy (NIR_{DCS}) and diffuse reflectance spectroscopy (NIR_{DRS}) have been developed for measuring changes in muscle oxygenation and mBF, and are able to compute mVO_2.[131] NIR_{DRS} methodology uses the unique approach of monitoring mBF by measuring the optical phase

shift caused by moving blood cells. NIR_{DCS} methodology is able to monitor tissue optical properties, such as the absorption coefficient (μa) and reduced scattering coefficient ($\mu s'$), without applying arterial occlusion or venous occlusion to a limb. The ability to measure mVO_2 and the mBF without occlusion is a strong potential advantage, although an extensive validation study in humans is needed before broadly applying this technique to practical and clinical use.

3.3 *Other Indicators*

NIRS is able to provide other indicators than those mentioned. SvO_2 is estimated by measuring changes in O_2Hb over tHb during venous occlusion,[132] and by the method based on the respiration-induced oscillations of the NIR absorption in tissues, named spiroximetry.[30] A method for measuring the compliance of the microvascular superficial venous system of the limb using NIRS has been developed.[133] More indicators have been proposed and used specifically in clinical science, which is addressed in the following section.

4 Near-Infrared Spectroscopy in Combination with Other Methodologies

NIRS has been used in combination with a large variety of other invasive and noninvasive methodologies to evaluate physiological and pathological changes in peripheral muscle and/or whole body metabolism. The noninvasive methods that have been used in combination with NIRS in recent studies (2000 to 2006), include: MRS,[88,128,134,135] magnetic resonance imaging (MRI),[78,135–138] electromyography (EMG),[68,71,136,139–143] ultrasound sonography and Doppler,[35,144–147] plethysmography,[76,148] respiratory gas analysis,[98,149–159] transcutaneous oxygen pressure measurement,[160–162] laser Doppler skin blood flow and skin oxygenation measurements,[163–167] pulse oximetry,[152,168] mechanomyography,[66,169,170] muscle force and power measurements,[78,94,171–173] muscle fatigue index measurements,[77] ankle-brachial (blood pressure) index measurements,[74,75] and sweat response measurements.[174] The invasive methods that have been used in combination with NIRS in recent studies include: blood gas measurement,[93,175,176] muscle sympathetic activity measurement,[145] blood biochemical measurements (including lactate),[34,69,98,177] muscle biopsy,[34,150,178] intramuscular pressure measurements,[169,179] and positron emission tomography.[180,181] Among them, substantial numbers of studies have been conducted to examine the relationship between respiratory gas indicators and NIRS indicators.[151–155,157] Recently, there have been several studies to evaluate oxygen uptake kinetics during exercise using NIRS indicators such as HHb delay, HHb mean response time, and HHb time constant at the onset of exercise.[35,149,150,156]

5 Examples of the Use of Near-Infrared Spectroscopy in the Assessment of Human Skeletal Muscle Function

5.1 *Healthy Subjects*

A number of different studies have evaluated the influence of increased activity as well as decreased activity on muscle function using NIRS. Costes et al. examined whether exercise-training-induced adaptations in muscles can be determined by NIRS.[182] Training did not change the pattern of muscle oxygenation, though a significant relationship was found between blood lactate and muscle oxygenation at the end of exercise. Ichimura et al. examined the interaction of age and habitual physical activity on recovery time of muscle oxygenation following maximal cycling exercise.[107] They found that NIRS measured recovery time was prolonged with aging, regardless of habitual physical activity levels. However, habitual physical activity may prevent the age-related prolongation in the recovery time of muscle oxygenation after maximal cycling exercise. Changes in skeletal muscle oxidative function were measured by NIRS in immobilized forearm muscles, evaluating the preventive effect of the endurance training protocol on deterioration of skeletal muscle.[124] Muscle oxidative function was determined by the time constant for the recovery of mVO_2, applying repeated transient arterial occlusions after exercise. This study suggested that NIRS can be used clinically for noninvasive monitoring of deconditioning and reconditioning of skeletal muscle oxidative functions.

NIRS has also been used for evaluating acute and chronic (training) effects of exercise on muscle oxygenation for athletes such as endurance cyclists,[13,149,152,183–186] sprinters,[187] endurance runners,[152,187] swimmers,[188] triathletes,[25,152,183] soccer players,[189] resistance-trained athletes,[190] skaters,[191] and cross-country skiers.[192] What has emerged from these studies is that several NIRS derived indicators can be useful for evaluating the effect of exercise training on muscle metabolism. These include the recovery time for muscle reoxygenation and the time constant for mVO_2 recovery after exercise in healthy subjects. However, most of the studies on the influence of training have been performed using cross-sectional study design, and there is a need for more longitudinal studies on exercise training that use NIRS measurements. Further, if NIRS is to be used in examining the alteration of intervention for longitudinal studies, it is imperative that the reliability of the technique be demonstrated. Currently there is limited research[193,194] that has documented the reliability of NIRS during exercise.

5.2 *Patients*

5.2.1 *Peripheral vascular disease*

A number of studies have used NIRS to evaluate patients with peripheral vessel disease (PVDs). Peripheral arterial disease (PAD) involves partial occlusion of arterial flow, usually to the legs, that impairs function. The impaired function can be quite severe, and is termed intermittent claudication. PAD has been shown to produce impaired oxidative metabolism,[195] despite observations of increased mitochondrial enzyme content.[196] The increase in mitochondrial volume indicates an adaptive response to the low DO_2.

A consistent finding with NIRS measurements in PAD patients is slower rates of calf reoxygenation after exercise.[74,75,197–199] The magnitude of the impairment could be very large, with recovery rates being up to five times slower than healthy control subjects.[109] Good correlation was found between measurements of Doppler pressure waveforms and ankle arm systolic pressures (AAI) and the NIRS recovery time constant.[109] An important aspect of this study was that

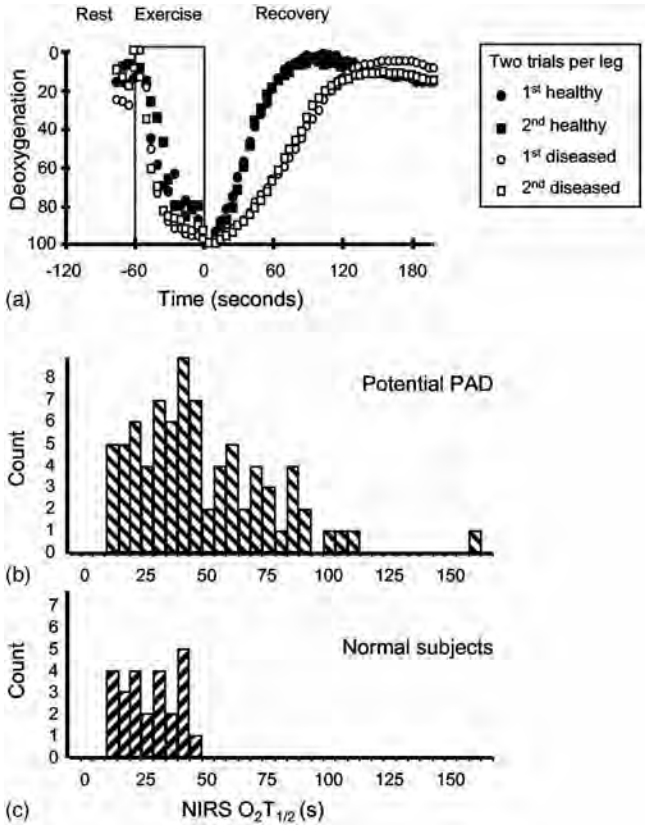

Fig. 5 An example of NIRS measurements of the rate of reoxygenation after exercise in patients with peripheral arterial disease (PAD). (a) Four measurements from one elderly male subject with PAD in only one leg. Note that multiple trials on one leg produce very similar results, while the diseased leg shows a much slower rate of recovery. (b) The distribution of reoxygenation rates in a population of older subjects with suspected PAD by self report. Note the wide and continuous range of responses. Subjects with faster recovery rates were shown to be normal on clinical examination, while those with slower recovery rates had PAD. (c) Recovery rates for healthy subjects for comparison. Copyright (c) The Gerontological Society of America. Reproduced by permission of the publisher.

the degree of impairment appeared to be continuous, demonstrating that clear separation of healthy and diseased people is difficult (Fig. 5). Komiyama et al. successfully classified patients with a varied severity of PVD by using patterns of calf oxygenation kinetics during treadmill exercise and recovery.[198] Impaired muscle O_2 usage at the exercise onset was also observed in PAD patients.[200] Interestingly, Mohler et al. reported an interaction between PAD and the presence or absence of diabetes mellitus (DM) using changes in muscle capillary blood expansion and reoxygenation recovery.[75] Capillary blood expansion was reduced in patients with DM, regardless of the existence of PAD; therefore, this parameter might be a good indicator for evaluating vascular impairment in DM patients. Taking into account that not all studies have shown positive results, NIRS appears to be able to identify and quantify the severity of patients with PAD.

Several studies have evaluated peripheral venous occlusive diseases using NIRS.[201–203] A calf venous blood filling index was tested on standing patients, and the calf venous retention index was monitored after exercise testing in patients with acute deep vein thrombosis from 1 to 12 months after treatment. These indicators were able to distinguish between successfully treated patients and those remaining with deep vein thrombosis after a period of 12 months.

5.2.2 *Heart diseases*

A number of studies have used NIRS to evaluate skeletal muscle in patients with heart disease. In addition to functional deficits associated with impaired cardiac function, heart disease has also been shown to be associated with impaired muscle metabolism.[204] This decrease in muscle metabolism has been linked to reduced exercise tolerance and decreased pVO_2, and increased risk of cardiovascular disease.[205,206]

NIRS measured muscle oxygenation kinetics have been studied in patients with congestive heart failure (CHF).[101,106,207–209] Wilson et al. concluded that CHF patients exhibited greater deoxygenation compared with the controls, due partly to the pump failure of the heart and the consequent skeletal muscle hypoperfusion. A correlation between changes in tHb and leg vessel conductance was found in patients with and without cardiac dysfunction during submaximal dynamic exercise, but there was some discrepancy between the NIRS and leg vessel conductance measurements at near maximal exercise levels.[148] Recently, skeletal muscle oxygenation was evaluated in heart transplant recipients (HTR).[151] The changes in HHb during submaximal exercise were steeper in HTR than in the control subjects, while the peak value of HHb was lower in HTR. The authors suggested that NIRS allows the detection of an impairment of both DO_2 and O_2 extraction in the HTR skeletal muscle.

To elucidate with heart failure, NIRS has been used to assess respiratory muscle deoxygenation in patients with CHF or HTR during leg cycling exercise.[159,210,211] The rationale for these studies is that exercise-induced dyspnea is common in patients with heart disease. The NIRS measurements were consistent with respiratory muscle hypoperfusion combined with the greater work of breathing in patients with CHF.

5.2.3 *Chronic obstructive pulmonary disease*

Patients with chronic obstructive pulmonary disease (COPD) frequently develop skeletal muscle and vascular abnormalities as complications of their disease, similar to patients with heart disease.[212,213] These observations suggest that deteriorated oxidative metabolism is related to lowered muscle oxidative capacity, elicited both by chronic inactivity and abnormal metabolic regulation, as well as reduced DO_2 to muscles. Evidence for a peripheral mechanism for exercise intolerance is supported by studies that have shown that exercise capacity was improved with endurance exercise training in patients with COPD.[213]

NIRS measured recovery of oxygen saturation after exercise has been shown to correlate with expired air pVO_2 off kinetics in COPD patients.[214] In a study measuring oxygen saturation in skeletal muscle with NIRS during incremental cycling exercise in 16 COPD patients and 10 age-matched healthy subjects, the slope of SO_2 was significantly steeper in COPD patients than in healthy subjects. The rate of the decrease in SO_2 with increasing exercise intensity in COPD patients significantly correlated with body mass index (BMI), suggesting that BMI contributes independently to the change

of muscle SO_2 with exercise.[215] NIRS was used to obtain the time constant of the deoxygenation recovery signal (HHb-Tc) during three constant work exercise tests, one below and two above the lactic acidosis threshold.[110] This study found significant correlations between changes in oxidative enzyme activity and changes in HHb-Tc and endurance time. It was concluded that leg training accelerates the speed of reoxygenation of the vastus lateralis muscle after exercise. This improvement is correlated to changes in the oxidative enzymes.[110]

5.2.4 *Muscle diseases*

NIRS measurements have been used to study patients with neuromuscular disorders. Exercise intolerance and fatigue are common complaints in patients with neuromuscular disorders.[216,217] Although neuromuscular disorders encompass a variety of pathologies, physical deconditioning often contributes to the limited exercise capacity in these chronic disorders. Previous studies using MRS have shown the utility of measuring muscle energetics in patients with cytochrome b deficiency.[218–220]

Using NIRS, an increase in muscle oxygenation at the onset of treadmill exercise has been detected in patients with cytochrome c oxidase deficiency,[221] in patients with mitochondrial myopathy caused by mitochondrial DNA mutations,[222] and in patients with Friedreich's ataxia.[223] This paradoxical oxygenation is due to the combination of impaired mVO_2 along with normal physiological increase of DO_2 (vasodilatation), stimulated by muscle pump and/or myogenic activity. Muscle hyperoxygenation measured with NIRS has been used as a diagnostic in many cases of suspected mitochondrial disease. Quite recently, patients with mitochondrial myopathies (MM) or myophosphorylase deficiency (McArdle's disease, McA) were tested for changes in the capacity for O_2 extraction, maximal aerobic power, and exercise tolerance during cycle exercise using NIRS.[69] HHb peak (percent of arterial occlusion), an index of O_2 extraction, was lower in MM ($25.3\pm12.0\%$) and McA ($18.7\pm7.3\%$) than in control subjects ($62.4\pm3.9\%$). These results suggest that NIRS is a promising tool for monitoring noninvasively the metabolic impairment in the settings of follow-up and in the assessment of therapies and interventions.

5.2.5 *Spinal cord injury*

NIRS has also been used to evaluate the extensive changes that occur to paralyzed muscles in the lower leg with spinal cord injury (SCI). Bhambhani et al. found a lower degree of muscle deoxygenation during maximal exercise and faster changes in muscle deoxygenation with respect to the pVO_2 during functional electrical stimulation cycle exercise in SCI patients when compared to healthy subjects.[86] Olive et al. found normal rates of reoxygenation after muscle stimulation exercise and ischemia in SCI subjects, although the SCI subjects had to have their legs warmed prior to testing to control for temperature.[224] NIRS has been used to evaluate potential therapies for SCI. Six motor-complete SCI subjects and four neurologically normal controls were placed on a gait-training apparatus that enabled the SCI subjects to stand and move their legs passively.[142] The O_2Hb level gradually increased, whereas the HHb decreased in the patients. This response differed from normal controls. Six SCI patients underwent electrical stimulation training (45 min daily for 3 days per week for 10 weeks) with different loads on muscle oxygenation of the paralyzed lower limbs using NIRS.[178] NIRS detected attenuated muscle deoxygenation after static training compared with prevalue.

5.2.6 *Renal failure*

NIRS has been used to evaluate the potential for vascular and metabolic dysfunction in patients with renal failure. Forearm vasodilator responses to 3-min arterial occlusion were measured by NIRS in patients receiving hemodialysis.[171] Vasodilator responses estimated by the ratio of the maximum value of O_2Hb after release of arterial occlusion to its minimum value before the release were significantly smaller in the renal failure patients compared with those in the controls (132 ± 20 versus $161\pm27\%$, $p<0.05$). No improvement in the vasodilator responses was observed after exercise training. Muscle oxygenation and metabolism were examined by using NIRS in ten children with end-stage renal disease (ESRD) before and after renal transplantation (ages 12.4 ± 3.1 years) and in ten controls (ages 12.8 ± 2.6 years) during submaximal hand grip.[81] The rate of initial decrease in oxygenation during transient arterial occlusion after exercise relative to the value at rest (S2/S1) and recovery time (TR) after exercise was used as an indicator of O_2 delivery to the muscle and aerobic capacity. S2/S1 and TR after exercise improved significantly after renal transplantation ($P<0.01$ and $P<0.05$, respectively) and were not significantly different from those of controls. These studies show that NIRS is able to detect muscle hypoperfusion in patients with renal failure as well as the functional alterations of muscle oxidative metabolism that occur after renal transplantation. The noninvasive nature of the NIRS measurements is an advantage in the study of children with renal failure as well as children with other diseases.[81,208,225]

5.2.7 *Diabetes mellitus*

NIRS has been used to evaluate the potential for vascular and metabolic disorders in skeletal muscle of patients with either type-1[138,225] or type-2 diabetes mellitus (DM).[138,225–227] After exercise, NIRS measured muscle reoxygenation rates as well as MRS measured PCr recovery rates were slower in patients with type-2 DM. Exercise duration correlated negatively with deoxygenation rates and HbAlc levels, while reoxygenation times correlated positively with HbAlc levels.[227] In patients with type-1 DM, the NIRS measured muscle reoxygenation rate correlated with percentage body fatness, visceral and abdominal subcutaneous fat volume, and dietary fat intake, but not with the duration of diabetes nor HbAlc.[138]

5.2.8 *Other diseases*

A number of other diseases and syndromes have been studied with NIRS. Muscle metabolism in chronic fatigue syndrome (CFS) was measured using NIRS and MRS.[228,229] These studies suggested that CFS may have altered control of blood flow, but this is unlikely to influence muscle metabolism. Patients with chronic compartment syndrome showed greater maximum relative deoxygenation during exercise and slower reoxygenation during recovery than the control patients.[230] Patients with traumatic acute compartment syndrome had

lower SO_2 values relative to the control patients, which was usually normalized after fasciotomy. NIRS evaluation may offer a rapid, noninvasive method of assessing extremities at risk for compartment syndrome.[231] Muscle perfusion and oxygen consumption have been measured in septic-shock patients[232,233] and in digit replantation patients.[234]

6 Conclusion

There is an increasing need to develop noninvasive and real-time methods for evaluating skeletal muscle metabolism in humans. NIRS has been developed to fill this need, and this work reviews some of the studies that have evaluated skeletal muscle oxidative metabolism and blood flow. Special reference is taken to examine the validity of the indicators determined by NIRS, and the application of these indicators for monitoring training-induced changes in oxidative metabolism in healthy and diseased muscles. For the most part, NIRS indicators are shown to be useful for the detection of changes in muscle metabolism and oxygen delivery in healthy subjects, as well as in patients with various organ diseases as well as muscle-specific disorders. The advantage of using NIRS over invasive techniques and MRS measurement is that the equipment itself is more portable and the procedure can be done more simply. The use of NIRS is therefore suitable for practical and clinical use. However, the variety of NIRS equipment that is available as well as the addition of new developed equipment will require continued validation studies. It can be argued that there are too many NIRS derived indices, and that standardization of testing approaches is needed to allow for greater ease of comparison between research studies. In addition, along with applied clinical studies, basic research is still needed, such as the origin of the NIR signal (which fractions from arterioles, capillary, and venules, as well as from Hb and Mb), the NIR penetration depth or measurement area in tissue with varying source-detector arrangement (orientation) in the multilayer model, including the effect of nonmuscular tissue, and changes in optical properties during a wide range of tissue oxygenation status, varying subjects, and exercise modality. Thus, NIRS technology remains a promising and continually development methodology. We are grateful for Jobsis' discovery of the NIR window into biological tissues, and we are proud to be among those who strive to continue his legacy by advancing the research of human skeletal muscle function with NIRS.

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Progress of near-infrared spectroscopy and topography for brain and muscle clinical applications

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Abstract. This review celebrates the 30th anniversary of the first *in vivo* near-infrared (NIR) spectroscopy (NIRS) publication, which was authored by Professor Frans Jöbsis. At first, NIRS was utilized to experimentally and clinically investigate cerebral oxygenation. Later it was applied to study muscle oxidative metabolism. Since 1993, the discovery that the functional activation of the human cerebral cortex can be explored by NIRS has added a new dimension to the research. To obtain simultaneous multiple and localized information, a further major step forward was achieved by introducing NIR imaging (NIRI) and tomography. This review reports on the progress of the NIRS and NIRI instrumentation for brain and muscle clinical applications 30 years after the discovery of *in vivo* NIRS. The review summarizes the measurable parameters in relation to the different techniques, the main characteristics of the prototypes under development, and the present commercially available NIRS and NIRI instrumentation. Moreover, it discusses strengths and limitations and gives an outlook into the "bright" future.
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Keywords: brain; muscle; near-infrared spectroscopy; near-infrared imaging; oximetry; tissue oxygenation.

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1 Introduction

This review celebrates the 30th anniversary of the first *in vivo* near-infrared (NIR) spectroscopy (NIRS) publication,[1] which was authored by Frans Jöbsis, who described his discoveries in two papers published in the *Journal of Biomedical Optics* 22 years after his original publication.[2,3]

Starting with the pioneering work of Jöbsis, noninvasive NIRS was first utilized to investigate cerebral oxygenation experimentally and clinically and, later on, muscle oxidative metabolism. In addition, since 1993, multichannel NIRS instruments have been largely applied to investigate the functional activation of the human cerebral cortex in adults[4–7] and later in newborns.[8] A number of recent detailed reviews describing the principles, the limitations, and the applications of NIRS have appeared in the literature.[9–18] The same is true for reviews describing the applications of NIRS on cerebral oxygenation monitoring in newborns and adults.[19–29]

The most recently available NIRS technology for monitoring cerebral oxygenation can contribute to the identification of deficits in cerebral oxygenation. Monitoring such deficits supports certain forms of therapy in reversing cerebral oxygenation issues and thereby preventing long-term neurological sequelae. Recently, it has been demonstrated that quantitative thresholds for cerebral oxygenation led to the identification of cerebral ischemia in the adult brain and thus increased the scope of clinical use of NIRS.[29] A number of recent detailed reviews describe the use of NIRS and NIRS imaging (NIRI) for human brain mapping[15,30–36] and muscle exercise pathophysiology.[37–43]

This review reports on the progress of the NIRS and NIRI instrumentation for brain and muscle clinical applications, 30 years after the discovery of *in vivo* NIRS. The review summarizes the measurable parameters in relation to the different NIRS techniques, the main characteristics of the prototypes under development, and the present commercially available NIRS and NIRI instrumentation. Moreover, a discussion on the strengths and limitations of NIRS and/or NIRI and an outlook into the "bright" future are reported.

2 Methods

Papers were retrieved by the authors through different strategies. First, a search on the two databases MEDLINE and INSPEC was performed using the keywords: "near infrared," "near infrared oximetry," "cerebral oximetry," "muscle oxygenation," "optical imaging," and/or "instrument." The references were screened and the full texts of relevant publications were retrieved. Next, the references of reviews were hand searched. The research was restricted to literature on the NIRS and/or NIRI instrumentation suitable for human muscle and brain measurements published or made available up to February 2007. Breast imaging instrumentation was not included, because its progress has recently been reviewed.[44–46]

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In addition, three-dimensional tomography was excluded, because it is covered by another paper in honor of Professor F. F. Jöbsis. The very recent proceedings of conferences organized by the following societies: Optical Society of America, The International Society of Optical Engineering (SPIE), Organization of Human Brain Mapping, American College of Sports Medicine, and the Polish Academy of Sciences were also consulted. Research groups known to be active in the field were contacted for gathering further information. The Web sites of the commercial systems were searched and visited for exploring the specifications of the instruments. After collecting all the documentation, a consensus was made by all authors to properly select material eligible for inclusion in this review. The material was sorted according to the type of NIRS and NIRI instrumentation and the parameters measured. Tables were generated to report the origin and properties of each instrument and all the measurable parameters.

3 Results

NIR from the 650- to 950-nm wavelength penetrates tissue relatively deeply. In this region of wavelength, chromophores such as oxyhemoglobin (O_2Hb in micromolar concentration), deoxyhemoglobin (HHb in micromolar concentration), cytochrome oxidase, water, lipids, and indocyanine green absorb light. Thus their concentration can in principle be measured by NIRS and NIRI. However, besides the light absorption, the strong light scattering of tissue in the NIR has to be taken into consideration. To quantify the measurements, theoretical models describing light transportation in tissue have been developed.[47] Because a general mathematical approach is not feasible, all the mathematical models rely on assumptions and approximations to simplify matters.[47] It is important to ensure that these assumptions are fulfilled, when applying NIRS and NIRI.

The most widely used approximations are the differential pathlength factor (DPF) method[48–50] and the diffusion approximation.[47,51–53] The DPF method is a relatively simple model that enables us to quantify changes in chromophore concentration. Absolute values cannot be obtained directly by the DPF method. Only changes in light attenuation are measured, and it is assumed that these changes reflect changes in the chromophore concentration. If geometrical or structural changes occur, they will be misinterpreted as changes in the chromophore concentration, which, for instance, might occur during motion artifacts. In addition, the DPF method assumes that the tissue and the change in chromophore concentration are homogeneous. To obtain quantitative values, the DPF, which accounts for the increased pathlength due to light scattering, has to be measured or taken from the literature.[54–59]

The diffusion approximation of the Boltzmann transport equation is another widely used mathematical model. The diffusion approximation has analytical solutions under the following assumptions: (1) tissue is homogeneous, (2) scattering is much larger than absorption, and (3) the tissue has a specific geometry—infinite, semi-infinite, slab, or two-layered.[47] To obtain correct values, it is again vital to observe these boundary conditions. The DPF method is in agreement with the diffusion approximation. The diffusion approximation can be used to measure absolute values of the absorption and scattering coefficients of tissue and from the absorption coefficient, absolute values of the chromophore concentration can be calculated. Generally, this requires measuring light intensity and the time of flight (i.e., the time the light takes to pass through the tissue).

Several techniques to physically carry out the measurements have been described and applied. Table 1 summarizes the different types of instruments and indicates key features, advantages, and disadvantages. The parameters that can be measured are outlined in Table 2.

Most of the parameters are based on the measurement of O_2Hb and HHb. In addition, NIRS's measurement of the changes in the redox state of oxidized cytochrome *c* oxidase (ΔoxCCO), as first proposed by Jöbsis,[1] has the potential to provide a unique method for monitoring changes of intracellular O_2 delivery.[9,60] Although much work has been done on the refinement of NIRS hardware and algorithms (utilized to deconvolute the light absorption signal), recent years have seen a vivid discussion in the literature on the possibility of measuring ΔoxCCO by NIRS. To improve the accuracy of the measurement of this NIRS parameter, most of the recent animal[61,62] and human[63,64] NIRS studies have been performed using a broadband approach with a continuous white light spectrum.

Continuous wave (CW) means that only changes in the light intensity are measured. Usually at least two different wavelengths are multiplexed to obtain spectral information. The ambient light level is also measured and subtracted by the NIRS instrument. CW can easily be used for imaging by using many source-detector pairs, which are distributed on the tissue of interest.[15,65–70] This method only allows the continuous quantification of relative values (except for absolute values of venous oxygen saturation[71,72]) and usually relies on the DPF method. Another disadvantage is represented by the fact that it is relatively sensitive to motion artifacts. The advantages are that CW is inexpensive and can be miniaturized to the extent of a wireless instrument,[73] even for imaging (Fig. 1). In addition, in many situations (e.g., studies of functional activity of the brain or intervention studies for testing reactions on drugs or changes in treatment[15,32,74]) relative values are sufficient (Fig. 2).

Spatially resolved spectroscopy (SRS) is also called multidistance spectroscopy and is based on light intensity being measured at several different source-detector distances.[75,76] One problem of NIRS and/or NIRI is that the light coupling between the optodes and the tissue is unknown, difficult to measure, and sensitive to changes on the tissue surface over time. SRS techniques assume that the coupling is the same for the different source-detector distances and, by measuring the intensity as a function of the distance, determine a parameter that is independent of the coupling.[76] This allows the determination of ratios of O_2Hb to total hemoglobin (O_2Hb+HHb) and thus tissue oxygen saturation. The application of cerebral NIRS in adults has been hampered by concerns over contamination from extracerebral tissues. Using SRS,[77] the brain was identified as the anatomic source of the signal on adult patients undergoing carotid endarterectomy. A change in brain oxygen saturation was predominantly associated with internal carotid artery clamping. The reason is that using a SRS approach, the superficial layers of tissue affect all the light bundles similarly and therefore their influence cancels out.

Table 1 Near-infrared spectroscopy and imaging instrumentation: Characteristics and main parameters directly measured.

	Single-Distance CW Photometers			1 or 2 Channels Oximeters				Imagers		
Parameters measured and instrument characteristics	Discrete wavelengths	Broadband second derivative	DWS	SRS CW	PMS MD	PMS MF	TRS	CW	PMS	TRS
[O_2Hb], [HHb], [tHb]	yes, changes[a]	yes, absolute value	no	yes, changes[a]	yes, absolute value	yes, absolute value	yes, absolute value	yes, changes[a]	yes, absolute value	yes, absolute value
Blood flow measurement	no	no	yes, relative	no	no	no	no	no	no	no
Scattering and absorption coefficient and pathlength measurement	no	yes, pathlength	no	no	yes	yes	yes	no	yes	yes
Tissue O_2Hb saturation measurement (SO_2,%)	no	yes	no	yes	yes	yes	yes	no	yes	yes
Penetration depth with a 4-cm source-detector separation	low	low	low	low, but deep for SO_2	deep	low	low	low	deep	low
Sampling rate (Hz)	≤100	1	≥5	≤6	≤100	≤1	≤6	≤100	≤50	1
Spatial resolution (cm)	n.a.	n.a.	feasible	n.a.	n.a.	n.a.	n.a.	≤1	≤1	≤1
Instrument size	very small	medium	medium	small	small	medium	medium	some bulky, some small	bulky	bulky
Instrument stabilization	n.r.	n.r.	required.	n.r.	n.r.	n.r.	required	n.r.	n.r.	required
Transportability	easy	easy	feasible	easy	easy	easy	easy	some easy, some feasible	feasible	feasible
Instrument cost	low	moderate	high	moderate	moderate	high	high	some low, some high	very high	very high
Caution for eye exposure to coherent sources	n.r.	n.r.	required	n.r.	n.r.	n.r.	required	depends on instrument	required	required
Stable optical contact	critical	critical	critical	not critical	not critical	critical	not critical	critical	not critical	not critical
Precise anatomical localization	no	no	no	no	no	no	no	scarce	scarce	scarce
Telemetry	available	n.a.	n.a.	available	difficult	difficult	difficult	available	difficult	not easy
Discrimination between cerebral and extracerebral tissue (scalp, skull, CSF)	n.a.	n.a.	feasible	n.a.	feasible	n.a.	feasible	n.a.	feasible	feasible
Possibility to measure deep brain structures	feasible on newborns	feasible on newborns	feasible on newborns	feasible on newborns	feasible on newborns	feasible on newborns	feasible on newborns	feasible on newborns	feasible on newborns	feasible on newborns

[a]When the differential pathlength factor (DPF) is included to calculate the tissue pathlength [=DPF×(source-detector separation)].
CSF=cerebrospinal fluid, CW=continuous wave, DWS=diffusing-wave spectroscopy or diffuse correlation spectroscopy, HHb=deoxyhemoglobin, MD=multidistance geometry, MF=multifrequency measurement, n.a.=not available, n.r.=not required, O_2Hb=oxyhemoglobin, PMS=phase modulation spectroscopy, SRS=spatially resolved spectroscopy, tHb=O_2Hb+HHb, TRS=time resolved spectroscopy.

Table 2 Parameters measured directly and indirectly by near-infrared spectroscopy and imaging instrumentation.

Parameter	Units	Modality	Applicability (during muscle exercise)	Author [reference]
ΔO_2Hb, ΔHHb, ΔtHb,				Delpy 1997[129]
$\Delta oxCCO$,	a.u., $\mu M \times cm$, μM	D	Yes	Tisdall 2007[64]
OI				Grassi 1999[130]
		D (by SRS)	Yes	Matcher 1995,[75] De Blasi 1993,1994,[104,105] Quaresima 2002,[131] Cuccia 2005[80]
Tissue O_2 saturation	%	D (by PMS)	Yes	Fantini 1995[76]
		D (by TRS)	Yes	Oda 1996[132]
		D (by calibration)	Yes	Benni 2005[133]
		Second differential	No	Matcher 1994, Cooper 1996[58,134]
Muscle SvO_2	%	I (by VOM)	No	Yoxall 1997[135]
		D	No	Franceschini 2002[136]
Muscle tHb	μM	D (by PMS)	Yes	Franceschini 1997[126]
	a.u.	D (by DWS)	No	Durduran 2003[95]
Muscle BF	mL/100 mL/min	I (by VOM)	No	De Blasi 1994[105]
		I (by ICG)	Yes	Boushel 2000[137]
Muscle Hb flow	μM/min	I (by VOM)	No	Wolf 2003[106]
Muscle VO_2	mL/100 g/min	I (by VOM)	No	De Blasi 1993, 1994[104,105]
		I (by AOM)		
Muscle recovery time	s	D	No	Chance 1992[138]
Muscle compliance	mL/L/mmHg	I	No	Binzoni 2000[139]
Cerebral SvO_2	%	I (by VOM)	No	Yoxall 1995[140]
		D	No	Wolf 1997[72]
Cerebral tHb	μM	D (by PMS)	Yes	Choi 2004[78]
		I (by O_2 swing)	No	Wolf 2002[141]
		I (by O_2 swing)	No	Wyatt 1990,[101] Wolf 2002[141]
Cerebral BV	mL/100 mL	SRS and second differential	No	Leung 2006[142]
		I (by ICG)	No	Hopton 1999[143]
	a.u.	D (by DWS)	No	Durduran 2004,[96] Li 2005[94]
Cerebral BF	mL/100 mL/min	I (by O_2 swing)	No	Edwards 1988[100]
		I (by ICG)		Roberts 1993,[144] Keller 2000[145]
Cerebral VO_2	mL/100 g/min	Combination cerebral SvO_2 and BF	No	Elwell 2005[146]

Δ=Relative changes from arbitrary baseline, AOM=arterial occlusion Method, a.u.=arbitrary units, BF=blood flow, BV=blood volume, DWS=diffusing-wave spectroscopy, D=directly, I=indirectly, ICG=indocyanine green, OI=oxygenation index (ΔO_2Hb-ΔHHb), oxCCO=cytochrome *c* oxidase redox state, PMS=phase modulation spectroscopy, SRS=spatially resolved spectroscopy, SvO_2=venous O_2 saturation, $tHb = O_2Hb + HHb$, TRS=time resolved spectroscopy, VO_2=oxygen consumption, VOM= venous occlusion method.

Fig. 1 Wireless imaging instrument attached to a newborn infant's head. The squares (blue) represent the detector locations, while the circles (red) depict source locations, each equipped with light emitting diodes at two wavelengths (730 and 830 nm). The electronics to the right includes a Bluetooth device for wireless transmission, drivers for the light emitting diodes, filters, analog-to-digital converters, a microprocessor, and a power supply based on a battery. The instrument weighs as little as 40 g, has a sample rate of 100 Hz, and the battery lasts for approximately 3 h. The wireless technology is comfortable to wear, easy to apply, and enables measurements in moving subjects and everyday situations. (Color online only.)

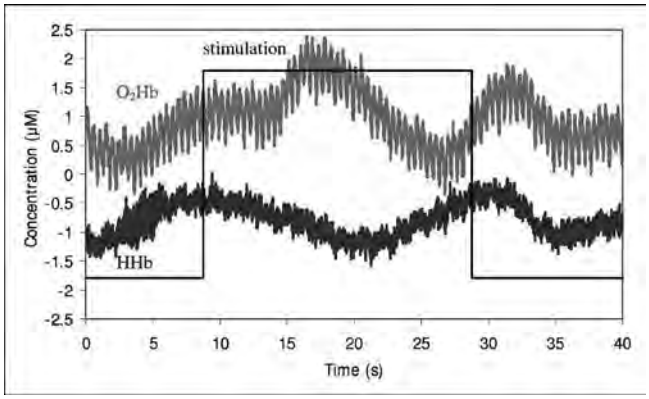

Fig. 2 A sample of a functional NIRs measurement with a 100-Hz sampling rate in a healthy neonate. The upper trace (red) depicts O_2Hb, and the lower trace (blue) HHb and the straight line (black) depict the duration of the visual stimulation. A number of physiological phenomena can be observed: (1) The arterial pulsations are visible in the O_2Hb tracing. The pulsations can be used to calculate the heart rate and arterial oxygen saturation. (2) Approximately every 10 s, there are fluctuations in the blood circulation (the so-called slow vasomotion). These changes are particularly evident in the O_2Hb tracing. (3) The O_2Hb increases and the HHb decreases during the stimulation. This corresponds to a typical functional cortical activation. Although the slow vasomotion partially masks the activation, the measurement can be repeated several times and thus the functional activation can be revealed statistically. (Color online only.)

Only deeper tissue layers have an effect on the values.[78,79] Using a single source-detector distance, however, the influence of the superficial tissues on the signals is relatively large. It depends on the source-detector separation. It can be minimized using large separations and a correction for an extracranial sample volume or both.[9]

The enhanced type of SRS, called spatial frequency domain measurements,[80] projects several bar patterns of different distances between bright bars and dark bars on the tissue. This type of imaging is able to determine absolute values.

Time resolved spectroscopy (TRS), also known as time domain spectroscopy,[49,81–85] is a technique that measures the time of flight in addition to the light intensity. It does so by emitting a short (~100 ps) pulse of light into the tissue and measuring the time point spread function of the light after it passes through the tissue. Due to the scattering process, the pulse will broaden and, due to absorption, the intensity will be reduced. The result of such a measurement is a histogram of the number of photons on the *y* axis and their arrival times on the *x* axis. The histogram also contains information about the depth of the photonic path, because photons that arrive later have a higher probability to have traveled deeper. The absorption and the reduced scattering coefficients are calculated from the histogram and the absorption coefficients are utilized to calculate the absolute values of the chromophores concentration. This technique is also used for three-dimensional imaging and tomography.[14,85,86] Thus, from the physicist's point of view, TRS is an excellent method because it yields a lot of information relatively rapidly and with a high dynamic range. However, it requires sophisticated instrumentation that is so far commercially unavailable. Because the instrumentation usually operates in photon counting mode, it is highly sensitive and can penetrate relatively large tissues (e.g., the head of a neonate). However, due to the low number of photons, TRS measurements are also characterized by a relatively high level of noise. From a clinical point of view, the disadvantages are represented by the physical size of the instrumentation, the use of glass fibers, and the photomultiplier tubes (i.e., the danger of destroying these detectors by excess ambient light). In the near future, technological advances in this field, in particular the miniaturization and reduction in cost of the instrumentation, will promote this technology.

Phase modulation spectroscopy (PMS) is also called intensity modulated or frequency domain spectroscopy. This technique is in principle equivalent to TRS except that it operates in the Fourier domain. This means that the light sources are intensity modulated at radio frequencies (50 MHz to 1 GHz). After passing through the tissue, the mean intensity (DC), amplitude (AC), and phase of the emerging wave are measured. The phase contains information about the time of flight. To obtain the same information as TRS, PMS requires scanning through all frequencies from 50 MHz to 1 GHz.[76,87–92] The result is a Fourier transform of the time point spread function of TRS. Only a few instruments are operated in scanning mode (also called multifrequency mode)[89–92] because the time resolution is relatively low. Most of the instruments are single frequency instruments and use a multidistance or SRS geometry.[76,87,88] It has been shown that the latter type of instrument is technically much simpler than TRS and provides measurements with a good signal-to-noise ratio and a high time resolution. In addition, unlike TRS instruments, SRS instruments can deal with a higher number of photons at the detector and thus with a higher signal-to-noise ratio. From a clinical point of view, the advantages are represented by the easier transportability and the commercial availability. How-

ever, compared to TRS, if only one frequency is used, PMS provides less information about the tissue. In addition, from a clinical point of view, the disadvantages are represented by the use of the glass fibers and the sensitivity of the photomultiplier tubes to excess light. In the near future, this technology might profit from technological advances and developments in the mobile communications industry, which lead to the miniaturization, optimization, and dramatic reduction in cost of crucial components such as synthesizers or demodulators.

Broadband imaging, or second differential spectroscopy,[89–93] means that white light is used instead of discrete wavelengths and, at the detection site, a spectrometer measures the whole range of wavelengths. The advantage is that a whole spectrum is available, which allows the discrimination of chromophores within the tissue with higher accuracy and less crosstalk. Using the second differential, even absolute values can be obtained if a certain water concentration can be assumed.[58] One disadvantage of second differential spectroscopy is that taking the derivative magnifies the noise level and thus measurements have a lower signal-to-noise ratio. Some groups also use a combination of broadband and PMS to be absolutely quantitative.[92] The disadvantage is that to utilize all wavelengths, the power of the light source needs to be higher and tissue warming may be a dangerous consequence.

Diffusing-wave spectroscopy (DWS), also called diffuse correlation spectroscopy, allows using lasers with a long coherence length and the speckle pattern that is created in the tissue.[94–98] Speckles, a pattern of bright and dark spots, are a result of the interference of light. This interference occurs when light with large coherence length (laser light) is going through the tissue by different paths, which may lead to constructive or destructive interference. Because in a tissue there is also movement, mainly of the blood, this interference pattern changes in time. The autocorrelation of the speckle pattern contains information about the blood flow. This technique is related to laser Doppler flowmetry, which measures superficial blood flow and is not included in this review. DWS is the fruit of a relatively recent development and the technology is relatively expensive. In the future, efforts for understanding the factors that affect the autocorrelation must be made to completely quantify blood flow.

NIRI, also called diffuse optical imaging (DOI) or topography, reconstructs two-dimensional images of the chromophore concentrations in tissue. The term "diffuse" in DOI refers to the fact that the theory is based on the diffusion approximation. This type of instrumentation operates usually in reflection mode. The resolution of the images achieved today is on the order of 1 cm.

Table 3 includes the main commercially available instruments, and Table 4 provides an overview of the most important recent noncommercial prototypes.

4 Discussion

Table 3 shows that quite a number of oximeters and imagers are commercially available. The presence of three big Japanese companies developing such devices underlines the consistent efforts made by this country in the field of NIRS and NIRI development. Unfortunately, so far, very few instruments have the approval of the American Food and Drug Administration. Therefore, their distribution has been limited to Japan and/or the European Community. Considering the high cost and the restricted clinical applications of the imagers, more oximeters than imagers have been sold particularly for monitoring adult brain oxygenation during heart surgery. It is not possible to report the exact number of the oximeters sold because the companies do not release such figures. However, it is possible to estimate that more than 2000 clinical oximeters are presently operating for different clinical applications.

The development of instrumentation and methodology has been proceeding in steps. At first, only CW instruments with one channel were available. These instruments allowed measurement of relative values only (i.e., changes in chromophore concentration). They provided useful information in many instances, particularly in intervention studies in which, for instance, the safety of drugs was tested (e.g., Ref. 99) or functional brain activity was investigated. In brain studies, absolute values of hemoglobin concentration or blood flow can be obtained using changes in oxygenation.[100–103] In muscle studies, the combination of relative concentration changes with a venous or arterial occlusion provides absolute quantitation of the oxygenation and blood flow.[104–106] In a second step, instrumentation based on spatially resolved or time resolved (TRS or PMS) methods led to the measurement of absolute values of concentration.[76] This considerable evolution enhanced the value of the NIRS measurements, because it allowed the comparison of concentration and oxygen saturation values among patients without any interventions. This paves the way for monitoring patients during treatment (e.g., in intensive care). In a third step, the use of multichannel instruments enhanced the scope of the measurements from single locations to two or three dimensions. This was another big step, because the single location measurements usually assumed that the values at a given location were representative for the whole area or organ. Imaging studies however showed that (1) this assumption is not true and (2) there may be considerable local variability in volume and/or flow and oxygenation.[106–109]

This leaves us with new problems that have to be solved to enhance NIRI advancement, for example, the placement of multiple channels, the handling of large amounts of data, and the algorithms for reconstructing images. However, NIRS and/or NIRI instrument development can be considered constant as witnessed, for instance, by the fact that every 2 to 3 years new models have been replacing the previous ones, particularly as far as oximeters are concerned. Usually, the new models are characterized by lower dimensions, weight, and cost, as well as improved data presentation, software, and precision. In addition, new techniques have been proposed and are under evaluation for improving the quantitation of oximeters (Table 4).

A large effort refers to the development of imaging instrumentation and image reconstruction algorithms. The main problem of imaging relies on the existence of the strong scattering of light in the NIR range and the very low number of light bundles. Most of the commercial imagers are based on CW light sources and are still very bulky and expensive (Table 3). The fact that several prototypes have been developed by industries and academic institutions using TRS and PMS approaches could suggest that these techniques would be utilized by the next generation of commercial clinical imagers

Table 3 Main commercial near-infrared clinical instrumentation.

Instrument		Technique	Number of channels	Company	Web site
Photometers	BOM-L1 TR	Single-distance CW	1	Omegawave, Japan	www.omegawave.co.jp
	HEO-200[a,b]	Single-distance CW	1	OMRON, Japan	n.a.
	Micro-RunMan[a]	Single-distance CW	1	NIM, Inc., USA	n.a.
	OXYMON MkIII	Single-distance CW	1 to 96	Artinis, The Netherlands	www.artinis.com
Oximeters	FORE-SIGHT[c]	Multidistance	1	Casmed, USA	www.casmed.com
	INVOS 5100C[c]	Multidistance	2 or 4	Somanetics, USA	www.somanetics.com
	InSpectra 325[c]	Multidistance	1	Hutchinson, USA	www.htbiomeasurement.com
	NIMO	Multidistance	1	NIROX, Italy	www.nirox.it
	NIRO-100	Multidistance	2	Hamamatsu, Japan	www.hamamatsu.com
	NIRO-200	Multidistance	2	Hamamatsu, Japan	www.hamamatsu.com
	O2C	Broadband	2	LEA, Germany	www.lea.de
	ODISsey[d]	Multidistance	2	Vioptix, Inc., USA	www.vioptix.com
	OM-220	Multidistance	2	Shimadzu, Japan	www.med.shimadzu.co.jp
	OxiplexTS	Multidistance PMS	1 or 2	ISS, USA	www.iss.com
	TRS-20	Multidistance TRS	2	Hamamatsu, Japan	www.hamamatsu.com
Imagers	Dynot	CW	up to 32	NIRx, USA	www.nirx.net
	ETG-4000[c]	CW	44	Hitachi, Japan	www.hitachimed.com
	ETG-7000[c]	CW	72	Hitachi, Japan	www.hitachimed.com
	Imagent	PMS	up to 128	ISS, USA	www.iss.com
	LED IMAGER	CW	16	NIM, Inc., USA	n.a.
	nScan D1200	CW	16 to 32	Arquatis, Switzerland	www.arquatis.com
	nScan W1200	Wireless CW	16	Arquatis, Switzerland	www.arquatis.com
	NIRO-200	CW	8	Hamamatsu, Japan	www.hamamatsu.com
	NIRS 4/58	CW	4 or 58	TechEn, Inc, USA	www.nirsoptix.com
	OMM-2001	CW	42	Shimadzu, Japan	www.med.shimadzu.co.jp
	OMM-3000	CW	64	Shimadzu, Japan	www.med.shimadzu.co.jp

[a]Wearable instrument.
[b]No longer commercially available.
[c]USA Food and Drug Administration's approval.
[d]30-min battery backup.
CW=continuous wave, n.a.=not available, PMS=phase modulation spectroscopy, SRS=spatially resolved spectroscopy, TRS=time resolved spectroscopy.

(Table 4). But why are there so many different instruments? One reason is that, unlike the other well-established imaging modalities such as magnetic resonance imaging (MRI) or computerized tomography (CT), the setup of NIRS and/or NIRI is highly dependent on the application performed and the tissue measured. Thus, each of the instruments optimizes a certain aspect. For example in neonatology, it is less important to utilize high sensitivity detectors, because neonatal tissue is relatively transparent, and neonatal measurements require soft and flexible probes to prevent lesions of the sensitive skin. An instrument, which optimally incorporates all the physical aspects of the technique (such as highly sensitive detectors) and therefore is capable of providing all the measurable parameters, might be impractical for any kind of

Table 4 Main recently developed near-infrared prototypes.

Name of the instrument or town of the university		Technique	Number of channels	University or firm	Author [reference]
Oximeters	Irvine	Broadband PMS	1	Irvine Univ., USA	Pham 2000,[147] Lee 2006[148]
	Keele	PMS	1	Keele Univ., UK	Alford 2000[149]
	Koblenz	Broadband SRS	1	Koblenz Univ., Germany	Geraskin 2005[150]
	NeoBrain	CW	8	Helsinki Univ., Finland	Nissila 2002[151]
	Philadelphia	Multidistance SRS	1	NIM, Inc., USA	Nelson 2006[152]
	IRIS-3	CW	1	INFM, Italy	Giardini[153]
	TSNIR-3	Multidistance SRS	1	Tsinghua Univ., China	Teng 2006[154]
	Zurich	PMS	1	Univ. Hospital Zurich, Switzerland	Brown 2004[155]
Imagers	Arlington	CW	64	Univ. of Texas, Arlington, USA	Kashyap 2007[156]
	Berlin	CW	22	Charité, Germany	Boden 2007[157]
	London	CW	20	Univ. College London, UK	Everdell 2005[158]
	NIROXCOPE 201	CW	16	BoğaziÇi Univ., Turkey	Akin, 2006[159]
	Nanjing	CW	16	Southeast Univ., China	Li 2005[160]
	New York	CW	var.	Columbia Univ., USA	Schmitz 2002[161]
	Philadelphia	CW	16	Drexel Univ., USA	Leon-Carrion 2006[162]
	St. Louis	CW	300	Washington Univ., USA	Culver 2006[163]
	Zurich[a]	CW	16	Univ. Hospital Zurich, Switzerland	Mühlemann 2006[73]
	Berlin	TRS	16	Physikalisch Technische Bundesaustalt, Germany	Liebert 2006[82]
	Boston	TRS	32	Harvard Univ., USA	Selb 2006[164]
	Hamamatsu	TRS	16	Hamamatsu, Japan	Ueda 2005[165]
	Milan	TRS	16	Politecnico of Milan, Italy	Contini 2006[166]
	Monstir	TRS	32	Univ. College London, UK	Schmidt 2000[167]
	Strasbourg	TRS	8	Strasbourg Univ., France	Montcel 2004[168]
	Warsaw	TRS	16	Academy of Sciences, Poland	Liebert 2005[169]
	Helsinki	PMS	16	Helsinki Univ., Finland	Nissila 2005[170]
	Seoul	PMS	16	Yonsei Univ., South Korea	Ho 2007[171]
	Hokkaido	SRS	64	Hokkaido Univ., Japan	Kek 2006[172]
	Irvine	SRS	CCD	Irvine Univ., USA	Cuccia 2005[80]

[a]Wearable instrument.
CCD=charge coupled device, the instrument uses a noncontact camera; CW=continuous wave; PMS=phase modulation spectroscopy; SRS=spatially resolved spectroscopy; TRS=time resolved spectroscopy; Univ.=university; var.=variable.

clinical application because, for instance, the detector is too sensitive to excess light and could therefore be easily destroyed.

The possibility to map the whole cerebral cortex convinced many cognitive neuroscience research groups to utilize NIRI instrumentation for human brain mapping studies. In this framework, sophisticated data processing methods have recently been investigated and applied to the analysis of NIRI data. Principal component analysis has been utilized for analyzing the spatial and spectral features of diffuse reflectance

data from brain tissue[110] and for suppressing systemic physiological contributions to the evoked hemoglobin-related signals.[111] Independent component analysis[112] and the continuous wavelet transform[113] have been proposed to detect activated cortical areas, whereas lagged covariance methods have been proposed to explore functional brain connectivity from event-related optical signals.[114] In the attempt to characterize the contributions of systemic parameters, such as the heart rate and the mean arterial blood pressure to the low-frequency oscillations in cerebral oxygenation,[115] researchers applied information transfer analysis. The recent and quickly growing emphasis placed on data processing procedures for NIRI data shows the importance that the NIRI field is attributing to the development of powerful and reliable data analysis tools. However, no standardized approach for NIRI data analysis has been established yet, laying further emphasis on the development of standard data processing schemes to elevate NIRI into a well-established human cortical imaging modality.[116]

One measured but not widely explored variable is the light scattering, which is related to tissue structure, cell membranes, and mitochondria. Unfortunately scattering and scattering changes are often disregarded when the focus is on the absorption. One example showing the potential value of scattering changes is their association with the neuronal activity.[117] The latter leads to small changes in light scattering at the neuronal level. Because the changes are small, they are difficult to detect. Although several groups report the detection of such changes,[118–122] there are some controversies.[123] New algorithms able to better separate the other physiological signals from the scattering changes might help to resolve this issue. Light scattering has also been investigated in NIR mammography for breast cancer detection.[124]

The progress of NIRS and/or NIRI is not as rapid as expected and hoped for.[22,125] There are several reasons for this. In fact, NIRS and NIRI have many pitfalls and limitations. Some typical examples can be summarized as follows. (1) For correct measurements, it is necessary to precisely know the assumptions in the physical models and to make sure that they are fulfilled (e.g., the boundary conditions assumed in the algorithms have to correspond to the geometry of the tissue under investigation). (2) An incorrect attachment of the sensor might lead to light piping and consequently large errors. (3) Heterogeneous tissue cannot be measured if the physical model assumes a homogenous tissue. (4) The different NIRS and NIRI approaches show a different degree of susceptibility to movement artifacts, single distance measurements are highly sensitive while multidistance geometries are relatively inert.[126] Often these pitfalls lead to errors that in turn are wrongly used to disqualify NIRS and/or NIRI results. A strong interdisciplinary collaboration between clinicians and scientists could facilitate the correct use of NIRS and NIRI. Another explanation for the slow progress is that there is not a unique ideal NIRS and NIRI instrument. Instead, different instruments could be optimal for a given clinical application. Another problem is that the clinical studies for understanding the meaning of a new parameter (such as tissue oxygen saturation), for establishing its normal values, and for determining limits requiring therapeutic or corrective actions (e.g., the administration of oxygen) call for time-consuming, extensive, and very expensive clinical studies.

There is considerable technical progress that, leading to a higher precision of the measurements and resolution of the images, could partly overcome the limitations of the technique. Also from the clinical perspectives there is considerable progress in view of the first clinical applications entering routine.[21,22,25–28,127] It can be predicted that the evolution of this progress will consist of an increasing variety of clinical applications in which NIRS and/or NIRI will become established techniques in hospitals.

5 Conclusion

Thirty years after NIRS's discovery, NIRS and NIRI are currently at a stage of transition from basic clinical research to an adjuvant in clinical applications. On average, two to three papers per day about the clinical applications of NIRS and NIRI are reported on MEDLINE and "Current Contents Connect" (Thomson Scientific, USA). In addition, several technical papers are published in journals not included in MEDLINE. In the next 5 years, additional efforts are expected in technology developments, commercialization, and clinical validation of oximetry and imager instrumentation. In particular, oximeters are expected to become capable of measuring absolute values, and this will give a consistent contribution for the expansion of their clinical applications. Multimodality imaging systems will be developed to integrate NIRI with various other well-established brain imaging techniques such as MRI and positron emission tomography.[128] Structural information of brain tissue that is obtained from conventional imaging tools, such as CT, MRI, and ultrasound, will provide highly useful coregistration and guidance that will ultimately improve the accuracy of NIRI image reconstruction. Because NIRS and/or NIRI have an inherently high contrast, technological and computational advances will enable image reconstruction with higher spatial resolution and sensitivity. NIRI techniques show a tremendous potential for noninvasive brain imaging by providing functional and metabolic maps of the activated brain cortex. The complementary information provided by changes in O_2Hb and HHb; the coregistration with electroencephalography and systemic parameters such as the heart rate, blood pressure, and respiratory rate; and the development of dedicated data processing algorithms are critically important for the analysis and interpretation of NIRI data.

In summary, although NIRS and NIRI have been growing slowly but constantly, NIRS and NIRI are on the verge of entering clinical everyday applications and have already brought many valuable insights in clinical research. There are good prospects that NIRS and/or NIRI will light up in the future, shed light on many physiological issues, and brighten the perspectives of many illnesses.

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Exercise-induced blood flow in relation to muscle relaxation period

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Abstract

Background: Dynamic exercise is characterized by relaxation periods between contractions. The relaxation period should be considered as a causal factor for determining the magnitude of blood flow during dynamic exercise. The purpose of this study was to investigate the effect of muscle relaxation periods determined by the response of each subject on the exercise-induced blood flow response.

Methods: Seven healthy female subjects performed dynamic plantar flexions twice in succession; the duration of each flexion was 1- s and they were performed at an intensity of 15%, 30% and 50% of the maximal voluntary contraction (MVC). Based on the blood flow response after a single contraction, we set up intervals between two successive contractions; the intervals corresponded to 50% (pre-T_{peak}), 100% (T_{peak}), and 150% (post-T_{peak}) of the time required to reach peak blood flow.

Results: In all the conditions, upon cessation of the contraction, there was a progressive, beat-by-beat increase in the blood flow through the popliteal artery that peaked by the 5th cardiac cycle. Peak values of blood flow achieved after exercise were significantly higher at pre-T_{peak} than at T_{peak} and post-T_{peak} ($p < 0.05$).

Conclusion: The result indicate that at three intervals based on the time taken to reach the peak value, the highest blood flow value was obtained at the pre-T_{peak} interval.

Background

The blood flow to an active muscle changes depending on the exercise intensity, contraction frequency, contraction-to-relaxation duty cycle, etc [1-9]. The blood flow increases markedly during the relaxation phase of dynamic exercise, whereas it remains at a lower level during the contraction period [10-14]. Thus, the magnitude of the blood flow during the relaxation phase of the dynamic exercise determines the magnitude of blood supply to the exercising muscles. Further, the manner in which an exercise protocols increases the blood flow during the relaxation phase of dynamic exercise needs to be clarified.

An earlier study on contraction-to-relaxation duty cycle indicated that the blood flow to an active muscle during dynamic exercise reflects the influence of alteration in the duration of the relaxation phase, rather than the effect of altering the contraction rate [9]. It was also reported that a second contraction of the same intensity during the

period of increased blood flow due to the first contraction induced a greater increase in the blood flow than that caused by the first contraction alone [15]. Therefore, the relaxation time between successive contractions should be a causal factor for the determination of blood flow during dynamic exercise. Hence, the time courses of changes in the blood flow immediately after dynamic contraction should be clarified.

The immediate post-exercise flow was approximately analogous to an interpolated blood flow during relaxation [10,13]. Moreover the blood flow early in recovery after exercise differed between subjects, including athletes and non-athletes [16]. Based on these findings, it is reasonable to hypothesize that exercise-induced hyperemia may vary between the subjects depending on the time taken to reach peak blood flow. To elucidate the changes in blood flow induced by the contraction-to-relaxation duty cycle, the relationship between the changes in the blood flow during relaxation phase and augmentation of blood flow during exercise should be clarified. However, the effect of relaxation time on the time course of changes in the blood flow has never been assessed previously.

Therefore, the aim of this study was to elucidate the effect of muscle relaxation periods that were determined from the blood flow response of each subject on the exercise-induced blood flow. The following approaches were employed. The three intervals were chosen based on the time taken to reach peak value of blood flow after a single contraction of plantar flexion exercise. Alternations in the blood flow after contractions were studied by comparing the 3 different time durations between contractions–the time corresponding to peak value of blood flow, before reaching the peak value, and after the peak value of blood flow was reached.

Methods

Subjects

Seven physically active women participated in the study after giving their informed consent. The age, body height and body mass (means ± SD) of the subjects were 21.9 ± 0.7 years, 162.5 ± 5.8 cm and 55.4 ± 5.3 kg, respectively. All the subjects were free of medical problems.

Experimental protocol

Exercise protocol

All the experiments were performed in the supine position. To fix the entire distance between shoulder and foot, the subjects were stabilized in a fixed position by a using a padded support plate. Each subject placed their respective right foot on the pedal of the ergometer with ankle and knee joints angle at 90° and 180°, respectively. The subject pressed the pedal with the ball of the foot to extend the ankle joint to 100°, and then the subject relaxed their foot to return the ankle joint to 90°. Dynamic plantar flexion was performed against the loads adjusted to 15%, 30%, and 50% of the maximal voluntary contraction (MVC). The MVC of the plantar flexors was determined isometrically and the average of 3 of 5 trials, i.e., excluding the highest and lowest values, was used as the representative MVC to standardize the load. The duty cycle comprised 0.5-second lifting, 0.5-second hold, and 0.5-second unloading. The cadence was determined using an auditory metronome. Prior to the experiments, the experimental approach was explained to all the subjects; the subjects practiced the exercise to ensure that they could maintain the contraction-relaxation schedule and cadence. The experiment was conducted in a room with the temperature and relative humidity set at 24°C and 60%, respectively.

Determination of the relaxation time

Two experimental protocols were tested in this study (Figure 1). In the first experiment, we investigated the popliteal artery blood flow after a single contraction during plantar flexion exercise to determine the time at which peak blood flow was achieved, i.e., the time taken to reach the peak value of blood flow after contraction.

In the second experiment, two successive plantar flexor contractions were performed at three intervals that were based on the results of the first experiment. The intervals

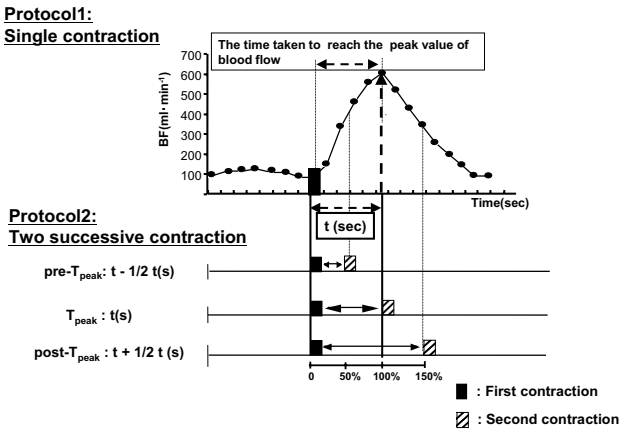

Figure 1

Exercise protocol. We set up the time intervals based on the time taken to reach the peak value of blood flow. In the first experiment, we investigated popliteal artery blood flow after a single 1-second contraction of plantar flexion exercise. Immediately after the cessation of contraction, the blood flow began to increase markedly and reached its peak value. The intervals between the contractions used in this study were 50%, 100%, and 150% of the time taken to reach the peak value.

between contractions used in this study corresponded with the following time durations: to 1) The time taken to reach the peak blood flow (T_{peak}), 2) the interval preceding T_{peak} (pre-T_{peak}), and 3) the interval following T_{peak} (post-T_{peak}). The time corresponding to pre-T_{peak} and post-T_{peak} were calculated as follows: pre-T_{peak} = t – 1/2t, post-T_{peak} = t + 1/2t, where t was the time taken to reach the peak value of blood flow.

Physiological measurement

The mean blood velocity and the vessel diameter of the popliteal artery were measured by using a Doppler and B-mode ultrasound method (HP SONOS 1000, USA). A 7.7 MHz linear array transducer was placed approximately 1 cm above the bifurcation of the popliteal artery into the anterior and posterior tibial arteries. The sampling volume was maintained at 8.9 mm and the angle of the beam to determine the direction of flow of blood was adjusted automatically to 60°.

The diameter of blood vessel based on the relative time periods of the systolic (1/3) and the diastolic (2/3) phases of the cardiac cycle was assumed to be the most representative of the diameter size for each cardiac cycle, and it was utilized for determining the cross-sectional area of the vessel ($A = \pi r^2$, where r is the radius of the vessel); this was used to calculate the blood flow.

Beat-by-beat popliteal artery blood flow was calculated by multiplying FI, HR, and πr^2, where FI is the flow integral during each cardiac cycle and HR is the heart rate obtained from the R-R interval of the electrocardiogram (ECG).

Statistical analysis

The group values are expressed as mean ± SE. Differences among means obtained from the 3 intervals were evaluated by using a one-way ANOVA with post hoc comparison using Fischer's PLSD. Difference between the blood flow during the relaxation period and post-contraction were analyzed using t test for paired samples. A p value of less than 0.05 was considered statistically significant.

Results

Blood flow and time to reach peak blood flow after a single contraction

Following the initiation of a decrease in tension after the 0.5-s hold, the blood flow began to increase immediately. Moreover, it continued to increase even after the developed tension returned to baseline and reached the peak values in 3.8 – 4.7 seconds (mean: 4.0 ± 0.2) (Figure 2). Table 1 shows the time taken to reach the peak blood flow and the coefficients of variation of the time to reach the peak blood flow for each subject at 3 intensities. There were no significant differences in the time taken to reach the peak value of blood flow among the 3 intensities; however, there were significant differences in the peak blood flow achieved, at different exercise intensities, and those obtained during exercise at 30% and 50% MVC were significantly higher than that obtained at 15% MVC ($p < 0.05$: Table 1).

The average of the beat-by-beat blood flow after a single contraction in the 7 subjects at all intensities is illustrated in Figure 3. The blood flow reached its peak value by the 4 th or 5 th cardiac cycle.

The relaxation time calculated using the time to reach peak blood flow after single contraction is listed in Table 2.

Blood flow and time to reach the peak blood flow after two successive contractions

The beat-by-beat blood flow after contractions at all contraction frequencies and intensities are illustrated in Figure 4. At all contraction frequencies and intensities, the peak value of blood flow was observed during the third cardiac cycle after two successive.

The peak value of blood flow immediately after two successive contractions are shown in Figure 5. A comparing of the three different intervals reveals that the highest blood flow values were obtained after the second contraction at the pre-T_{peak} interval at all intensities ($p < 0.05$). In contrast, the blood flow value was the lowest during the post-T_{peak} interval further, the blood flow after the contraction in the post-T_{peak} interval was lowers than that after a single contraction at 15% and 30%MVCs.

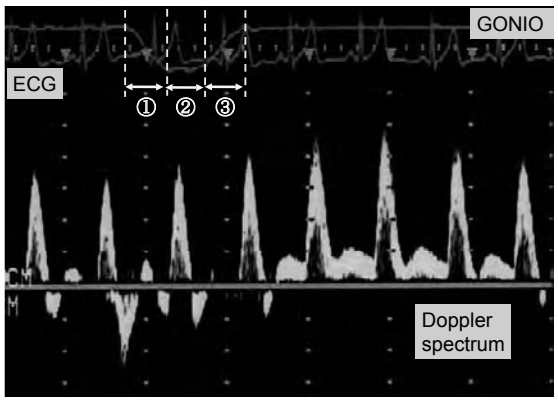

Figure 2
Blood velocity signal before, during and after a single contraction.

Table 1: Peak blood flow and the time taken to re ach the peak blood flow after a single contraction

	15%MVC	30%MVC	50%MVC
Peak BF (ml/min Mean ± S	**149 ± 15**	**416 ± 41**	**488 ± 55**
The time taken to reach the peak BF (s)	**3.8 ± 0.3**	**4.7 ± 0.2**	**3.9 ± 0.2**
The coefficients of variation (%)	**23**	**12**	**14**

Data are obtained from after single contraction. Peak value of blood flow at 30% and 50% MVC were significantly higher than that at 15% MVC. Peak BF: Peak value of blood flow.
*p < 0.05 as compared to 15% MVC

Discussion

The major finding of this study was that the blood flow was augmented to a greater extent when the second contraction occurred prior to the time of the peak hyperemic response. The contraction interval in this study was based on using the time taken to reach peak blood flow after a single contraction. We set up at three intervals using the time duration reaching peak value; the time shorter and longer the time reaching peak value after a single contraction. As a result, the highest blood flow value was obtained from interval using the time before reaching peak value after a single contraction.

As reported by previous studies, the blood flow after a single contraction began to increase markedly immediately after contraction [15,17,18]. After a single contraction, a beat-by-beat increase in the blood flow was observed, and the peak value was obtained between the 4 th and 5 th cardiac cycles. At all contraction intervals and intensities, after two successive contractions, the blood flow showed a progressive, beat-by-beat increase peaked by the 3rd cardiac cycle. These results are similar to those reported by

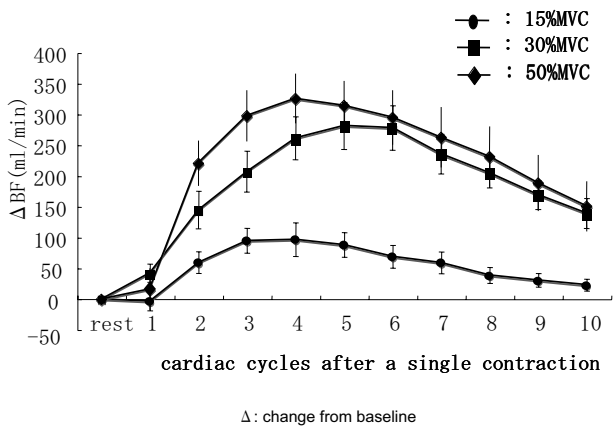

Figure 3
Beat-by-beat blood flow after a single contraction.

Table 2: Determination of the relaxation time

	pre-T_{peak} (sec)	T_{peak} (sec)	post-T_{peak} (sec)
15% MVC	**2.0 ± 0.2**	**3.9 ± 0.4**	**5.7 ± 0.4**
30% MVC	**2.3 ± 0.1**	**4.6 ± 0.3**	**6.7 ± 0.3**
50% MVC	**2.1 ± 0.1**	**3.9 ± 0.2**	**5.8 ± 0.4**
			(Mean ± SE)

Data are the relaxation time calculated using the time to reaching peak blood flow after a single contraction.

Tschakovsky et al [19]. Although all subjects required a similar number of cardiac cycles to reach the peak blood flow, the time taken to reach peak blood flow differed between subjects because of differences in the R-R intervals of the subjects.

In this study, immediately after the tension in the muscle began to decrease during unloading, the blood flow began to increase and continued to do despite the return of the tension to resting levels. This rapid increase is most likely a consequence of the mechanical effects of the muscle pump on alterations of the perfusion pressure gradient across the capillary bed [20]. The rapid vasodilation after a single contraction was detectable within approximately 0.5 – 2 s [15,19]. Considering from the time taken to reach the highest blood flow (3.8– 4.7 s), we cannot exclude the possibility of vasodilation mechanism due to the local release of any vasodilators [15,17].

A novel featuring of this study was that the relaxation times for each subject were set up by using relative time

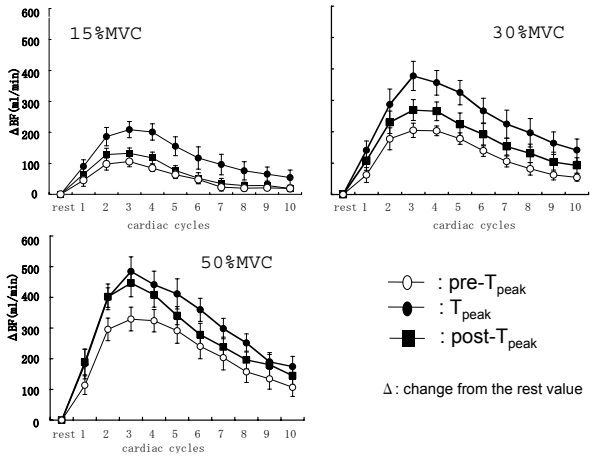

Figure 4
Beat-by-beat blood flow after two successive contractions. At all contraction frequencies and intensities, a beat-by-beat progressive increase in the popliteal artery blood flow was observed following the cessation of contraction, and the peak value was obtained during the third cardiac cycle.

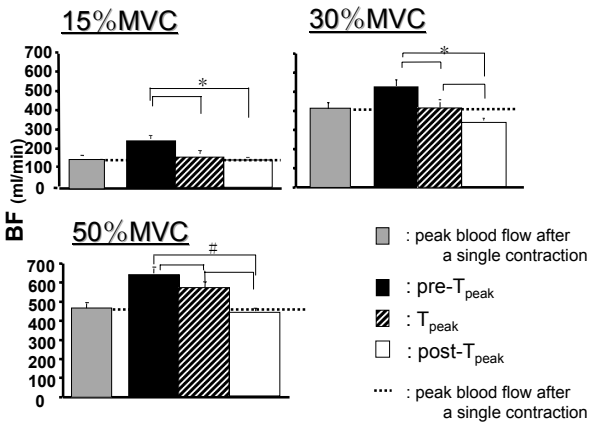

Figure 5
Peak blood flow in exercise at three different relaxation times. The pre-Tpeak interval showed the highest blood flow value and the value decreased as the relaxation period increased. *p < 0.05 pre-T_{peak} compared with T_{peak} and post-T_{peak} at 15% MVC and during the three relaxation intervals at 30% MVC. #p < 0.01 during the three relaxation period at 50% MVC.

based on the time taken to reaching peak value of blood flow after a single contraction. The advantage of the use of relative time is that the timing of the second contraction was adjusted for change in the blood flow changes of each subject. As a result, it indicates that the blood flow will markedly increase during two successive contraction model used in this study if the second contraction comes 50% of time for reaching peak blood flow. Corcondilas et al [15] reported that amount of blood flow increase was different when second contraction was performed four seconds and ten seconds after a single contraction. It is possible to suppose that the effect of the exercise stimulus (mechanical or metabolic stimulus, central command etc) to the vessel caused by a single contraction may be summated when the second contraction comes before post-contraction blood flow reaches the peak. On the other hand, the summation may not occur when the second contraction comes at or after the time for the peak post-contraction hyperemia. Further physiological mechanism remains to be studied.

The three relaxation times that were used in this study corresponded to 2.1– 2.3 s (pre-T_{peak}), 3.9– 4.6 s (T_{peak}) and 5.7– 5.6 s (post-T_{peak}). Among the three relaxation times, the highest blood flow was obtained at the pre-T_{peak} contraction interval. This is in agreement with the results of Byström and Kilbon [7] who demonstrated that the blood flow during exercise with short intervals were higher than that during exercise with long intervals. The contraction-to-relaxation duty cycle in this study corresponded to a frequency of 19–20 contractions per min (cpm), 11–13 cpm, and 8–9 cpm at the pre-T_{peak}, T_{peak}, and post-T_{peak} intervals, respectively. Several studies have indicated that an increase in the blood flow and contraction frequency was paralleled at lower contraction frequency [8,21-23]. With regard to higher contraction frequencies, the results obtained were inconsistent with those of some studied that showed it increased blood flow [21,22] and the others showing decreased blood flow [9]. The contraction frequency used in this study was lower than that used in the previous studies. The effect of contraction intervals shorter than that used in the present study on the blood flow remains to be studied.

With respect to the exercise intensities (15%, 30%, and 50% MVC) used in this study, the peak blood flows after contraction increased with the increase in the exercise intensity. This might be either due to the number of muscle fibers recruited [24] or the increased tension produced due to the increase in the exercise intensity [3]. Moreover, Hamann et al [25] indicated that the blood flow response to a single muscle contraction is not solely determined by the rate at which work is performed; muscle fiber recruitment also contributes independently to the changes in the blood flow.

Conclusion

Dynamic plantar flexion contractions were performed twice successively at three different intervals, which were determined based on the time taken to reach peak value of blood flow after a single contraction. We demonstrated if the second contraction occurs before the peak value of blood flow is reached subsequent to the previous contraction, the increase in the blood flow is higher as compared to the case if the second contraction occurs after the peak blood flow is reached.

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ORIGINAL ARTICLE

Transient increase in femoral arterial blood flow to the contralateral non-exercising limb during one-legged exercise

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Abstract We studied the effect of exercise intensity and duration on blood flow to the non-exercising leg during one-legged dynamic knee extension. Femoral arterial blood flow (FBF) to the non-exercising leg, blood pressure (BP), and heart rate (HR) were monitored during one-legged dynamic knee extension exercise at 15, 30, and 45% maximal voluntary contraction (MVC) in seven healthy females. There was an interaction between exercise intensity and duration for FBF and FVC ($P < 0.01$). During the initial phase of contralateral leg exercise at all intensities, FBF and femoral vascular conductance (FVC) of non-exercising leg increased, and the increase was larger at higher intensities ($P < 0.01$). After initial vasodilatation, FBF and FVC decreased to baseline, which suggests the vasoconstriction. However, FBF and FVC gradually increased during exercise at 15% MVC. We conclude that transient vasodilatation at the onset of exercise is followed by gradual change to vasoconstriction in non-exercising limb during dynamic one-legged exercise and these changes are exercise intensity- and duration-dependent.

Keywords Ultrasound Doppler · Exercise intensity · Exercise duration · Heart rate · Blood pressure

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Introduction

Exercise induces redistribution of blood flow by elevating sympathetic nerve activity mainly by local accumulation of various metabolites in the active muscles (the muscle pressure reflex) and this reflex contributes to increase blood flow to the exercising muscles. Thus, flow to non-exercising muscles and especially the splanchnic area decreases (Hohimer et al. 1983; Osada et al. 1999; Saito et al. 1990; Sinoway et al. 1989). Recent findings regarding blood flow to nonworking limbs are, however, controversial. Several studies indicate that blood flow to the inactive forearm increases during leg cycling exercise (Ahlborg et al. 1975; Kagaya and Homma 1997; Tanaka et al. 2006; Taylor et al. 1989). Increased shear stress to the vessels in the nonworking limb was considered a possible mechanism. On the other hand, Green et al. (2002a, b, c) found that leg cycling exercise at least at a low intensity decreases blood flow in the inactive forearm.

In regard to blood flow to the nonworking leg, blood flow in the calf is reduced during handgrip exercises (Saito et al. 1990). In contrast, Tanaka et al. (2005) demonstrated that femoral arterial blood flow (FBF) increases during arm cranking exercises and Gaffney et al. (1990) reported an initial elevation in blood flow to the inactive contralateral leg during static exercise.

Considering these findings, it may be that forearm and leg vasculatures are differentially controlled during exercise (Taylor et al. 1989). Also different types of exercises present different hemodynamic stimuli to the endothelium, which may result in differential effects of shear stress on the vasculature (Green et al. 2005). However, the mechanism by which exercise induces an increase, or a decrease, in blood flow in non-exercising limbs has not been determined. Additionally, muscle sympathetic nerve activity

(MSNA) that induces vasoconstriction depends on the intensity and duration of the exercise (Saito 1995; Saito et al. 1997; Seals 1993). Therefore, the exercise intensity (Taylor et al. 1989) and its duration (Gaffney et al. 1990) should be considered as important factors in modifying the circulatory response to exercise. However, no data are available regarding the effects of exercise intensity and its duration, or the interaction between these factors on the blood flow to the non-exercising leg.

The purpose of this study was to determine the effect of exercise intensity, duration of leg exercise, and the interaction between these two variables on the blood flow in the contralateral leg during dynamic knee extension exercises. The time course of changes in the blood flow to the femoral artery of the non-exercising contralateral leg was studied during one-legged knee extension exercise conducted at various intensities and continued to exhaustion.

Methods

The participants of this study were seven healthy females with a mean (±SD) age, height, and body mass of 23 (±2) years, 166 (±3) cm, and 61 (±7) kg, respectively. Voluntary consent was obtained from all the participants after they were informed of the purpose of the experiment, the procedure, and the possible risks involved. The study was approved by the Ethics Committee of the Japan Women's College of Physical Education in accordance with guidelines of the Declaration of Helsinki of The World Medical Association.

Experimental protocol

Right leg maximal voluntary contraction (MVC) of knee extension was assessed by an "Action meter device" (VINE, Tokyo, Japan), which changes the resistance electrically. An average of three attempts was considered as the subject's MVC. On separate days, the subjects performed one-legged dynamic knee-extension exercise of the right leg in the upright position with the knee joint angle extended from 90° to 120° (180° = full extension). The exercise comprised contraction and relaxation for 1 s each, as indicated by a metronome. The exercise intensities corresponded to 15, 30, and 45% of the MVC. Following a 10-min rest period, the subjects performed the knee extension exercise at a given load until exhaustion. However, the activity was stopped after 15 min if the subjects could continue to exercise.

Physiological measurements

Common FBF in the left leg was determined using a Doppler instrument (HP 8500-GP, Hewlett-Packard, USA). A 7.5 mHz linear array transducer was placed on the skin over the femoral artery. The measurements were performed below the inguinal ligament at ~2 cm proximal to the bifurcation of the common femoral artery in order to minimize artifacts from turbulent flow. B-mode ultrasound sonography was used to measure the diameter of the artery and Doppler-mode was used to measure blood flow velocity. Blood flow was obtained every 15 s for 90 s during exercise and at exhaustion.

Blood flow was calculated as:

$$\dot{Q} = \text{flow integral for each cardiac cycle} \times 60/\text{RR interval} \times \pi r^2,$$

where $\dot{Q}$ is the blood flow (ml min^{-1}) and r is the radius of the artery (cm).

Heart rate was determined from the RR intervals of the electrocardiogram, and blood pressure (BP) was measured on beat-by-beat basis throughout the experiment (Finapres model 2300, Ohmeda, USA). The blood pressure monitoring device was attached to a finger of the right hand and supported at the heart level. Mean arterial pressure (MAP) was calculated as: diastolic pressure +1/3 (systolic pressure–diastolic pressure).

Data acquisition and analysis

To determine the femoral vascular conductance (FVC), MAP was adjusted to the level of the femoral artery (Keller et al. 2003):

$$\text{FVC} = \dot{Q}/[\text{MAP} + 0.75\,\text{mmHg} \times (\text{height difference between the heart and femoral artery in cm})].$$

Statistics

Values are presented as mean ± SEM, unless indicated otherwise. In order to assess exercise intensity and duration, comparisons of the time courses of the parameters during exercise were assessed by one- or two-way ANOVA for repeated measures. Post hoc analysis was performed by Fisher's least significant difference (LSD) test Statistical significance was set at $P < 0.05$.

Results

The exercise durations were 900 ± 0, 217 ± 21, and 135 ± 8 s for exercise at 15, 30, and 45% MVC, respectively.

FBF

At 15 s, FBF increased at all the intensities, and the changes in blood flow reached a maximum at 45% MVC

(Table 1; Fig. 1). After 15 s in the 15% MVC session, the FBF returned to the resting level; however, it increased again at the end of exercise. At the 30 and 45% MVC, FBF remained elevated until 45 s (30% MVC) and 60 s (45% MVC). At the end of the exercise at 15% MVC, blood flow was higher than that at the end of the 30 and 45% MVC sessions (Fig. 3). Interaction was observed between the exercise intensity and duration ($P < 0.01$).

Mean blood pressure and heart rate

An increase in the MBP was observed after 30 s of exercise at 15% ($P < 0.01$) and 30% MVC ($P < 0.01$), whereas it was observed after 45 s of exercise at 45% MVC ($P < 0.01$) (Table 1). The HR increased immediately at the onset of exercise and continued to increase throughout exercise.

FVC

At the onset of the exercise at all intensities, FVC increased ($P < 0.01$) (Table 1). The change in FVC was the highest at 45% MVC (Fig. 2). At 15% MVC, the FVC increased again after having being reduced to the resting level, and high FVC values were observed at the end of exercise (Fig. 3). At 30 and 45% MVC, FVC remained elevated until 30 s (30% MVC) and 60 s (45% MVC), and it thereafter decreased with time. At the end of exercise, a decrease was observed in FVC at 45% MVC as compared to the resting level.

Discussion

This study examined the influence of exercise intensity and duration besides the interaction between these factors on blood flow in the femoral artery of the non-exercising leg. The major finding was that blood flow and vascular conductance of the leg vessels in the contralateral non-exercising leg demonstrated biphasic time-dependent changes, in that they increased at the onset of exercise to decrease during continued exercise.

Vasodilation in the non-exercising leg during the initial phase of exercise

Blood flow and vascular conductance in the non-exercising leg during dynamic contralateral leg exercise exhibited an increase for the first 15–30 s, and the increase dependent on exercise intensity. The initial increase in the blood flow in the contralateral leg and vascular conductance were in agreement with the results reported for static leg exercise (Fisher and White 2003; Fisher et al. 2005; Gaffney et al. 1990). These studies on static leg exercise indicate that blood flow to the contralateral leg increases momentarily. The explanation for these results may include two possible mechanisms: changes in neural control and changes in blood flow stimuli to the vessel walls. In contrast to arm exercise, during leg exercises, both static and dynamic, muscle sympathetic activity decreases during the early stages of exercise (Ray et al. 1992, 1993) and returns to the baseline with time. Therefore, a reduction in MSNA is a

Table 1 Average values of femoral blood flow (FBF), femoral vascular conductance (FVC), mean blood pressure (MBP), and heart rate (HR) determined at rest and during exercise

MVC	Time							
	Rest	15 s	30 s	45 s	60 s	75 s	90 s	Exhaustion or 900 s
FBF (ml min^{-1})								
15% MVC	251 ± 32	362 ± 34**	300 ± 28	259 ± 27	258 ± 36	233 ± 35	269 ± 46	452 ± 94**
30% MVC	237 ± 28	393 ± 55**	347 ± 34**	335 ± 54*	312 ± 48	278 ± 34	256 ± 28	219 ± 20
45% MVC	260 ± 31	458 ± 45**	468 ± 52**	531 ± 82**	501 ± 92**	341 ± 57	277 ± 32	220 ± 26
15% MVC	2.4 ± 0.3	3.4 ± 0.4**	2.6 ± 0.3	2.2 ± 0.3	2.2 ± 0.4	1.9 ± 0.3	2.2 ± 0.5	3.8 ± 1.0*
30% MVC	2.2 ± 0.3	3.6 ± 0.7**	2.9 ± 0.3*	2.7 ± 0.5	2.5 ± 0.4	2.1 ± 0.3	2.0 ± 0.3	1.5 ± 0.1
45% MVC	2.4 ± 0.3	4.4 ± 0.6**	4.1 ± 0.5**	4.4 ± 0.7**	4.0 ± 0.8**	2.6 ± 0.5	2.0 ± 0.3	1.5 ± 0.2
MBP (mmHg)								
15% MVC	81.5 ± 5.1	82.8 ± 5.3	89.9 ± 4.9**	91.4 ± 5.5**	95.2 ± 5.8**	96.8 ± 5.7**	98.5 ± 5.9**	102.5 ± 9.4**
30% MVC	85.8 ± 4.6	86.5 ± 5.0	94.7 ± 4.1**	98.6 ± 4.2**	102.6 ± 3.9**	104.9 ± 4.2**	106.3 ± 5.9**	117.0 ± 6.0**
45% MVC	84.0 ± 5.0	80.2 ± 4.8	90.4 ± 3.1	97.3 ± 3.3**	102.7 ± 4.2**	108.6 ± 3.3**	111.0 ± 3.4**	118.7 ± 5.3**
HR (bpm)								
15% MVC	64.3 ± 3.0	76.6 ± 2.9**	81.0 ± 2.5**	81.0 ± 2.9**	77.8 ± 4.1**	80.0 ± 3.8**	82.3 ± 3.0**	85.4 ± 4.2**
30% MVC	69.3 ± 5.6	82.4 ± 4.1**	84.9 ± 4.8**	86.0 ± 5.2**	87.4 ± 4.6**	89.9 ± 4.2**	91.3 ± 4.9**	94.6 ± 5.5**
45% MVC	70.4 ± 4.5	85.7 ± 3.5**	91.2 ± 4.4**	93.1 ± 4.9**	91.2 ± 4.9**	92.9 ± 5.1**	94.4 ± 5.3**	97.6 ± 6.9**

* $P < 0.05$, ** $P < 0.01$ versus rest

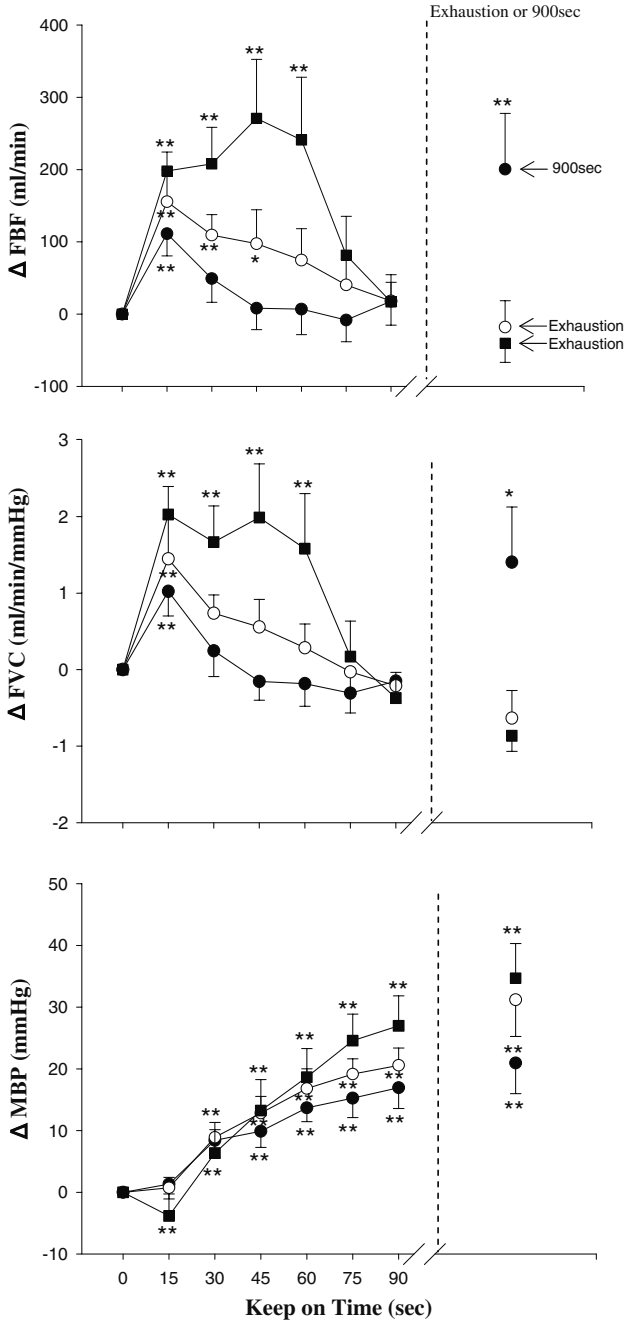

Fig. 1 Changes in the femoral arterial blood flow (*FBF*), femoral vascular conductance (*FVC*) of the resting leg, and mean blood pressure (*MBP*) during one-legged dynamic exercise with the contralateral leg. For 30% (*open circle*) and 45% (*filled square*) MVC exercise, the values at exhaustion are illustrated, and for 15% (*filled circle*) MVC, values at the very right are those obtained at 15 min. Main effect for exercise duration was observed ($P < 0.01$). Interaction was observed between exercise intensity and duration ($P < 0.01$). *$P < 0.05$, **$P < 0.01$ versus rest

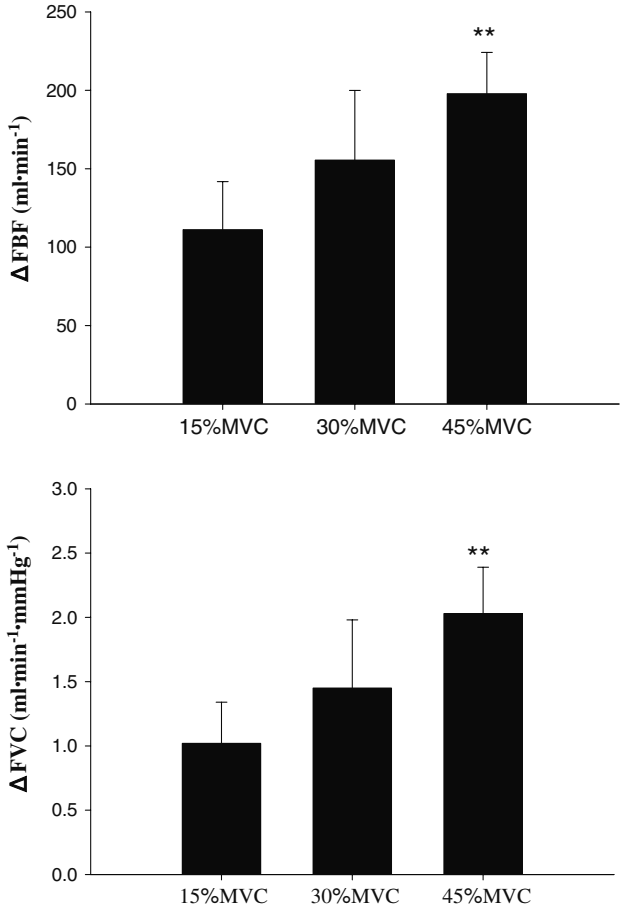

Fig. 2 Mean changes in the femoral arterial blood flow (Δ*FBF*) and femoral vascular conductance (Δ*FVC*) of the resting leg at 15 s of dynamic knee extension exercise of the contralateral leg. *$P < 0.05$, **$P < 0.01$ versus 15% MVC

probable mechanism for increased blood flow and vascular conductance in the non-exercising leg at the early stages of exercise. However, the reduction in the MSNA at the onset of exercise does not increase with exercise intensity (Ray et al. 1993) and it is, therefore, unlikely that lowering of MSNA is the only factor underlying the intensity-dependent increase in blood flow to the non-exercising leg. Fisher et al. (2005) found that increased vascular conductance during contralateral isometric exercise is unrelated to the decrease in MSNA.

In the active muscles, blood flow increased immediately and remarkably upon initiation of exercise, and this increase was related to exercise intensity (Rådegran and Saltin 1998). As blood flow to the femoral artery passes through the abdominal aorta, which branches into femoral arteries of active and non-active legs, an increased FBF to the active limb during exercise induces increase in upstream blood flow of the abdominal aorta in an intensity-dependent manner (Osada et al. 1999). If MSNA is reduced but the vasoconstriction of the contralateral leg vessels is not yet augmented, the gradient of flow resistance to the femoral arteries on both sides may not be high enough to prevent blood flow to the non-exercising regions. Furthermore, accelerated blood flow due to exercise may stimulate the endothelium and lead to the release of nitric oxide

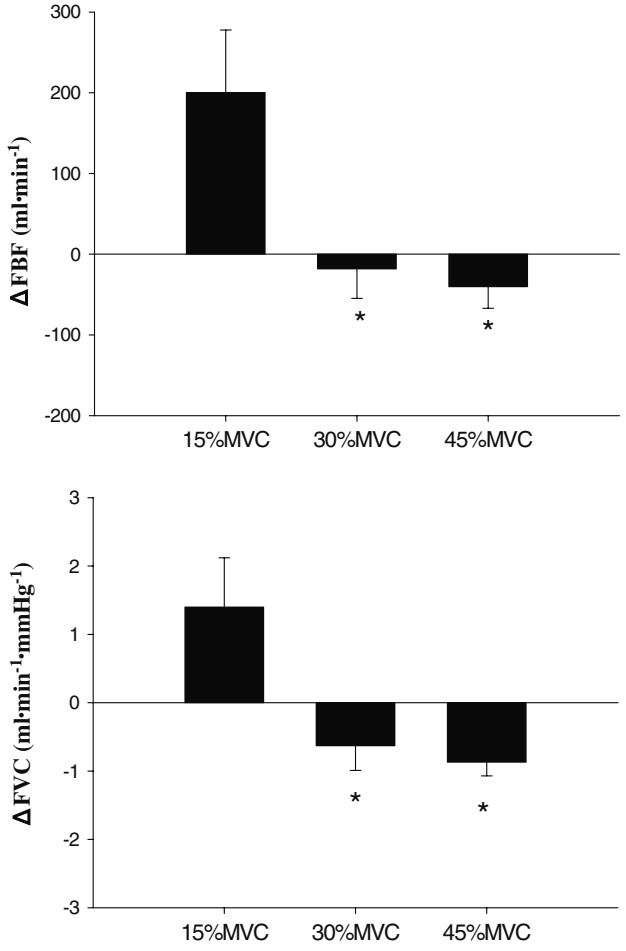

Fig. 3 Mean changes in the femoral arterial blood flow (ΔFBF) and femoral vascular conductance (ΔFVC) of the resting leg at the end of dynamic knee extension exercise of the contralateral leg. $^{*}P < 0.05$, $^{**}P < 0.01$ versus 15% MVC

(NO), which is a strong vasodilatator (Green et al. 2002a; Gilligan et al. 1994). The intensity-dependent vasodilation at the initial phase of leg exercise in the contralateral non-exercising leg could be explained by the reduced MSNA and increased shear stress to the vessel due to the passively increased perfusion.

Time-dependent vasoconstriction in the non-exercising leg during contralateral leg exercise

After the initial phase of exercise, we observed different changes in blood flow depending on the exercise intensity. At 15% MVC, flow to the non-exercising leg returned to the resting level and then increased again after 900 s. One mechanism for this increase in flow could be the release of NO. Green et al. (2002a, b, c) demonstrated that brachial arterial blood flow increased during cycling exercises, but intra-arterial infusion of a NO synthase inhibitor decreased brachial arterial blood flow. Another possibility is that core temperature increases during exercise and blood flow to the cutaneous vasculature increases proportionately (Kolka and Stephenson 1997).

At 30 and 45% MVC, blood flow to the non-exercising leg remained elevated until 45 and 60 s from the onset of exercise and FBF and FVC thereafter decreased to below the baseline level. The results of this study were consistent with the finding by Taylor et al. (1989) who reported that vascular resistance in the calf of the non-exercising leg increased in a time- and intensity-dependent manner. These changes may be caused by augmented MSNA via metaboreflex from the exercising muscles (Ray et al. 1993). Saito (1995) demonstrated that MSNA is markedly activated by exercise at intensities above 30% MVC. Considering this, the SNA occurring in the late phase of exercise at 30 and 45% MVC in the present study may be mediated by an increase in metabolites in the exercising muscles. The consequent activation of muscle metaboreflex may have resulted in reduction of vasoconstriction and blood flow in the non-exercising leg.

Another mechanism to explain the late vasoconstriction observed in this study could be the release of endothelin-1 (ET-1), which is the most potent endothelium-derived constricting factor and it contributes to regulation of peripheral vascular tone. Maeda et al. (1997) showed that the ET-1 concentration increased in the circulation of the nonworking muscle after one-legged dynamic exercise.

Dynamic leg exercise induces intensity-dependent transient increase in the blood flow and vascular conductance in the contralateral limb. The explanation of our results might involve an increase in shear stress due to passively increased blood perfusion to the non-exercising limb, although other explanations are possible. After initial vasodilation, vasoconstriction manifests during exercise at higher intensities (30 and 45% MVC) but not at lower intensities (15% MVC). Time- and exercise intensity-dependent responses of the vasculature were indicated in the contralateral non-exercising limb during leg exercise.

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ORIGINAL ARTICLE

Resistance exercise training enhances sympathetic nerve activity during fatigue-inducing isometric handgrip trials

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Abstract Muscle sympathetic nerve activity (MSNA) was investigated 1 week before (pre-training), 1 week after, and 4–6 weeks after strength training using fatigue-inducing handgrip exercises and post-exercise forearm occlusion. Eighteen volunteers underwent forearm training, which consisted of 30 maximal effort, 10-s-duration static handgrips, 4 days per week for 4 weeks. A second group of 18 volunteers served as a control. MSNA was recorded from the tibial nerve by microneurography. Maximal handgrip force increased at 1 week post-training. The MSNA response during fatigued handgrip also increased at 1 week post-training, as compared to pre-training (52.6 ± 5.8 vs. 40.6 ± 4.4 bursts min^{-1} (mean $\pm$ SEM), respectively). However, at 4 weeks post-training, MSNA activity returned to the pre-training level (44.0 ± 5.2 bursts min^{-1}; $p < 0.0001$ by ANOVA), while the control group showed no changes throughout this period. The MSNA response during post-exercise forearm occlusion was constant throughout the experiment in both groups. Our results indicate that an increased MSNA response after strength training is likely to be the result of central neural factors rather than the muscle metaboreflex.

Keywords Muscle sympathetic nerve activity · Central command · Muscle metaboreflex · Muscle mechanoreflex

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Introduction

The modulating effect of exercise on the cardiovascular response to muscular exercise is well documented (Fisher and White 1999), and these adaptive changes have been attributed to the autonomic sympathetic nervous system. Muscle sympathetic efferent nerve activity (MSNA) during exercise is attenuated by muscle training *via* the attenuation of muscle reflexes (Ray 1999; Sinoway et al. 1996; Somers et al. 1992), including the decreased stimulation of muscle metaboreceptors (Somers et al. 1992) and mechanoreceptors (Sinoway et al. 1996). However, resistance exercise training does not alter the MSNA response during muscular contractions (Carter et al. 2003; Ray and Carrasco 2000). This discrepancy may be the result of the training mode used; endurance training improves muscle oxidative metabolic activity (Kent-Braun et al. 1990), whereas resistance training improves mainly the muscle strength associated with increased central neural activity, rather than metabolic potentials (Kraemer et al. 1996; Narici et al. 1989). MSNA during muscle contraction is controlled by both central command and the reflexes from contracting skeletal muscles (Mitchell 1990). The relative contributions of endurance or resistance training effects on central command and muscle reflexes, such as the metaboreflex, may underlie the conflicting results obtained for the MSNA response during exercise.

Many studies on strength exercises have indicated that strength training develops muscle force and delays the onset of muscle fatigue, which is associated not only with peripheral factors (i.e., muscle reflexes), but also with central neural factors (i.e., central command) (Gandevia 2001; Rube and Secher 1990; Sale 1988). Increased muscle force after short-term resistance training (i.e., less than 6 weeks) is due primarily to increased central motor command, rather

than muscle properties (Sale 1988). After the cessation of resistance training, muscle force decreases in line with decreased motor neural activity (Houston et al. 1983, Narici et al. 1989). Therefore, we hypothesised that if high-intensity resistance training increases central motor command, followed by a decrease after cessation of training, this would, in part, modulate the MSNA response during muscular exercise. Central command is one factor that stimulates MSNA during static handgrip, although this effect was only observed during a strong contraction or effort (Victor et al. 1989, 1995). Indeed, the MSNA response during fatigued isometric handgrip was found to be greater in athletes than in sedentary subjects (Ng et al. 1994), and physical inactivity, such as bed rest, attenuated the MSNA response during muscle contraction (Kamiya et al. 2000, 2003).

We re-examined whether resistance exercise training influences the MSNA response during muscle contraction. The exercise test was carried out after strength training and at 4 weeks after halting training (i.e., detraining). However, since both the central motor command and muscle reflexes act simultaneously during voluntary contraction, it is impossible to separate their contributions to MSNA modulation during exercise. For this reason, the following exercise tests were conducted to activate differentially the central motor command and muscle receptors: (1) a standard 2-min isometric handgrip performed at 33% of maximal voluntary force (MVC); (2) a rhythmic handgrip with forearm ischaemia performed at maximal effort, to stimulate forearm muscle metaboreceptors and mechanoreceptors with high-intensity contraction; and (3) a fatigued isometric handgrip performed at 33% of maximal handgrip force, to stimulate central motor command.

Methods

Subjects

All 36 subjects were volunteers and provided written informed consent before participating. This study was approved by the Human Subject Ethics Committee of the Toyota Technological Institute. Participants were provided with information about the study and were randomly assigned to the resistance training group (TG, $n = 18$) or the control group (CG, $n = 18$). The subjects were aged 22 ± 2 years (mean $\pm$ SD), with a mean height of 172 ± 4 cm and mean body mass of 65 ± 9 kg. One of the trained subjects was left-handed and 17 were right-handed. All subjects were in good health and had recently participated in leisure sports, but none had engaged in any activity that specifically used the arms, such as racket sports.

Handgrip exercise test

For the exercise tests, three different static handgrips were performed in a supine position: (1) a 2-min isometric handgrip performed at 33% of maximal voluntary contraction (MVC); (2) a rhythmic handgrip (40 contractions per min) with forearm ischaemia performed at maximal effort; and (3) a fatigued isometric handgrip performed at 33% of MVC, until the subject could no longer maintain grip force. Each handgrip was followed by a 2-min post-exercise forearm occlusion. Nine of the trained subjects performed the isometric exercise first, followed by the fatigued handgrip after an interval of 20 min on the same day; the remaining nine subjects performed the rhythmic handgrip, and one of these subjects also performed the isometric handgrip test. The subjects were asked to breathe as normally as possible and to not hold their breath or contract any muscles other than those directly involved in the handgrip contraction. All subjects were introduced to the routine 1 day prior to the experiment, to become familiar with the equipment and procedures.

Measurements

MSNA was recorded from the tibial nerve at the popliteal fossa, using an inserted tungsten microelectrode with a shaft diameter of 0.1 mm (Saito et al. 1989). The nerve action potential (amplified by a factor of 100,000) was filtered at 500–3000 Hz, rectified, and integrated (time constant, 0.1 s) to obtain a mean voltage neurogram. MSNA was identified as a MSNA burst rhythm that corresponded to the heartbeat rhythm. The Valsalva manoeuvre was used to enhance MSNA, and the burst rhythm and activity were unchanged by arousal stimuli. The burst amplitude of the original mean voltage neurogram was normalised against the highest MSNA burst amplitude during baseline recording, which was set at an arbitrary value of 20. The MSNA burst was inspected by the experimenter, and the data are expressed as the burst frequency (BF; bursts per min) and percent change in total activity (TSNA; sum of the burst area in arbitrary units). MSNA and other physiological data were recorded from 3 to 1 min before exercise (i.e., a 2-min window of baseline data) and for each 30-s period of exercise and post-exercise forearm occlusion in the isometric and rhythmic handgrip exercises. In the fatigued handgrip test, MSNA was determined in the same manner as in the isometric handgrip; a 2-min handgrip was used as the common non-fatiguing point, and the last 30 s of the exercise were used for the fatigue data.

Heart rate was determined using the R–R interval of an electrocardiogram (ECG), which was performed using bipolar electrodes positioned on the chest (AB118;

Nihonkhoden, Tokyo). Blood pressure was measured using a Finapres blood pressure monitor (Ohmeda Englewood, CO) with the finger cuff on the middle finger of the resting hand. Heart rate and blood pressure were determined in the same segments as the MSNA analysis. Respiratory movements were monitored using a facemask attached to a flow meter with a hot wire (RT-6; Minato Medical, Tokyo). Handgrip force was monitored using a strain gauge attached to a hand dynamometer (TKK5710b; Takei Co., Tokyo), and maximal handgrip force was calculated as the highest value among three trials of a 3-s maximal effort performed over 2–3 min in a standing position. Work performance of the handgrip exercise was represented by the integration of the handgrip force curve.

Exercise tests were performed 2 weeks prior to training (pre-training), 1 week after the cessation of training (1 week post-training), and between 4 and 6 weeks from the end of training (4 weeks post-training). All signals were digitised at 200 Hz through an analogue-digital converter (MP100; Biopac Systems, Goleta, CA) for later processing on a personal computer that was equipped with an online data acquisition programme.

Training

Although strength training could be reveal any specific strength the gain the important factors initial strength gain attributable to neural factors is very high intensity (Kraemer et al. 1996). Thus, intermittent handgrip exercise with maximal effort was used for resistance training, to enhance central motor activity and the number of activated motor units, which correlates with the intensity of muscle force (Grimby 1977). We tested the nondominant arm, as it is used less frequently in daily activities than the dominant arm and is expected to show a greater physiological response to training and at 4 weeks post-training. The training regimen involved 10-s isometric handgrip contractions performed at maximal effort, repeated 10 times at 10-s intervals for three sets per day, 4 days per week for 4 weeks. Subjects in the control group were asked to maintain their normal daily activities.

Statistics

The significance of the main effect was tested by one-way analysis of variance (ANOVA) using time (resistance training) and handgrip exercise, followed by a Tukey-Dunnet post hoc test to detect significant differences (Prism 5; Graph Pad Software, CA). Values are expressed as the mean ± standard error (SEM). A value of $P < 0.05$ indicates statistical significance.

Results

Effects of training

Resistance training increased maximal handgrip force by 6.6% in the TG, whereas the CG showed no change over the same time period (Fig. 1). Total handgrip work during the fatigued handgrip increased by 17.6% after training in the TG. Although endurance time tended to increase after training, the differences among the values for pre-training, 1 week post-training, and 4 weeks post-training (171 ± 32, 190 ± 30, and 185 ± 18 s, respectively) were not significant. No changes were observed in the CG (Fig. 1). Total handgrip work was unchanged for the rhythmic and isometric handgrip exercises in both groups.

MSNA increased from the basal control during the handgrip exercises, and higher activity persisted during post-exercise forearm occlusion in the isometric, rhythmic, and fatigued handgrip exercises (Tables 1, 2, 3, respectively). In the TG, the increase in MSNA was greater during the fatigued handgrip exercise at 1 week post-training (Fig. 2), whereas no change occurred during the isometric or rhythmic handgrip exercise. In the CG, no significant change was noted during any exercise (Fig. 2). The MSNA response did not change during forearm occlusion after any exercise in the TG or CG.

The mean blood pressure was elevated during exercise, and remained high during post-exercise forearm occlusion. No significant difference was observed in the mean blood pressure response at pre-training versus 1 or 4 weeks post-training for the three different handgrip exercises, and the magnitude of the response was identical in the TG and CG. In the TG, the heart rate increased during the handgrip exercises, but no difference in heart rate was observed between the control resting state and during post-exercise forearm occlusion (Tables 1, 2, 3). In the CG, the blood pressure and heart rate responses were identical before and after the experimental period.

Effects of halting resistance training

In the TG, training resulted in an 8% increase in maximal handgrip force, which persisted throughout the subsequent 4 weeks of detraining (Fig. 1). Handgrip force remained stable in the CG throughout the study period. The integrated handgrip force during the rhythmic and fatigued handgrip exercises did not differ in comparison to that observed pre-training (Fig. 1).

At 4 weeks post-training, the MSNA response during the fatigued handgrip exercise decreased compared to the 1 week post-training response and was similar to the pre-training response (Fig. 2). No significant difference in MSNA was noted during the isometric versus rhythmic handgrip exercise. After the detraining period, the MSNA response during post-exercise forearm occlusion did not

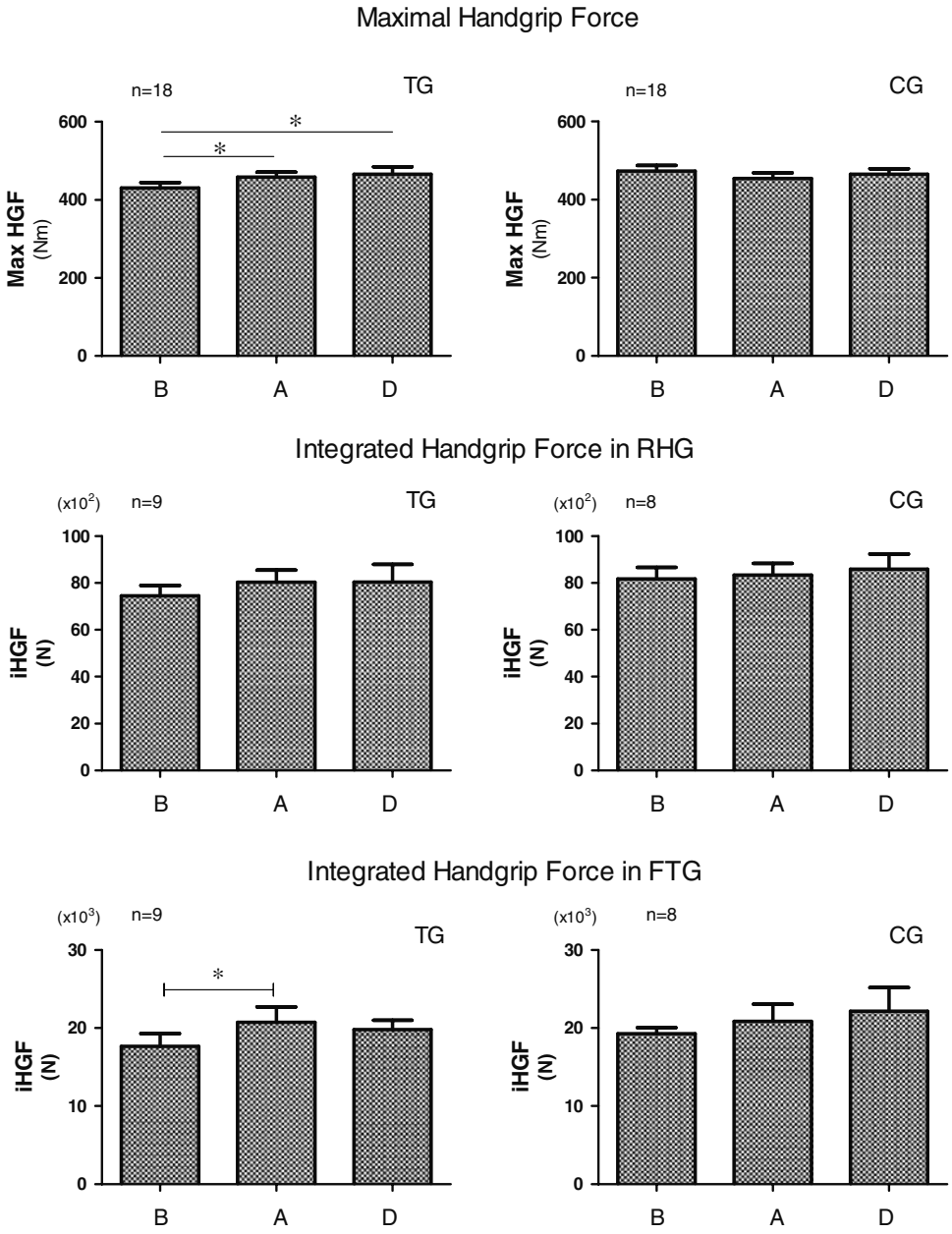

Fig. 1 Maximal handgrip forces (*Max HGF*) and integrated handgrip forces (*iHGF*) in the training (*TG*) and control (*CG*) groups during the rhythmic and fatigued handgrip exercises at pre-training (*B*), 1 week post-training (*A*) and 4 weeks post-training (*D*). * $p < 0.05$ compared to the pre-training values, *n* number of data points

differ from the pre-training or 1 week post-training response, irrespective of exercise mode. In the CG, no significant change in MSNA was observed during any handgrip exercise or post-exercise forearm occlusion.

In both the TG and CG, the responses in heart rate and mean blood pressure during exercise and post-exercise forearm occlusion did not differ significantly at 4 weeks post-training compared to the pre-training or 1 week post-training values (Tables 1, 2, 3).

Discussion

Our results demonstrate that strength training increases MSNA during fatiguing static handgrip exercise, whereas MSNA is restored to the pre-training levels after training is stopped for 4 weeks (i.e., detraining). However, sympathetic activity during post-exercise circulatory occlusion did not change at 1 or 4 weeks post-training. Furthermore, maximal handgrip force increased after strength training, and persisted at this level at 4 weeks post-training.

Training effects on performance

Four weeks of high-intensity resistance training increased the maximal handgrip force. In previous studies, resistance training for less than 6 weeks was typically associated with improved force of muscle contraction, which was produced primarily by increased motor unit recruitment with little muscle hypertrophy or muscle fibre alteration (Lewis et al.

Table 1 Burst frequency (*BF*), total sympathetic nerve activity (*TSNA*), heart rate (*HR*), and mean blood pressure (*MBP*) during the handgrip exercise and post-exercise forearm occlusion (*OCL*) for the isometric handgrip exercise at pre-training, 1 week post-training, and 4 weeks post-training in the training and control groups

			n	Base	IHG1	IHG2	OCL1	OCL2
Trained group								
Pre-training	BF	Bursts min^{-1}	9	19.3 ± 3.5	24.2 ± 1.4	36.2 ± 4.4*	29.7 ± 3.0*	31.5 ± 2.7*
	TSNA	Unit	9	45 ± 3	59 ± 4	111 ± 21*	91 ± 13*	96 ± 16.1*
	HR	bpm	9	67 ± 1	79 ± 3*	85 ± 2*	72 ± 2	69 ± 2
	MBP	mmHg	8	79 ± 3	100 ± 6*	108 ± 6*	98 ± 6*	95 ± 7*
1 week	BF	Bursts min^{-1}	9	18.2 ± 3.4	19.3 ± 3.6	33.2 ± 5.2*	30.0 ± 2.9*	29.8 ± 4.3*
Post-training	TSNA	Unit	9	43 ± 9	48 ± 9	94 ± 19*	92 ± 11*	88 ± 13.9*
	HR	Beats/min	9	67 ± 1	76 ± 2.7*	82 ± 2*	72 ± 2	73 ± 3
	MBP	mmHg	9	76 ± 4	95 ± 8*	105 ± 8*	104 ± 5*	101 ± 6*
4 weeks	BF	Bursts min^{-1}	9	20.3 ± 3.1	26.7 ± 4.4	36.8 ± 6.4*	30.3 ± 4.2*	35.3 ± 4.7*
Post-training	TSNA	Unit	9	49 ± 8	58 ± 12	95 ± 23.4*	76 ± 16	92 ± 18.6*
	HR	bpm	9	65 ± 2	75 ± 2.1*	82 ± 2.6*	73 ± 2*	72 ± 2.2*
	MBP	mmHg	8	77 ± 3	94 ± 6*	104 ± 4*	99 ± 4*	100 ± 4*
Control group								
Pre-training	BF	Bursts min^{-1}	8	14.8 ± 1.1	23.2 ± 2.6*	34.3 ± 2.4*	25.1 ± 2.2*	26.7 ± 2.9*
	TSNA	Unit	8	34 ± 5	63 ± 8.3*	122 ± 13.2*	92 ± 10*	91 ± 12*
	HR	bpm	8	64 ± 1	76 ± 2*	82 ± 2*	70 ± 2.4*	72 ± 2.4*
	MBP	mmHg	8	78 ± 2	103 ± 4*	114 ± 4*	105 ± 4*	107 ± 4*
1 week	BF	Bursts min^{-1}	8	13.5 ± 2.7	22.0 ± 2.4*	37.7 ± 3.6*	23.3 ± 2.8*	24.2 ± 4.3*
Post-training	TSNA	Unit	8	31 ± 7	48 ± 6	122 ± 15.7*	75 ± 10.9*	80 ± 18.5*
	HR	bpm	7	61 ± 2	74 ± 1.3*	81 ± 2.4*	67 ± 3.4*	67 ± 3*
	MBP	mmHg	8	75 ± 2	105 ± 4*	114 ± 4*	103 ± 4*	103 ± 4*
4 weeks	BF	Bursts min^{-1}	8	18.8 ± 1.9	23.6 ± 2.9	42.3 ± 4*	29.2 ± 3.8*	30.6 ± 4.1*
Post-training	TSNA	Unit	8	46 ± 7	59 ± 10	113 ± 11.9*	80 ± 13.5*	85 ± 15.2*
	HR	bpm	8	65 ± 2	77 ± 2*	85 ± 3*	71 ± 2	73 ± 3*
	MBP	mmHg	8	82 ± 2	108 ± 4*	120 ± 5*	106 ± 3*	106 ± 4*

Values represent the mean ± standard error (SEM)

IHG1 and *IHG2* represent the first and second minute of the isometric handgrip, respectively, *OCL1* and *OCL2* represent the first and second minute of the post-exercise forearm occlusion, respectively, *n*, number of data points

* $p < 0.05$ compared to the control base

1984; Narici et al. 1989; Rube and Secher 1990; Sale 1988). Increased central motor nervous activation after training was also reported (Aagaard et al. 2002; Gandevia 2001). This phenomenon may explain the increase in maximal handgrip force observed in the present study. Force output during the fatiguing handgrip exercise increased by 17% after training, whereas the increase in force output during the rhythmic handgrip exercise was insignificant (7%). These findings suggest that short-term strength training improves endurance for isometric contraction, but has only a small effect on anaerobic performance, similar to that seen during an ischaemic rhythmic handgrip (Hansen 1961).

Effect of resistance training on MSNA

Training increased MSNA during contraction in the fatiguing handgrip exercise, whereas no change was observed during the isometric or rhythmic handgrip exercise. In contrast, Ray and Carrasco (2000) found no significant difference in MSNA response during fatiguing isometric handgrip exercises between pre- and post-training. This discrepancy may be attributable to differences in training regimen. The previous study used a 3-min submaximal isometric handgrip at a tension of 30% MVC. In contrast, to activate high-threshold motor neurons, we used an intermittent handgrip performed at maximal effort. The involvement of a greater number of motor units than that involved in a submaximal isometric contraction (Grimby 1977) may stimulate sympathetic muscle efferent activity to a greater extent. In cross-sectional studies, whole-body resistance training decreased the MSNA response (Sinoway et al. 1992) or MSNA remained unchanged (Carter et al. 2003) during fatiguing static handgrip trials, as compared to controls. This discrepancy

Table 2 Burst frequency (*BF*), total sympathetic nerve activity (*TSNA*), heart rate (*HR*), and mean blood pressure (*MBP*) during the handgrip exercise and post-exercise forearm occlusion (*OCL*) for the rhythmic handgrip exercise at pre-training, 1 week post-training, and 4 weeks post-training in the training and control groups

		n	Base		RHG1	RHG2	OCL1	OCL2
Trained group								
Pre-training	BF	Bursts min^{-1}	10	17.7 ± 2.2	30.2 ± 1.5*	38.2 ± 2.8*	23.1 ± 2.2	28.6 ± 2.4*
	TSNA	Unit	10	43 ± 5	89 ± 8*	135 ± 10*	66 ± 6	72 ± 7*
	HR	bpm	10	73 ± 3	91 ± 3*	94 ± 2*	76 ± 3	76 ± 3
	MBP	mmHg	10	99 ± 3	119 ± 4*	127 ± 4*	114 ± 5*	115 ± 5*
1 week	BF	Bursts min^{-1}	10	17.1 ± 2.2	31.0 ± 3.5*	42.2 ± 5.3*	28.4 ± 3*	32.2 ± 2.7*
Post-training	TSNA	Unit	10	40 ± 6	104 ± 15*	157 ± 19*	82 ± 8*	93 ± 12*
	HR	bpm	10	67 ± 2	92 ± 2.8*	96 ± 3.5*	76 ± 3.9*	76 ± 3.8*
	MBP	mmHg	10	92 ± 3	116 ± 6*	122 ± 7*	118 ± 6*	114 ± 7*
4 weeks	BF	Bursts min^{-1}	7	18.4 ± 1.2	31.4 ± 3*	44.8 ± 4*	28.1 ± 2.2*	28.7 ± 2.8*
Post-training	TSNA	Unit	7	48 ± 4	108 ± 6*	152 ± 13*	79 ± 10*	82 ± 7*
	HR	bpm	7	67 ± 2	88 ± 3.2*	92 ± 3*	74 ± 3.2*	74 ± 3.3*
	MBP	mmHg	7	83 ± 3	98 ± 8*	108 ± 8*	103 ± 4*	104 ± 3*
Control group								
Pre-training	BF	Bursts min^{-1}	9	11.2 ± 1.7	23.5 ± 2.2*	35.7 ± 3.4*	22.2 ± 2.7*	22.9 ± 3*
	TSNA	Unit	9	28 ± 5	74 ± 10*	141 ± 16*	80 ± 17*	76 ± 21*
	HR	bpm	9	68 ± 2	82 ± 2.1*	86 ± 3.2*	72 ± 2	71 ± 2
	MBP	mmHg	9	84 ± 2	95 ± 2*	108 ± 2*	106 ± 4*	107 ± 4*
1 week	BF	Bursts min^{-1}	9	12.8 ± 2.2	22.4 ± 2.4*	37.1 ± 3.3*	30.6 ± 3.1*	26.7 ± 3.3*
Post-training	TSNA	Unit	9	31 ± 6	68 ± 9	142 ± 17*	100 ± 16*	86 ± 17*
	HR	bpm	9	66 ± 2	91 ± 2.3*	96 ± 3.1*	76 ± 4*	76 ± 4.2*
	MBP	mmHg	9	78 ± 2	99 ± 3*	108 ± 4*	107 ± 5*	108 ± 5*
4 weeks	BF	Bursts min^{-1}	8	16.7 ± 2.6	24.0 ± 2.1	40.7 ± 2*	29.2 ± 2.6*	28.1 ± 3.1*
Post-training	TSNA	Unit	8	41 ± 7	85 ± 9*	167 ± 11*	92 ± 10*	84 ± 11*
	HR	bpm	8	67 ± 2	88 ± 2.5*	92 ± 2.6*	73 ± 3.5*	74 ± 2.9*
	MBP	mmHg	8	78 ± 3	97 ± 3*	107 ± 3*	105 ± 4*	104 ± 4*

Values represent the mean ± standard error (SEM)

* $p < 0.05$ compared to the control base

RHG1 and *RHG2* represent the first and last 30 seconds of the rhythmic handgrip, respectively, *OCL1* and *OCL2* represent the first and second minute of the post-exercise forearm occlusion, respectively, *n* Number of data points

may reflect differences in subjects or the training of different muscle groups.

When constant handgrip exercises are performed until fatigue, motor nerve activity increases with the onset of muscle fatigue (Sale 1988), and the concomitant increase in perceived exertion and the surface electromyogram are both correlated with increased MSNA (Saito et al. 1989; Seals and Enoka 1989). However, the development of fatigue during sustained muscle contraction decreases after resistance training (Gandevia 2001; Lewis et al. 1984; Rube and Secher 1990), signifying that not only peripheral factors, but also central fatigue factors are involved. In the current study, using the standard 2-min isometric handgrip test, the MSNA response during the handgrip exercise remained unchanged during the subsequent post-exercise arterial occlusion. Furthermore, the MSNA response during post-exercise arterial occlusion after the fatigued handgrip exercise remained unchanged throughout the study period, despite the increase in total handgrip force and a non-significant trend toward increased endurance time (11%) at 1 week post-training. These results suggest that no alteration of metaboreflex intensity reached the maximal level. Therefore, our subjects were thought to be naïve to training and showed sustained central activity during fatigue compared to pre-training (Bigland-Ritchie et al. 1978; Gandevia 2001). Therefore, we propose that an increase in central activity after resistance training contributes to an increased MSNA response.

The MSNA response during rhythmic handgrip performed at maximal effort was not altered post- training, although it increased during the fatigued handgrip exercise. This difference in response may be due to the pattern of

Table 3 Burst frequency (*BF*), total sympathetic nerve activity (*TSNA*), heart rate (*HR*), and mean blood pressure (*MBP*) during the handgrip exercise and post-exercise forearm occlusion (*OCL*) for the fatigued handgrip exercise at pre-training, 1 week post-training, and 4 weeks post-training in the training and control groups

			n	Base	FTG1	FTG2	OCL1	OCL2
Trained group								
Pre-training	BF	Bursts min^{-1}	9	17.1 ± 2.2	37.8 ± 4.2*	40.6 ± 4.4*	24.0 ± 2.5*	28.6 ± 3*
	TSNA	Unit	9	34 ± 4	127 ± 26*	163 ± 32*	81 ± 11*	98 ± 16
	HR	bpm	9	68 ± 2	89 ± 2*	94 ± 3.4*	73 ± 2.4*	72 ± 2
	MBP	mmHg	9	85 ± 4	122 ± 8*	133 ± 9*	111 ± 5*	113 ± 5*
1 week	BF	Bursts min^{-1}	9	18.0 ± 3.4	42.2 ± 5*	52.6 ± 5.8*	30.0 ± 4.2*	32.2 ± 4.2*
Post-training	TSNA	Unit	9	39 ± 6	122 ± 14*	294 ± 147*	96 ± 19*	92 ± 18*
	HR	bpm	9	69 ± 2	88 ± 2.3*	94 ± 3.2*	78 ± 2.1*	79 ± 2*
	MBP	mmHg	9	82 ± 2	113 ± 6*	123 ± 5*	103 ± 5*	100 ± 6*
4 weeks	BF	Bursts min^{-1}	9	20.6 ± 1.9	39.1 ± 4.4*	44.0 ± 5.2*	33.1 ± 4.3*	32.6 ± 3*
Post-training	TSNA	Unit	9	49 ± 4	109 ± 16*	145 ± 34*	84 ± 12	84 ± 14
	HR	bpm	9	67 ± 2	88 ± 6.1*	93 ± 5*	77 ± 2.9*	73 ± 3
	MBP	mmHg	8	82 ± 2	115 ± 5*	123 ± 5*	106 ± 4*	105 ± 5*
Control group								
Pre-training	BF	Bursts min^{-1}	9	16.8 ± 2.6	34.7 ± 3.8*	41.3 ± 3.4*	27.2 ± 3.4*	26.2 ± 3*
	TSNA	Unit	9	41 ± 5	101 ± 10*	148 ± 14*	84 ± 12*	80 ± 12*
	HR	bpm	9	64 ± 2	83 ± 2.8*	90 ± 3*	72 ± 2	72 ± 2
	MBP	mmHg	9	84 ± 3	98 ± 5+	111 ± 4	106 ± 5	106 ± 5
1 week	BF	Bursts min^{-1}	9	15.5 ± 2.7	34.7 ± 4.2*	41.1 ± 4.3*	26.1 ± 2.6*	30.1 ± 2.7*
Post-training	TSNA	Unit	9	36 ± 6	95 ± 13*	147 ± 20*	90 ± 10*	89 ± 14*
	HR	bpm	9	63 ± 3	81 ± 2*	88 ± 3.4*	72 ± 3	73 ± 3
	MBP	mmHg	8	84 ± 3	105 ± 4*	121 ± 6*	108 ± 6*	108 ± 6*
4 weeks	BF	Bursts min^{-1}	7	17.4 ± 1.4	30.5 ± 3.6*	37.1 ± 3.7*	23.8 ± 2.9	28.2 ± 1.9*
Post-training	TSNA	Unit	7	43 ± 5	81 ± 6*	129 ± 19*	73 ± 13	81 ± 11
	HR	bpm	7	65 ± 1	80 ± 3.4*	91 ± 5.7*	73 ± 4	73 ± 3
	MBP	mmHg	7	82 ± 4	106 ± 4*	120 ± 6*	106 ± 6*	106 ± 6*

Values represent the mean ± standard error (SEM)

* $p < 0.05$ compared to the control base

FTG1 and *FTG2* represent the second minute and last 30 s of the handgrip exercise, respectively, *OCL1* and *OCL2* represent the first and second minute of the post-exercise forearm occlusion, respectively, *n* number of data points

muscle contraction. Even if the activity of higher-threshold motor units increases during the post-training rhythmic handgrip exercise, central motor activity is periodically associated with rhythmic muscle contraction, meaning that one half of the exercise duration corresponds to a pause in central motor neuron activity. Thus, the extent of the impinging central sympathetic neurons at a given time during rhythmic handgrip should be small in comparison to the continuous central motor command during fatigued isometric contraction, which may result in an insignificant change in the MSNA response. In addition, maximal rhythmic handgrip with forearm ischaemia was used to stimulate maximally the muscle receptors for a given duration, and the metaboreflex MSNA response was identical to that during the fatigued handgrip. Thus, the strong but relatively small efferent volley from central motor neurons during rhythmic handgrip versus static contraction may have been masked by the central command-induced MSNA increase by enhanced muscle reflexes.

Effects of halting training

Maximal handgrip force remained high at 4 weeks post-training, whereas the MSNA response during the fatigued handgrip exercise decreased after training was stopped and eventually returned to the pre-training level. If an increase in central motor activity after training is a factor in increased maximal handgrip force, a higher MSNA response should be maintained after detraining; however, this was not the case. The observed dissociation may have been caused by the difference in the duration of muscle contraction (e.g., contraction for several seconds in the

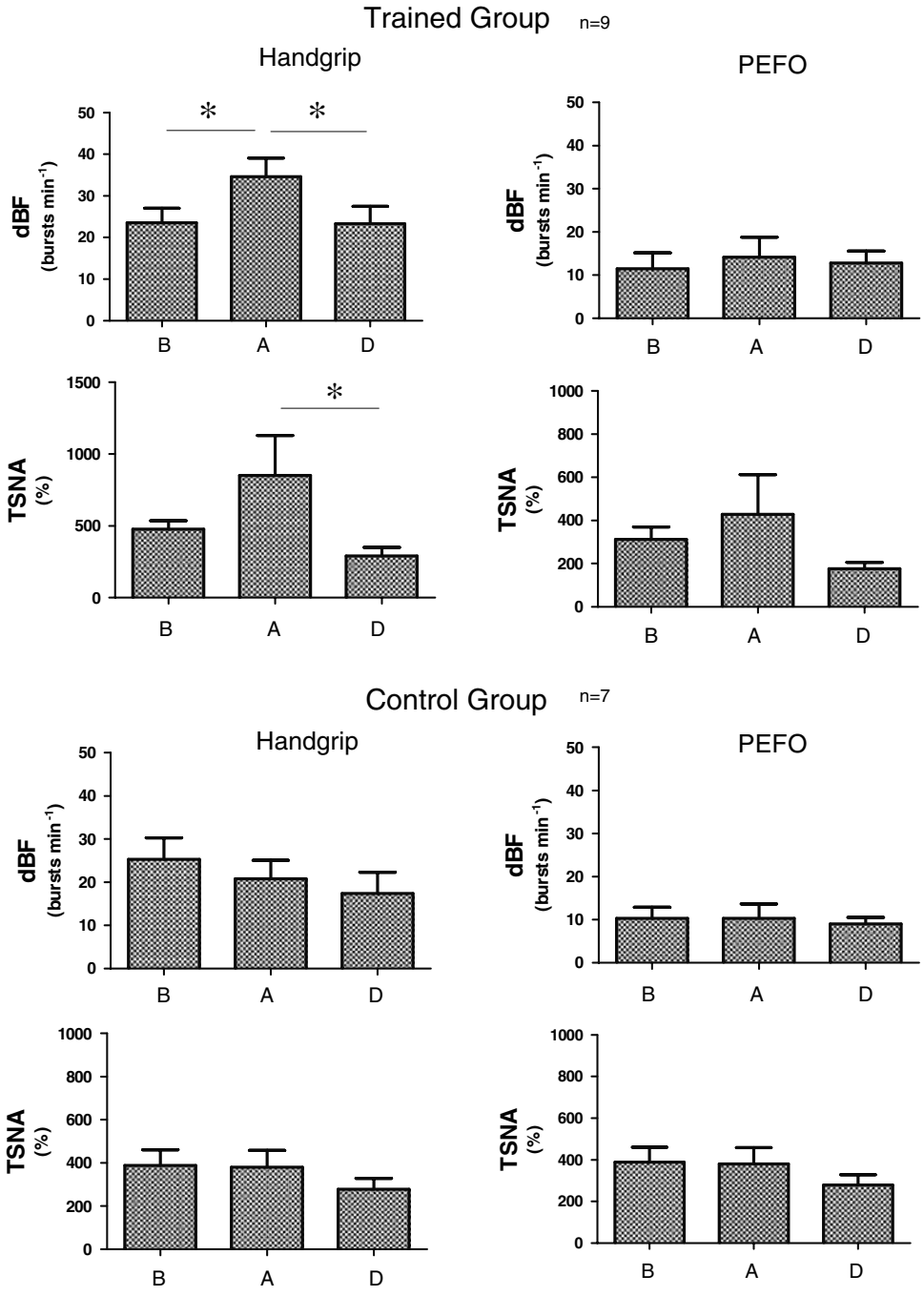

Fig. 2 Comparisons of the changes in burst frequency (*dBF*) and total sympathetic nerve activity (*TSNA*) during fatiguing handgrip exercises (Handgrip) and post-exercise forearm occlusion (*PEFO*) at pre-training (*B*), 1 week post-training (*A*), 4 weeks post-training (*D*) in the training and control groups. * $p < 0.05$ compared to the pre-training or post-training values; *n*, number of data points

maximal handgrip exercise versus contraction for several minutes in the test exercise). Cessation of training may cause a decrease in central motor activity and a subsequent increase in the development of central fatigue during prolonged contraction (Gandevia 2001). Thus, it is believed that neural efferent activity from the central nervous system to the sympathetic nervous centre decreases rapidly after training is halted. At 4 weeks post-training, the MSNA responses during handgrip exercises returned quickly to the pre-training level, even though the metaboreflex MSNA response during post-exercise forearm occlusion was unchanged.

Dissociation of MSNA and blood pressure

The pre-training blood pressure response during fatiguing contraction was similar to that after resistance training, despite the observed increase in MSNA. This dissociation may be explained by differences in sympathetic outflow to the various organs, such as muscle, skin, kidney, and

viscera (Saito et al. 1990). Alternatively, the training of sympatholysis may enhance the modulation of vasodilatation in not only trained skeletal muscle, but also in resting muscle vessels (Green et al. 1994), by increasing the nitrite level. Several studies have demonstrated that the nitrite concentration correlates with the extent of MSNA in resting humans (Skarphedinesson et al. 1997) and with the plasma norepinephrine levels during strenuous exercise (Node et al. 1996).

In summary, short-term high-intensity resistance training resulted in an increased MSNA response during fatigued isometric handgrip, which returned to the pre-training level at 4 weeks after training was ceased, although no significant changes were observed for the metaboreflex responses throughout the experiments. In the standard isometric and ischaemic rhythmic handgrip exercises, the MSNA response was constant throughout the study. Neither the heart rate nor the blood pressure changes at pre-training compared to 1 or 4 weeks post-training, irrespective of the exercise performed. The enhanced MSNA response to exercise after strength training probably involves activation of the central nervous system rather than alteration of the metaboreflex, which indicates that central motor command plays an important role in determining MSNA during exercise and may vary with strength training or effort.

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運動準備期の大脳皮質運動野周辺における酸素動態と循環応答の対応

岩館　雅子[1]　　定本　朋子[2]

要　旨：本研究では，運動準備期の大脳皮質運動野周辺の脳酸素動態と心拍数，血圧および前腕屈筋群の酸素動態を同時計測し，掌握運動の準備関連活動と循環応答の対応を検討した。その結果，運動準備によって，脳のoxyHbとtotalHb，心拍数，筋oxyHbの増加が認められ，血圧には変化がみられなかった。この結果から，運動準備期には，大脳皮質運動野の活動と心拍数および筋血流速度の上昇を同時に生じるという関連性が示唆された。(J Jpn Coll Angiol, 2008, **48**: 389–396)

Key words: near-infrared spectroscopy, heart rate, muscle oxygenation, motor preparation

緒　言

運動時の循環調節には，セントラルコマンドと呼ばれる，高位中枢からの制御が重要な役割を担うといわれている。筋収縮を発現させる運動指令が高位の運動中枢から脊髄α運動ニューロンへと下行する際，それと平行して延髄の心血管中枢に連絡をもち，その経路を介して伝えられる情報をセントラルコマンドと呼んでいる[1]。このようなセントラルコマンドの起源が，徐脳ネコを用いた自発床歩行時には視床下部や中脳にあるとする研究もあるが[2]，島皮質[3]や内側前頭皮質[4]といった大脳皮質にあることを示す研究もみられている[5,6]。また，これらの大脳皮質領域と並び，運動指令に直接かかわる大脳皮質運動野が循環反応の調節に重要であることを示す報告も，動物実験ではみられている。筋収縮発現がない運動閾値下の電気刺激を運動野に与え筋血流が増大することを示した報告[7]や，神経筋遮断により筋収縮のない条件で運動野を刺激すると，活動肢となるべき骨格筋の血流が増加し[8]，また同時に腎のような非活動部位では血流減少がみられることを示す報告[7,9]がある。いずれの研究も運動時の循環調節に運動野の興奮が関与することを示している。このような大脳皮質運動野の賦活と循環反応との関係を検討することは，セントラルコマンドの調節を知るうえで重要な課題である。しかし，ヒトにおける検証は未だ数少なく，これは，動物実験と同様に運動野を電気刺激し，その刺激により生じる筋収縮を無効にする筋麻痺条件(反射性制御をなくす)といった侵襲的手法を適用することが難しいからであったと考えられる。

このような問題があるため，セントラルコマンドに関するヒトの研究では，運動野の直接刺激ではなく，筋収縮のない運動の準備や想起(イメージ)という手法により間接的に運動野を賦活させ，その際にみられる循環反応を検討するという手法がとられてきた。それらの成果によると，運動準備期[10]，運動想起時[11]には運動遂行時に類似した循環反応が生じることが報告されている。しかし，大部分の研究では，運動野の活動指標が同時計測されておらず，皮質活動と循環反応が対応するという実証が得られてはいなかった。また皮質活動を計測した研究では，放射性物質が必要な計測法であるSPECT(単光子放射線コンピュータ断層撮影)が用いられているため[11]，結果を追試することが難しく，また刻々と変動する循環反応との時系列的対応関係という点では限界もみられていた。

一方，運動制御に関する神経科学の研究では，非侵襲的手法である脳波を用い，大脳皮質運動野の活動が

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運動準備期[12]や運動想起時[13]にみられることは多数報告されている。しかしこれらの研究では，研究視点の違いもあり，循環反応との対応についての検討がなされてはこなかった。その理由は，脳波を用いた研究では，加算平均を行うため被験者に同一試行を数十回繰り返し行わせるが，この繰り返しによる慣れや疲労が循環反応を変化させ，両変数の対応関係の検討を困難にするためと考えられた。

以上のような状況の中で，新しい計測手法であるが，近赤外分光法(near-infrared spectroscopy: NIRS)を用いた大脳皮質酸素動態の計測は，非侵襲的に皮質活動を示す指標として注目され，実際に適用されるようになっている[14, 15]。NIRSは時間分解能にも比較的優れ，脳波のような加算を必ずしも必要としないことから，変動しやすい循環反応との対応関係をみるには，現時点では最も適しているといえる。

このような先行研究および実験手法等の問題点を踏まえ，本研究では，運動を遂行しないが皮質運動野が賦活されると考えられる運動準備期という実験条件を設定し，また脳酸素動態をNIRSを用いて計測することにより，運動準備期における大脳皮質運動野の賦活と循環反応との対応関係を検討することにした。

方　法

(1)被験者

右利きの健康な成人女性13名を対象とした[年齢：22 ± 1歳(平均値 ± 標準偏差)，身長：159 ± 4cm，体重：59 ± 9kg，掌握運動による随意最大筋力(maximum voluntary contraction: MVC)：22 ± 1kg]。

(2)実験条件と手続き

被験者は頭部を楽な位置に固定できる椅子に座り，右腕を握力計，左腕を血圧測定台に置いた。握力計および血圧測定台はいずれも心臓位の高さに調節した。本研究は，静的掌握運動を行わない対照条件と運動を行う運動条件の2条件で構成されている(**Fig. 1**)。「運動の準備」以外の意識や構えが条件間で異ならないようにするため，声を出さずに音信号数を数える計数作業を同時に課した。なお，運動準備期に関する先行研究[12]では約10秒以内の比較的短時間の準備期が設定されてきたが，心拍数(heart rate: HR)および動脈血圧は，呼吸性変動(約5秒周期)およびMayer波(約10秒周期)といった長い周期的変動の影響を受けるため，比較的長い運動準備期を設定する必要があった。また予備実験において被験者の眠気や集中力の変化等の影響を少なくするため，本研究では50秒の運動準備期とした。

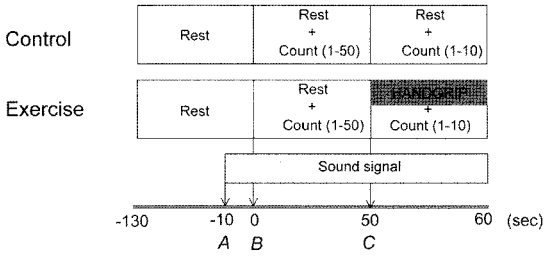

Figure 1　Experimental protocol.
A, start of sound signal; *B*, start of counting the sound signal from one to fifty; *C*, re-start of counting from one to ten while subjects in the Control condition were quietly sitting and the subjects in Exercise condition were sustaining static handgrip contraction.

Fig. 1 に示すように，約2分間の安静の後に，1Hzの音信号を発生させ(**Fig. 1** 内*A*)，その10秒後に「計数開始」の指示が与えられた。指示と同時に，被験者は音信号にあわせて1，2，3…，と信号音を数え始め(**Fig. 1** 内*B*)，50回まで数えた後，再び1から10まで数えた(**Fig. 1** 内*C*)。計数時には声を出したり，回数を予測したりせずに丁寧に数えること，また実験終了後に数えた数の合計値の回答を求めること等を説明した。計数作業の練習後に，対照条件を先に，続いて運動条件を実施した。対照条件では，「掌握運動を行わない条件であるので，安静にして計数作業をする」よう教示した。運動条件で用いる30% MVCの負荷と運動の仕方を練習したのち，運動条件の開始前には，「運動を行う条件であるので，1から10までの再計数作業と同時に右手の掌握運動を行う」よう教示した。本研究では，対照条件を1試行おこなった後，運動条件を1試行おこなった。また，運動条件を後に実施するようにしたが，その理由は，被験者の内省報告において運動条件が先に実施されると運動の想起や構えが対照条件でも起こりやすいことが，予備実験で確かめられたからである。

(3)測定項目

大脳皮質運動野周辺における，酸素化ヘモグロビン(oxyHb)，脱酸素化ヘモグロビン(deoxyHb)および総ヘモグロビン(totalHb)の変化を近赤外分光装置(OMM-3000，島津製作所)により計測した。測定は，大脳皮質左運動野手領域に相当する部位(脳波国際10－20法に基づくC3)に受光プローブを置き，照射プローブは受光プローブを中心に前後および内側・外側方向へ3cm離れた4点に置き，運動野周辺領域全体の酸素動態が計測できるようにした。4点からの照射信号を1つの受光プローブで各々計測し，その4つの計測値を合計して，運動野皮質周辺のoxyHb，deoxyHb，totalHbの測定値とした。これらの信号のサンプリング間隔は装置の最小間隔である10Hzとした。

循環応答の指標として，HR，平均血圧(mean arterial blood pressure: MAP)，心拍出量(cardiac output: CO)を計測した。HRは胸部双極誘導法より導出した心電図波形のR-R間隔により測定した(R-TRIG UNIT，メディセンス)。フィノメータ血圧測定装置(Finometer®，Finapres Medical System)を用いて，連続指動脈波形を測定し，1心拍ごとの指動脈圧波形の積分値の1/2をMAPとした。またフィノメータが内蔵するModel Flow法の解析プログラムを用いて圧波形から1回拍出量を算出し，また1回拍出量とHRの積からCOを算出した。さらに，掌握運動時には主働筋となる前腕屈筋群の酸素動態(oxyHb，deoxyHbおよびtotalHb)を，近赤外分光装置(NIRO-200，浜松ホトニクス)を用いて計測した。計測部である右深指屈筋の筋厚を，あらかじめ超音波Bモード法により測定し，筋厚の最大部位表面に照射と受光のプローブを4cm離して貼付した。計測部位の皮下脂肪厚は0.5±0.1cmであった。データ取込のサンプリング間隔は装置の最小間隔である2Hzとした。

(4)データ処理と検定

各測定項目のデータについて，安静開始後30秒から90秒(**Fig. 1**の−100から−40にあたる)を基準値として，基準値からの変化量を算出した。そしてその変化量を5秒ごとに平均して代表値とした。本研究では，計数開始時(**Fig. 1*B***)から運動直前までの「運動準備期50秒間における代表値」を，条件(対照と運動)×時間(10点の値)の対応のある2元配置分散分析を用いて検定した。なお，結果の図には静的掌握運動開始時のデータを描画しているが，統計的検定データには含まれていない。分散分析の結果，条件の主効果および交互作用が有意と認められた場合，時間ごとの2条件間の平均値の差をpaired t-testを用いて検定した。有意水準を5%未満とした。データは平均値±標準偏差で示した。

結　果

Fig. 2は，運動準備期における左運動野周辺の酸素動態を示している。運動条件では，対照条件に比べoxyHbおよびtotalHbが高く，また安静時基準値(0値)よりも高くなっていた。一方deoxyHbは低下傾向を示すがほぼ基準値に近く，また条件間の相違がみられなかった。

Fig. 3は，運動準備期におけるHR，MAPおよびCOの変化を示している。運動条件のHRおよびCOは，安静時よりも高く，また対照条件よりも高い値を示した。一方，MAPについては2条件間の差がみられなかった。次に右前腕屈筋群における酸素動態の変化(**Fig. 4**)をみると，oxyHbおよびdeoxyHbにおいて条件間の相違がみられた。oxyHbでは運動条件が対照条件よりも高く，deoxyHbでは運動条件の方が低いという相違がみられた。このようなoxyHbおよびdeoxyHbの和であるtotalHbには，条件間の差がみられなかった。

考　察

本研究は，運動を行う運動条件と運動を行わない対照条件の準備期間における大脳皮質運動野周辺の酸素動態と循環応答の変化について検討した。それによって得られた結果から運動野の活動と循環応答との対応について考察する。

(1)脳酸素動態

本研究結果において，運動条件のoxyHbとtotalHbは基準値よりも上昇し，対照条件より有意に高くなっていた。oxyHbが局所脳血流変化の最適指標であるという先行研究[14, 15]を踏まえると，運動野周辺領域における脳血流が運動条件では増加したと考えられる。またラットの脳モデルを用いて，脳血流速度変化による脳血流の増減がある場合と脳酸素消費率上昇に伴う脳血流増加がある場合における変化を比較・検討したHoshiら[16]の研究から，次のようなことがうかがえる。脳酸素消費率の変化がなく脳血流量のみが増加した場合には，本研究と同様にoxyHbとtotalHbが上昇するが，加えてdeoxyHbの低下が典型的で

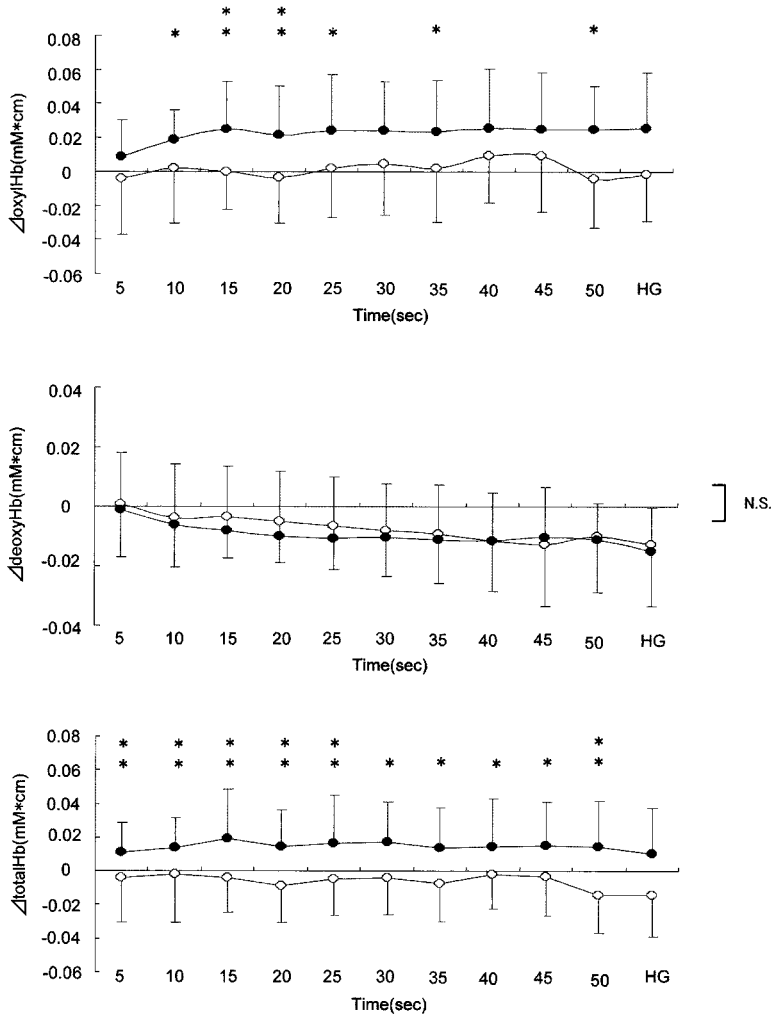

Figure 2 Changes in oxygenated hemoglobin (oxyHb), deoxygenated hemoglobin (deoxyHb) and total hemoglobin (totalHb) obtained from left motor cortex during the preparatory period before handgrip exercise (HG).
Values are means ± SD in 13 subjects. ○, control condition; ●, exercise condition; *, $p < 0.05$; **, $p < 0.01$.

あると報告されている。一方，脳酸素消費率が上昇した場合にはそれを上回る脳血流増加があるため[17]，oxyHbとtotalHbの上昇が観察されるが，deoxyHbは必ずしも「基準値よりも低い」とは限らず，本実験結果でみられたような「基準値に等しい」，あるいは「基準値よりも高い」という種々の反応を示すことが報告されている。このような知見に従うと，本研究でみられた基準値に等しいdeoxyHbの反応は，脳酸素消費率上昇に伴う局所脳血流の増加を反映している可能性が高いと考えられる。

以上のことから，本研究における運動条件では，運動野周辺部位において，神経活動賦活に伴った局所脳血流量の増加が生じたのではないかと推察される。

(2)循環反応と筋酸素動態

循環変数の指標として計測したHRおよびCOにおいては，運動条件の方が対照条件よりも高いという結果が示された。このようなHRの上昇は，運動前の予期心拍反応に関する先行研究によると，ヒトでは心臓迷走神経活動の抑制[18, 19]に起因すると報告されている。一方，意識下動物では心臓交感神経活動の亢進[20]がかかわると指摘されている。本研究においては，どちらの仕組みが運動条件のHR上昇をどの程度説明するのかについては明らかではなく，今後の検証が必要と思われる。

MAPには条件間の相違がなかったが，この結果は，運動条件ではCOが高く総末梢血管抵抗(total peripheral

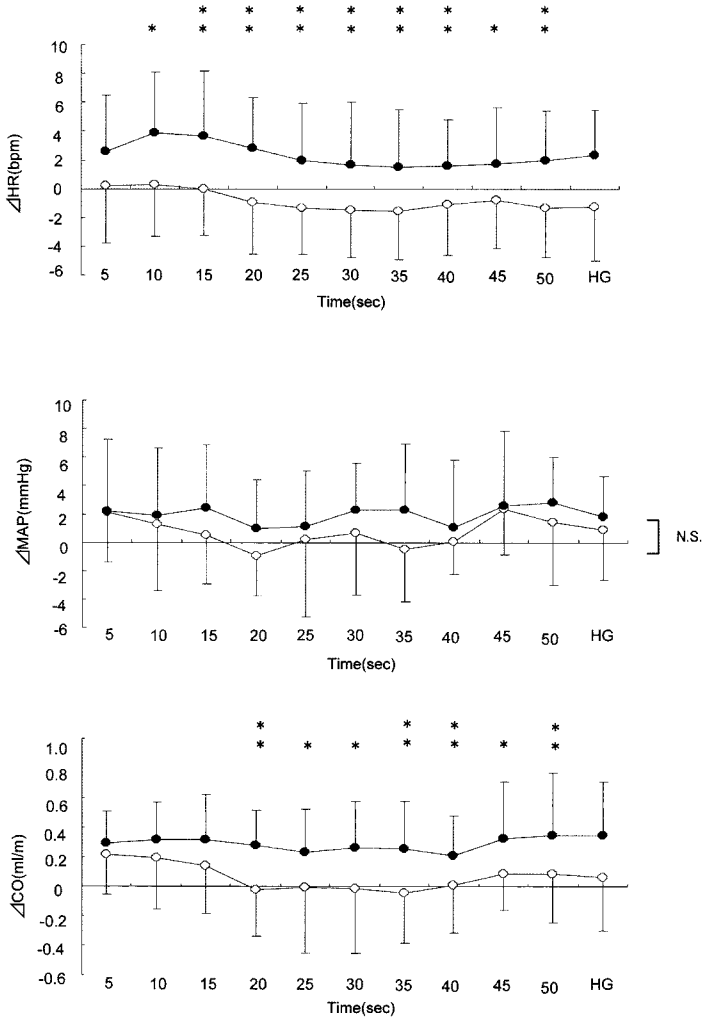

Figure 3 Changes in heart rate (HR), mean arterial blood pressure (MAP), and cardiac output (CO) during the preparatory period before handgrip exercise (HG).
Values are means ± SD in 13 subjects. ○, control condition; ●, exercise condition; *, $p < 0.05$; **, $p < 0.01$.

resistance: TPR)が対照条件よりも低下していることを示している。その部位の正確な同定は難しいが，TPRの低下部位のひとつとして，前腕の筋血管抵抗の関与が考えられる。しかしながら，後述するように，筋酸素動態の結果(**Fig. 4**)において，totalHbに有意差がみられなかったことから，TPRの低下に対する筋血管抵抗の関与は，ごくわずかであったと推察される。

握力発揮の主働筋である前腕屈筋群において(**Fig. 4**)，運動条件においてはoxyHbが基準値よりも上昇しdeoxyHbが低下していた。このような対照条件にはみられない結果は，被験者が筋をわずかに収縮させた結果であるという説明が考えられるかもしれない。しかし，実際に静的掌握運動時の前腕屈筋群のNIRSによる酸素動態を検討したHomma & Kagaya[21]によると，10%MVC以下のような低強度の筋収縮では，酸素の需要と供給が均衡しているため，oxyHbとdeoxyHbは安静時値から有意な変化を示さないと指摘されている。この結果を踏まえると，本研究でみられた運動条件のoxyHbの上昇とdeoxyHbの低下という結果は，筋収縮が引き起こした反応とは考え難い。また，「oxyHbの上昇，deoxyHbの低下，totalHbが変化しない」という運動条件の反応は，Hoshiら[16]の研究成果によると，酸素消費が変化せず，血流速度がわずかに上昇した場合にみられる反応に一致するといえる。これらのことを踏まえると，本研究の運動

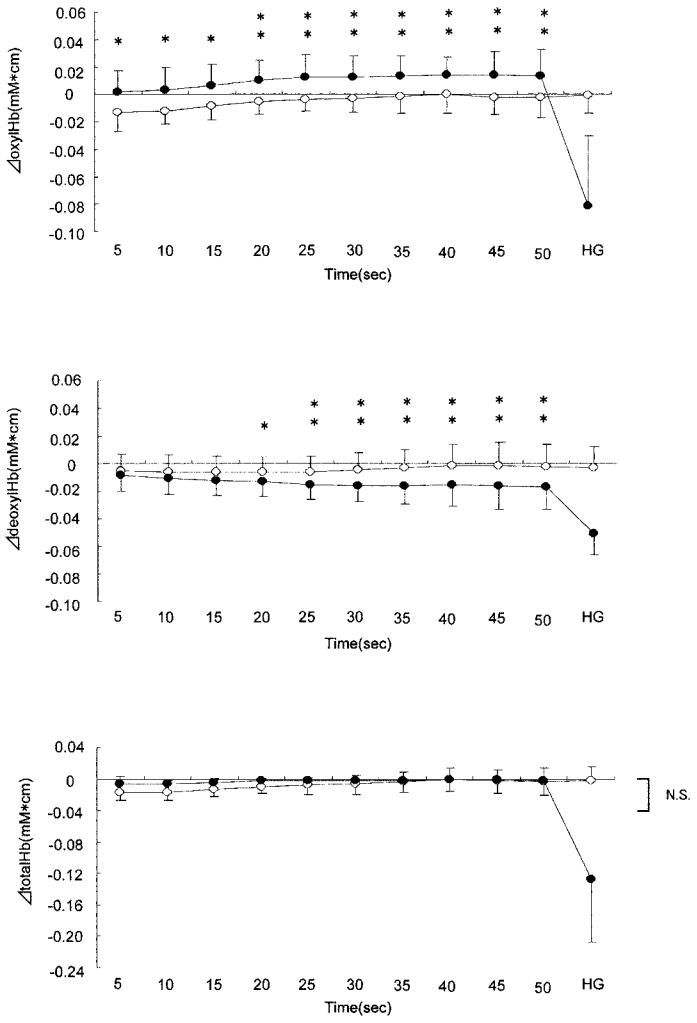

Figure 4 Changes in oxygenated hemoglobin (oxyHb), deoxygenated hemoglobin (deoxyHb), and total hemoglobin (totalHb) obtained from right forearm flexor muscles during the preparatory period before handgrip exercise (HG).
Values are means ± SD in 13 subjects. ○, control condition; ●, exercise condition; *, $p < 0.05$; **, $p < 0.01$.

条件では，安静にしているにもかかわらず，活動肢となる前腕屈筋群において，筋血流速度が上昇していたのではないかと考えられる。

では，このような運動条件におけるHR上昇および前腕血流速度の上昇がなぜ生じたのだろうか。最も考えられる説明は，前述した運動条件における皮質運動野周辺の神経活動の高進の関与であると考えられる。

種々の先行研究において，HRおよび筋血流が大脳皮質活動の影響を受けることが報告されている。例えば，運動をイメージしたり[11]，筋麻痺条件下において運動(attempted exercise)を行う場合には[6]，運動遂行時に類似したHRの上昇が生じることが示されている。また，大脳皮質運動野周辺の神経活動は循環反応の調節に関連することが，皮質電気刺激[7,8]，運動野の機能障害[22]などの報告により示唆されている。いずれの研究においても，運動野の神経活動の変化によって筋血流や心拍または血圧などの循環変数に変化が生じることが報告されており，運動野が循環調節にかかわることが示唆されている。また，運動野と心血管中枢間の連絡については，錐体路ニューロンを刺激することで循環反応がみられることから，錐体路を介する投射が重要であると考えられている[23]。さらに，錐体路ニューロンが結合している脊髄の運動ニューロンにおいて，運動準備期に脊髄介在ニューロン活動の高進が生じていることが近年報告されている[24]。

(3)本研究の制限

本研究ではヒトにおいて運動準備にかかわる皮質活動と循環反応とのかかわりを検討するため，NIRSによる非侵襲的手法を用い，被験者の心理的・生理的拘束が少ない状態で実験ができるようにした。そして，NIRSによって得られる脳血流動態の変化から，運動野周辺の神経活動変化を推察した。しかし，NIRSを脳活動計測に適用する際には，筋への適用時のような較正[25]が不可能であるため，酸素消費量の定量化が難しいといえる。このため，測定データの解釈には制限を伴うといえる。また筋血流の指標として考察を進めた筋酸素動態の変化についても，直接筋組織血流を計測したものではない。さらに，呼吸性およびMayer波による循環応答の変動を避け，運動準備にかかわる脳血流反応と循環応答との関係を取り出すために，本研究では運動準備期を約50秒と長く設定した。このことは安定したデータをもたらせたが，結果の解釈においては，運動準備期に関する神経科学分野の先行研究との比較を困難にしたといえる。

結　論

本研究では，運動を行う運動条件と行わない対照条件という，運動以外の教示はすべて等しく設定した実験プロトコールを用いて，50秒間の準備期における脳酸素動態と心拍数，平均血圧，および筋酸素動態の変化について条件間で比較した。その結果，運動条件の準備期には，大脳皮質運動野周辺において酸素消費率上昇に伴う脳血流量の増加が生じ，心拍数と前腕屈筋群の血流速度も同様に上昇することが示された。このことから，運動開始前から運動準備にかかわる大脳皮質活動の高進と心拍数および筋血流の変化が共に生じる仕組みがあると推察した。

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Relationship between Cortical Oxygenation in the Motor Area and Cardiovascular Responses during the Resting Preparatory Period before Voluntary Exercise

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Key words: near-infrared spectroscopy, heart rate, muscle oxygenation, motor preparation

The present study investigated cortical oxygenation in the motor area (MA) and the concomitant cardiovascular responses during a resting preparatory period either followed by the right handgrip exercise (Ex) or no exercise (Con) in 13 healthy subjects. The oxygenated hemoglobin (oxyHb), deoxygenated hemoglobin (deoxyHb), and total hemoglobin (totalHb) in the left motor cortex were measured by near-infrared spectroscopy. Heart rate (HR), cardiac output (CO), mean arterial blood pressure, and oxyHb, deoxyHb, and totalHb in the right forearm flexor muscles were simultaneously recorded in both Ex and Con experiments. During the preparatory period in Ex, the oxyHb and totalHb in the motor cortex were significantly higher than those in Con, while deoxyHb was similar to that in Con. These changes in Ex indicated a significant increase in regional cerebral blood flow resulting from neuronal activation in MA. In accord with the cerebral changes, HR, CO, and muscle oxyHb were elevated significantly in Ex but not in Con. These results suggested that the increases in HR, CO, and muscle flow rate in Ex were coupled with the cortical activation in MA resulting from exercise preparation.

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Research Report

Quantification of delayed oxygenation in ipsilateral primary motor cortex compared with contralateral side during a unimanual dominant-hand motor task using near-infrared spectroscopy

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ABSTRACT

Using near-infrared spectroscopy (NIRS) techniques, it is possible to examine bilateral motor cortex oxygenation during a static motor task. Cortical activation was assumed to be reflected by increased oxygenation. The purpose of the present study was to examine the time course of oxygenation in the bilateral motor cortex during a low-intensity handgrip task. Six healthy, right-handed subjects participated in the study. The near-infrared spectroscopy probes positioned over the bilateral motor cortex were used to measure the cortical activation throughout a handgrip task carried out. The subjects performed a 3-min handgrip task with increasing intensity in a ramp-like manner [10–30% of the maximal voluntary contraction (MVC) at 6.67% MVC.min^{-1}]. Contralateral motor cortex oxygenation increased significantly from 100 to 180 s after the start of the motor task compared with the baseline value ($p<0.05$). Ipsilateral motor cortex oxygenation also increased significantly from 130 to 180 s after the start of the motor task ($p<0.05$). The onset of increase in oxyhemoglobin ([HbO_2]) and decrease in deoxyhemoglobin ([Hb]) in contralateral motor cortex area (M1) were significantly earlier than in ipsilateral M1 (respectively, $p<0.05$). These results show that there is a delayed oxygenation in ipsilateral primary motor cortex area compared with contralateral side during a unimanual dominant-hand motor task.

1. Introduction

Musce fatigue is characterized by an exercise-induced loss of power- and force-generating ability of the muscle during the course of or after exercise (Bigland-Ritchie and Woods, 1984; Booth and Thomason, 1991; Nybo and Nielsen, 2001; Gandevia, 2001).

Cortical activation was assumed to be reflected by increased oxygenation (Colier et al., 1997, 1999; Kleinschmidt et al., 1996; Obrig et al., 1996). It was recently reported that the

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bilateral primary motor cortex area (M1) reaches a point of deoxygenation during an exhaustive motor task, which suggested the existence of an interhemispheric connection during a motor task (Shibuya and Kuboyama, 2007). An increase in voluntary effort during the prolonged performance of a low-intensity motor task is indicated by an increase in electromyographic (EMG) signals recorded from the contracting muscle (Fuglevand et al., 1993, 1995; Loscher et al., 1996; Yue et al., 1997). These signals indicate that the nervous system attempts to recruit additional motor units to compensate for the decrease in force. Along with the increase in motor recruitment during a fatiguing motor task, there should also be an increased activation of the motor cortex, which sends then efferent commands to the contracting muscle groups. Previous studies have shown that activation in the contralateral M1 increases gradually during motor task and then decreases as exhaustion approaches (Shibuya and Kuboyama, 2007). In our previous study (Shibuya and Kuboyama, 2007), however, oxygenation in the ipsilateral M1 could not be confirmed. Oxygenation in the bilateral M1 decreased at exhaustion simultaneously, which indicates that a connection between bilateral hemispheres was formed during the motor task. The connectivity between bilateral M1 might concern in the familiarization with the motor task, because the familiarization would be plasticized the intercortical neural connectivity. If the subjects in that study (Shibuya and Kuboyama, 2007) would have been more familiar or less familiar with the pinching motor task, or if the intensity of pinching task were lower than that protocol, oxygenation in the ipsilateral M1 might be found. It is needed to confirm the existence in interhemispheric connection during general low-intensity motor task.

Dai et al. (2001) reported bilateral M1 activation during a handgrip task lasting approximately 30 s. This indicates the possibility of the existence of an interhemispheric interaction at or before the start of the motor task. In that case, there should be simultaneous bilateral M1 oxygenation along with increasing intensity of the motor task without reaching exhaustion. If there is delayed oxygenation in the ipsilateral M1 compared with the contralateral M1, it can be considered that the interhemispheric interaction is activated during the course of the motor task. It is important to know when the interhemispheric interaction occurs during the course of a motor task. This can be inferred by observing the increase in bilateral M1 oxygenation during a low-intensity motor task using high temporal resolution techniques (e.g., near-infrared spectroscopy: NIRS).

NIRS allows for noninvasive monitoring of regional changes in cortical tissue oxygenation in response to various stimuli (Colier et al., 1999; Kleinschmidt et al., 1996; Mehagnoul-Schipper et al., 2000; Obrig et al., 1996, 2000). It also permits monitoring of changes in the oxyhemoglobin ([HbO_2]) and deoxyhemoglobin ([Hb]) levels with high temporal resolution. The NIRS method is based on absorption changes that depend on concentration changes of [HbO_2] and [Hb] in the tissue under investigation. In addition, NIRS can monitor changes in cerebral oxygenation during dynamic motor task with high temporal resolution. Using NIRS techniques, it is possible to examine bilateral M1 oxygenation during a static motor task. The purpose of the present study was to examine

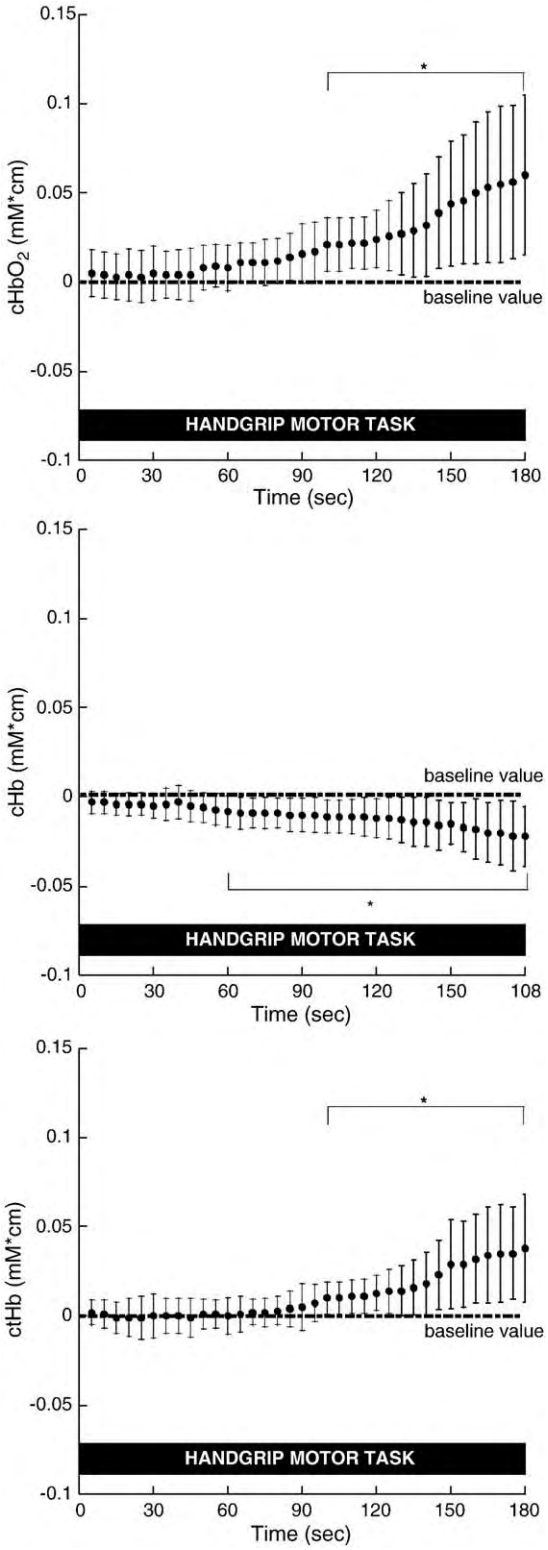

Fig. 1 – Oxygenation in contralateral motor cortex. Changes from baseline values in oxyhemoglobin concentration ($cHbO_2$), deoxyhemogrobin (cHb) and total-hemoglobin (ctHb) in the contralateral motor cortex during a motor task. Values are means ± SD. Asterisks show significant differences, $p < 0.05$.

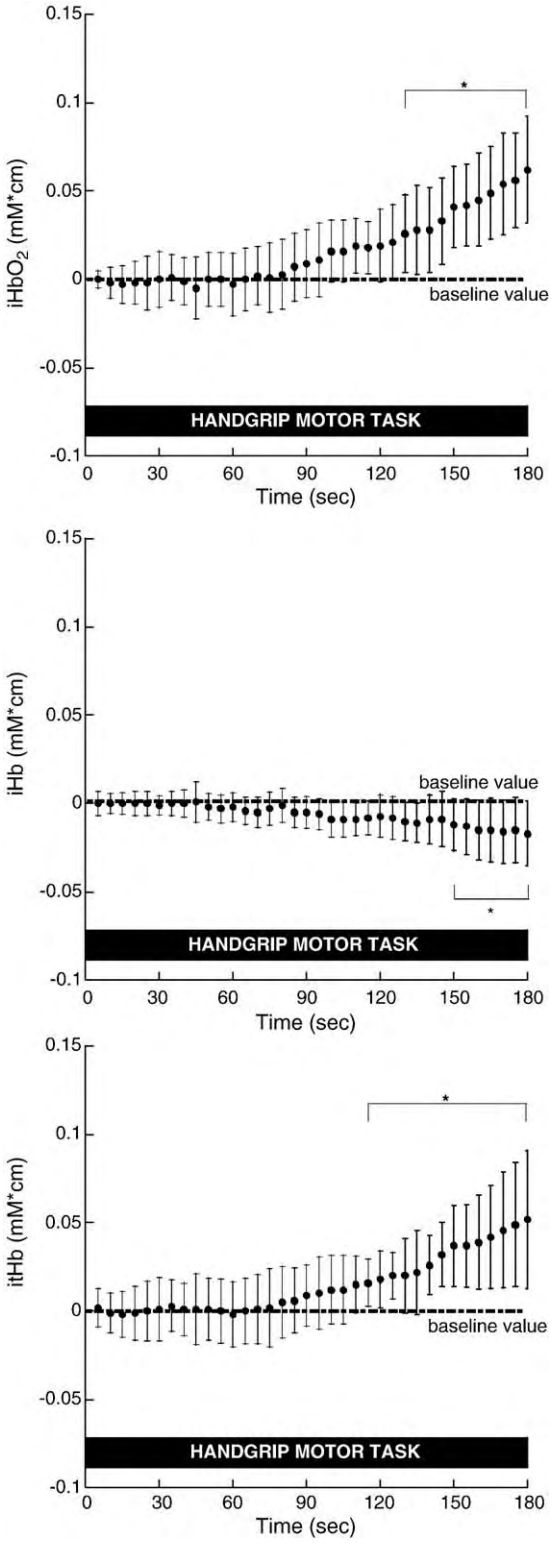

Fig. 2 – Oxygenation in ipsilateral motor cortex. Changes from baseline values in oxyhemoglobin concentration ($iHbO_2$), deoxyhemogrobin (iHb) and total-hemoglobin (itHb) in the ipsilateral motor cortex during a motor task. Values are means ± SD. Asterisks show significant differences, $p<0.05$.

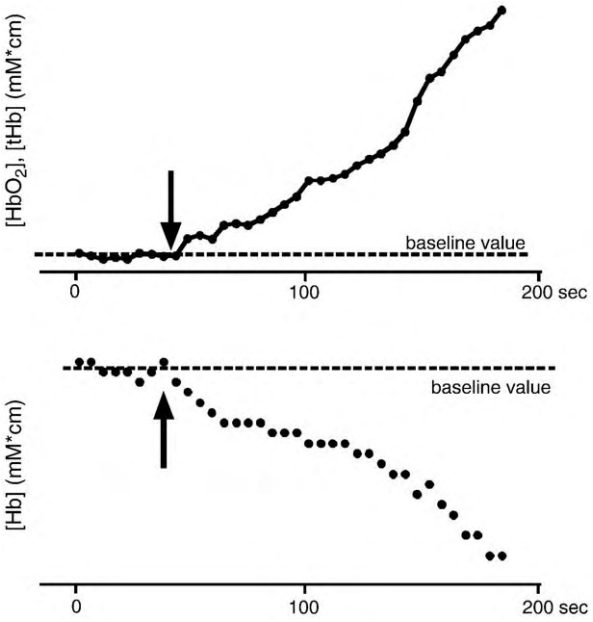

Fig. 3 – Example of the oxygenation response to motor task. Arrows indicate the onset of response to motor task.

bilateral M1 oxygenation during a low-intensity unimanual handgrip task.

2. Results

2.1. *Contralateral (left-sided) M1 oxygenation*

The kinetics of oxygenation in the contralateral M1 during the course of the motor task are shown in Fig. 1. The contralateral [HbO_2] levels changed significantly during the motor task ($F=6.5172$, $p<0.0001$). Compared with the baseline value, the contralateral [HbO_2] levels increased significantly in all subjects, from 100 s (equivalent to 21.1% of the maximal voluntary contraction (MVC)) to 180 s (equivalent to 30% MVC) after the start of the motor task ($p<0.05$).

The contralateral [Hb] levels also changed significantly during the motor task ($F=3.734$, $p<0.0001$). In all the subjects, the contralateral [Hb] levels decreased from 60 to 180 s after the start of motor task compared with the baseline value, more significant from 65 s onward (equivalent to 17.2% MVC) ($p<0.05$).

The contralateral total hemoglobin ([tHb]: [HbO_2]+[Hb]) level changed significantly during the motor task ($F=4.087$, $p<0.0001$). The contralateral [tHb] levels significantly increased from 100 (equivalent to 21.1% MVC) to 180 s after the start of motor task compared with the baseline value ($p<0.05$).

2.2. *Ipsilateral (right-sided) M1 oxygenation*

The kinetics of oxygenation in the ipsilateral M1 during the course of the motor task are shown in Fig. 2. The ipsilateral [HbO_2] levels changed significantly during the motor task ($F=14.799$, $p<0.0001$). In all the subjects, the ipsilateral [HbO_2]

Table 1 – The time for oxygenation after the start of motor task

	Contralateral	Ipsilateral	
HbO_2	50.8±35.4	60.0±31.3	*
Hb	32.5±15.7	94.2±38.1	*
tHb	45.0±17.3	64.2±9.2	*

Asterisks show significant differences between the response on hemispheres ($p<0.05$).

levels increased from 125 s to 180 s after the start of motor task compared with the baseline value, more significantly from 130 s onward (equivalent to 24.5% MVC) ($p<0.05$).

The ipsilateral [Hb] levels also changed significantly during the motor task ($F=3.738$, $p<0.0001$). In all the subjects, the ipsilateral [Hb] levels decreased from 135 to 180 s after the start of motor task compared with the baseline value, more significantly from 155 s onward (equivalent to 27.2% MVC) ($p<0.05$).

The ipsilateral [tHb] level changed significantly during the motor task ($F=3.950$, $p<0.0001$). The ipsilateral [tHb] levels significantly increased from 115 (equivalent to 22.8% MVC) to 180 s after the start of motor task compared with the baseline value ($p<0.05$).

2.3. *The kinetic analysis in bilateral M1 oxygenation*

The hemodynamics ([HbO_2], [Hb] and [tHb]) during the early phase of motor task did not change compared with the resting value (cf. Fig. 3). Then, the oxygenation increased or decreased from the baseline values. The onset of increase in [HbO_2] and [tHb] and decrease in [Hb] was shown in Table 1. The onset of increase in [HbO_2] in contralateral M1 was significantly earlier than in ipsilateral M1 ($t=2.803$, $p<0.05$). The onset of decrease in [Hb] in contralateral M1 was significantly earlier than in ipsilateral M1 ($t=3.323$, $p<0.05$). The onset of decrease in [tHb] in contralateral M1 was significantly earlier than in ipsilateral M1 ($t=3.781$, $p<0.05$).

3. Discussion

Changes in cerebral oxygenation reflect cerebral functional activation (Colier et al., 1997, 1999; Kleinschmidt et al., 1996; Obrig et al., 1996). In the present study, we observed a bilateral increase in M1 oxygenation during the course of a low-intensity static motor task. The increase in ipsilateral M1 oxygenation was delayed compared with the increase in contralateral M1 oxygenation. To the best of our knowledge, this is the first report showing that ipsilateral M1 oxygenation is delayed compared with contralateral M1 oxygenation during the course of a motor task.

It is a well-known fact that EMG signals increase with the passage of time during low-intensity fatiguing exercises. This is because of the recruitment of additional motor units to compensate for the decrease in muscle force production (Bigland-Ritchie and Woods, 1984; Fuglevand et al., 1993, 1995; Yue et al., 1997). The increase in EMG signals during the maintenance of a target force is an indication of fatigue. The M1, which sends efferent commands to contracting muscle groups, should increase its activity to compensate for the decrease in force. Then, it can be easily conceived that the ipsilateral M1 is recruited during the fatiguing motor task in compensation for the contralateral M1 (Ghacibeh et al., 2007). Actually, a few studies have reported that ipsilateral motor activity increases as a response to a greater voluntary effort to perform a motor task (Dai et al., 2001). However, there are no reports about the time lag between contralateral and ipsilateral M1 activation and/or oxygenation during a motor task as assessed using high temporal resolution techniques. The time lag between activation of the contralateral and ipsilateral M1 allows us to study the interhemispheric connection, hemispheric dominancy. In the present study, ipsilateral M1 oxygenation was delayed for approximately 30 (in [HbO_2] changes) to 90 s (in [Hb] changes) compared with contralateral M1 oxygenation. As shown in Table 1, the onset of change in [tHb] in contralateral M1 was faster than [HbO_2] and [Hb] in contralateral M1, while the onset of change in [tHb] in ipsilateral M1 was slower than [HbO_2]. These might reflect the relative delay of blood volume distribution to the activation in ipsilateral M1 compared with in contralateral M1. These findings suggest the existence of an interhemispheric connection and the delayed oxygenation in ipsilateral primary motor cortex compared with contralateral side during a motor task. NIRS permits measurement of cerebral oxygenation (Jobsis, 1977) and has been used to assess brain activation (Chance et al., 1993). While BOLD-fMRI is based on the magnetic field distortions produced by the cerebral blood oxygenation changes, NIRS detects more direct hemodynamic parameters such as changes in [HbO_2] and [Hb]. An increase in neural activation typically produces an increase in [HbO_2] and occasionally a decrease in [Hb] in NIRS measurements (Vilringer and Chance, 1997; Mochizuki et al., 2006). The delayed kinetics in [Hb] in the present study would be due to the lower sensitivity of [Hb] changes than [HbO_2] or [tHb] changes in NIRS measurement (Madsen and Secher, 1999). This is an issue for future study using NIRS and fMRI.

The mechanisms of this phenomenon remain unclear. However, these changes might reflect the interhemispheric modulation of motor activity, perhaps through transcallosal connections or secondary to other cortical projections to the motor cortex on both sides. The increasing oxygenation in the ipsilateral motor cortex shown in the present study suggests the presence of a real-time interaction between bilateral hemispheres during the course of the motor task. The pathways mediating the ipsilateral responses and their relationship to the contralateral corticospinal projections have not been fully defined (Chen et al., 2003). Further research is needed to clarify the interaction between bilateral hemispheres.

NIRS is not a direct measure of synaptic activities or action potentials of cortical neurons. An increase in neural activity in a cortical region increases the local blood flow. On the other hand, the consumption of oxygen in the region does not increase or increases only slightly (Fox and Raichle 1986; Fox et al., 1988). Consequently, the increased blood volume might have a greater proportion of venous relative to arterial blood in the illuminated area. As a result, oxygenation is increased in the area where the uncoupling of the changes in blood flow and oxygen consumption occurs. Nevertheless, the meaning of data obtained from NIRS is still under discussion. In particular,

it is debated whether the NIRS signals reflect the intracerebral blood volume of pial circulation or the blood volume of a more superficial circulation. For example, hyperventilation at rest induces a reduction in [HbO_2] levels, not because of decreased cerebral oxygenation but because the circulating blood volume is reduced as a result of peripheral vasoconstriction (Rostrup et al., 2002).

The NIRS signal changes may be due to excitatory or inhibitory neuronal activity. However, it is impossible to prove whether the NIRS signal changes in the present study are due to excitatory of to inhibitory activity on M1. Therefore, the results of the present study might suggest that ipsilateral M1 activates inhibitory transcallosal systems to inhibit intracortical inhibitory interneurons, leading to increased facilitation of the contralateral M1 in an adaptive mechanism. Further studies are needed to clarify the meanings of the changes of oxygenation in M1 during motor task that derived in the present study, as proposed by the recent previous studies (Benwell et al., 2006).

In the present study, the intensity of voluntary contraction was increased in a ramp-like manner. Contralateral M1 oxygenation increased with the passage of time, which reflected the elevation of required force production. Dettmers et al. (1995) and Dai et al. (2001) reported a linear regression between force production and M1 activation. The results of the present study are consistent with the results of these previous studies. This could be an evidence for monitoring the M1 oxygenation in the present study and that the NIRS signals reflect the cerebral activities.

In conclusion, the results of the present study show a delayed oxygenation in the ipsilateral primary motor cortex during the course of a unimanual low-intensity motor task. The increasing oxygenation in the ipsilateral motor cortex suggests a real-time interaction between bilateral hemispheres during a motor task.

4. Experimental procedures

4.1. *Subjects*

Six right-handed, healthy volunteers (age: 21.4±0.2 y, height: 159.1±1.3 cm, weight: 56.3±1.9 kg, MVC: 315.6±11.8 N) participated in the present study. Informed consent was obtained from each subject after a full explanation of the nature of the study procedure and its noninvasiveness. Throughout the study, the subjects were seated on a comfortable chair in a quiet room. All subjects had no remarkable medical history with sign of cardiovascular, pulmonary, renal, endocrinological, and neurological disorders. The subjects were told not to train hard on the day before the testing and not to exercise on the day of testing. They were also asked to refrain from consuming food or beverages containing caffeine before the test.

4.2. *Near-infrared spectroscopy*

NIRS techniques have been described elsewhere (Elwell et al., 1994). We used a three-wavelength NIRS apparatus (780, 805, and 830 nm; NIRStation, OMM3000, Shimadzu Co., Kyoto, Japan) for measuring motor cortex oxygenation. The optical probe consisted of one emitter and one detector (comprising three separate sensors). These probes were guided on the subjects' heads using glass fiber bundles and positioned over the bilateral motor cortex areas. The distance between the transmitting and the receiving probes was 3.0 cm. The probes were positioned over bilateral motor cortex areas for hand enclosing C3, according to the modified international EEG 10–20 system (American Electroencephalographic Society, 1994), which was checked during a handgrip motor task of the right and left hands to induce functional oxygenation. If no oxygenation changes were detected in response to the task, the probes were moved over several millimeters by trial and error until a consistent oxygenation response was found (Colier et al., 1999; Shibuya and Tachi, 2006; Shibuya and Kuboyama, 2007).

The probes were then fixed to the motor cortex areas. A description of room luminance and any procedures implemented to reduce light interference with the measurements. For quantification of changes in [HbO_2] and [Hb] and total hemoglobin concentrations ([tHb] = [HbO_2] + [Hb]) levels (Delpy et al., 1988), a modified Lambert–Beer law was used, which describes optical attenuation in a highly scattered medium.

The NIRS data were collected with a sample frequency of 10 Hz. The baseline values of [HbO_2] and [Hb] were calculated as an average of 900 data points (90 s) taken during rest at 3 min before the start of the motor task. The values of [HbO_2] and [Hb] during exercise were calculated as an average of 50 data points (5 s).

4.3. *Protocol*

Before the start of the study, the subjects were familiarized with the protocol. They performed a static 3-min right-handgrip task with a ramp-like increase in intensity from 10% MVC to 30% MVC (6.67% min^{-1}). The subjects were seated and were given a handgrip meter (Meiko-sha, Co. Japan) which was held at heart level. During the NIRS experiment, the subjects gripped the device by right hand to match the target force provided by a visual feedback system. The force applied by pinching was sensed and converted to a voltage signal by the pressure transducer in the hydraulic system. The laboratory was air-conditioned and the temperature was maintained at 19–22 °C.

4.4. *Statistical analysis*

To assess for the presence of changes in oxygenation with the passage of time, a repeated ANOVA was applied. Post-hoc analysis using Dunnett's correction was performed on the time series of oxygenation changes in [HbO_2], [Hb] and [tHb] levels. To assess the difference in oxygenation kinetics between hemispheres, it was compared the onset of increases in [HbO_2] and [tHb], and decrease in [Hb] from the baseline values as shown in Fig. 3, then Student's paired *t*-test was performed. A p value <0.05 was considered statistically significant.

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Auxiliary Muscles and Slow Component during Rowing

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Key words
- oxygen uptake kinetics
- muscle oxygenation
- muscle activation

Abstract

The aim of this study was to investigate the contribution of the auxiliary muscles, utilized to sustain the subject's position on the ergometer, to the oxygen uptake slow component phenomenon. Three tests were performed at the same severe relative intensity on a rowing ergometer: a standard rowing exercise test, a rowing exercise performed with the arms and one performed with the legs only. During the three exercise modalities, oxygen uptake, local oxyhemoglobin saturation and surface electromyography signals of the trapezius and vastus lateralis muscles were measured. The slow component amplitude, in absolute values, resulted statistically lower for rowing (343.9 ml·min^{-1}) than for arms (795.6 ml·min^{-1}) and legs (695.8 ml·min^{-1}) exercise modes. The same result was found when the slow component amplitude was calculated as percentage of $\dot{V}O_{2peak}$ (7.1% for rowing; 17.2% for arms; 17.3% for legs). The lower slow component amplitude measured for the rowing exercise mode with respect to both arms and legs modes, demonstrates that the auxiliary muscles involved in the exercise contribute to the increasing energetic cost due to the slow component.

Introduction

In the heavy and severe intensity domain of exercise, the oxygen uptake ($\dot{V}O_2$) response is characterized by three distinct phases. First, comes the cardiodynamic phase, where the increase in $\dot{V}O_2$ measured at the mouth primarily reflects an increase in cardiac output. Second, after ~ 10 – 20 s of exercise, there is the primary response, whereby the $\dot{V}O_2$ increases exponentially as a function of the muscle oxygen uptake. Finally, after ~ 90 – 110 s of exercise, a third or slow component emerges and drives the $\dot{V}O_2$ to above what would be predicted based on the submaximal relationship between $\dot{V}O_2$ and work rate [17]. The slow component phase has been consistently reported to be exercise mode dependent, thereby generating significantly higher results for cycling than for running in all studies comparing the $\dot{V}O_2$ response profile using different exercise modes with the same participants [7,11,14,16 – 18]. Several physiological and mechanical differences between treadmill running and cycle ergometry may account for the observed differences in the amplitude of the slow component. During high-intensity cycling, an increased handlebar grip and rocking of the torso can be observed as subjects' fatigue. It is thus possible that the contraction of auxiliary muscles contributes to the increased energetic cost of cycling, while during running a larger muscle mass is actively involved in maintaining constant the athlete's velocity [11]. On the other hand, rowing involves even more upper and lower-body exercise than running [31]. In particular, the capability to perform better in the rowing ergometer test might, in part, relate to the muscle recruitment alternation strategy evident during fatiguing workouts. Indeed, the optimal muscle recruitment alternation strategy for continuous rowing has been reported to be: starting with all muscles, and then switching between the quadriceps and back muscles at 1-min intervals throughout the rest of the exercise bout [29].

At present, it is impossible to specifically isolate the contribution of discrete muscle groups in the performance of coordinated high-intensity exercise. In an attempt to define the contribution to the slow component coming from muscles used to support the athletes position on the ergometer, rowing was chosen because it is considered to involve most of the body muscle masses [21],

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but also for the possibility to isolate part of the stroking movement making the athletes perform it with the upper or the lower part of the body only. Thus, to verify the hypothesis that auxiliary muscles can actually contribute to the increased energetic cost of exercise, we tested high-level rowers during three rowing modalities performed at the same relative constant workload, each engaging different primary muscle masses. The first one (rowing) consisting of the standard rowing exercise involved no auxiliary muscles; the second one (arms) was a rowing exercise performed with the upper part of the body only, where the auxiliary muscles were those of the hips and limbs, and the third one (legs) consisted of a rowing exercise performed with the lower part of the body only, where the auxiliary muscles were those of the arms and trunk. Moreover, being difficult to objectively quantify the physiological and mechanical contribution of the auxiliary muscles given to the performance of the primarily engaged muscles, we assessed their involvement during the three exercise modes by surface electromyography (sEMG) and tissue oximetry of the vastus lateralis and trapezius muscles.

Methods

Subjects

Twelve male high-level rowers volunteered for the study. However, only seven of them were included in the analysis, mostly due to the difficulty of the youngest athletes to constantly maintain the requested target power for the 8-min duration of the constant intensity tests, especially when the exercise had to be performed in the arms and legs modality. All subjects signed a written informed consent to the experimental procedures. The risks of participation were also fully explained to them and tests procedures were approved by the Institutional Review Board that financed the study (cod. 134/06). The subjects were then instructed to report to the laboratory in a rested and fully hydrated state, at least 3-hours postprandial and to avoid strenuous exercise in the 48 h preceding the tests. To minimize the effects of diurnal biological variations, all tests took place at the same time of day (± 1 h). Subjects mean age, height, and body weight were 18.3 ± 4.9 years, 188.0 ± 5.9 cm, 87.1 ± 5.6 kg, respectively.

Protocol

Participants performed three exercise modalities at the same relative constant workload on a rowing ergometer (Concept II, Concept, Morrisville, VT, USA), which was modified by fixing two handles at the side of the sliding seat. The first one (rowing) consisted of the standard rowing exercise; the second one (arms) was a rowing exercise performed with the upper part of the body only, while the legs were kept straight forward, the feet were positioned on the foot-board and the sliding seat was fixed by a bolt at a distance from the foot-board individually set for each subject according to the length of his legs; the third one (legs) consisted of a rowing exercise performed with the lower part of the body only, while the trunk was kept still and the hands gripped the two handles positioned at the side of the sliding seat. Actual power afforded by the athletes was measured directly on the flywheel, in fact the Concept II ergometer has been reported to underestimate the power developed by the rower by approximately 25 W [10].

To make a valid comparison of $\dot{V}O_2$ kinetics across exercise modes, the tests workloads were normalized using as reference either the mechanical power at which anaerobic threshold (AT) occurred or the mechanical power at which the peak of oxygen uptake ($\dot{V}O_{2peak}$) occurred, determined individually for each exercise mode (rowing, arms and legs). Thus, for each exercise mode, first a pretest was necessary to assess AT and the power at which AT occurred (pAT). Second, another pretest was necessary to assess $\dot{V}O_{2peak}$ and the power at which $\dot{V}O_{2peak}$ occurred ($p\dot{V}O_{2peak}$). From these results the workloads for the constant intensity tests (p70%Δ) were calculated as pAT plus 70% of the difference between $p\dot{V}O_{2peak}$ and pAT ($p70\%\Delta = pAT + [(p\dot{V}O_{2peak} - pAT) \times 0.7]$). The constant intensity tests performed at p70%Δ were carried out a few days later. The three exercise modes procedure (rowing, arms and legs) were administered in a random order on three different days.

Pretests

In the Concept II ergometer resistance is generated by the spinning flywheel, thus, the faster the athlete makes the flywheel spinning, the more resistance there will be. However, in our study the flywheel was attached to the sliding sledge during rowing and legs exercises, while during the arms exercise it was attached to the handlebars. Due to the longer movement excursion allowed to the handlebars (70 – 110 cm) with respect to the sledge (45 – 55 cm), during the arms exercise the athletes were able to produce a greater mechanical power than during the legs exercise. Therefore, the requested initial mechanical power for arms pre-tests was set to a higher value than for the legs exercise, the highest initial power was requested for rowing as this exercise utilizes the larger muscle mass to actively produce mechanical power. Before starting the AT tests, subjects warmed-up for 15 min, rowing at a freely chosen intensity on the rowing ergometer and then spent 5 min recovering. At the end of the 5-min recovery period, a first capillary blood sample was collected. The initial workload was 100 W for the rowing exercise mode, and 80 W and 40 W for the arms and legs exercise modes, respectively. Subjects completed 4 – 5 stages of 6-min duration each, with a workload increase of 50 W and 40 W between stages for the rowing and for the arms and legs exercise modes, respectively. Between stages, 40 – 60 s of rest was necessary to collect capillary blood samples and immediately analyze them for the determination of blood lactate concentration ($[La]_b$). The tests were completed when $[La]_b$ reached a value equal to or higher than 5 mM. The pAT was assessed as the mechanical power corresponding to an increase in $[La]_b$ of at least 1 mM between 3.5 and 5 mM [2].

Approximately two hours later, subjects underwent a continuous incremental test to determine $\dot{V}O_{2peak}$. Subjects started the exercise at a workload of 100 W for the rowing exercise mode, and of 80 W and 40 W for the arms and legs exercise modes, respectively. The workload was then increased by 25 W every min up to volitional exhaustion for the rowing exercise mode and by 20 W for both the arms and legs exercise modes. Beyond volitional exhaustion attainment, the achievement of $\dot{V}O_{2peak}$ was also ensured by one of the following criteria: a $\dot{V}O_2$ change less than 2.1 $ml \cdot kg^{-1} \cdot min^{-1}$ between workloads, heart rate reaching ± 5 bpm of the age adjusted maximal, respiratory exchange ratio higher than or equivalent to 1.15, and blood lactate accumulation higher than 8 mM. Gas exchanges were continuously recorded at every breath and $\dot{V}O_{2peak}$ was considered as the highest value obtained from the $\dot{V}O_2$ data averaged over 30 s. $p\dot{V}O_{2peak}$ was determined as the lowest workload at which $\dot{V}O_{2peak}$ occurred.

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Constant intensity tests

Before starting the test, subjects warmed-up for 15 min, rowing at a light intensity freely chosen by each subject and then recovered for 5 min. The test protocol consisted of 2 min of seated rest on the rowing ergometer, during which resting values were recorded (baseline $[La]_b$, $\dot{V}O_2$ and local muscle oxygen saturation [SO_2]), followed by 8 min of exercise at the mode specific p70%Δ. The workload sustained by the subjects was recorded by a computer connected to the monitoring and storing device of the ergometer (PM3 LogCard, Concept, Morrisville, VT, USA). Subjects were asked to repeat the test in case the range of excursion exceeded ± 10 W from the predetermined workload. During the test, local muscle oxyhemoglobin saturation and surface electromyographic activity were monitored on the vastus lateralis and trapezius muscles, since both muscles are reported to be involved in most of the rowing phases [21].

Blood lactate concentration

For $[La]_b$ measurement, twenty µl of arterialized capillary blood were taken from the earlobe and $[La]_b$ values were determined by an amperometric method (EBIO Plus, Eppendorf, Hamburg, Germany). For all pretests and constant intensity tests, $[La]_b$ was measured before, right at the end of the test and after 3, 6 and 9 min of recovery. For the AT tests, $[La]_b$ was also measured at any recovery period between stages.

Surface electromyography

During the constant intensity tests, sEMG was recorded from left trapezius and vastus lateralis muscles (Opto 16, Prima s.r.l., Turin, Italy) for each exercise mode. The sEMG was sampled at 2048 samples per second. After gathering, data were band pass filtered (0 – 350 Hz) and full-wave rectified. Due to enormous bulk of data derived from such a high sample frequency and since our analysis focused on the third phase of oxygen uptake kinetics, muscle activation was recorded only during the last 2 min of exercise.

Local muscle oxyhemoglobin saturation

Local muscle oxyhemoglobin saturation was continuously assessed (with a sampling time of 0.175 s) during the three constant intensity tests by near infrared spectroscopy (NIRS). This technique, based on the relative transparency of muscle tissue to the near-infrared light (700 – 1100 nm), measures the relative concentration changes in oxyhemoglobin [O_2Hb] and deoxyhemoglobin [HHb] besides tissue SO_2. The principles and the apparatus of NIRS, in general, as well as its applications on muscle studies have been reviewed [8,9,15,22]. Left vastus lateralis and trapezius SO_2 were measured simultaneously by a two-channel, four-wavelength tissue oximeter (NIRO-300, Hamamatsu Photonics, Hamamatsu City, Japan). The design, the features, the calibration of this device and the measured parameters have been previously described [30]. SO_2, calculated as $[O_2Hb/(O_2Hb + HHb) \cdot 100]$, reflects predominantly the mean arteriolar, capillary and venular O_2 saturation with a minor (less than 20%) contribution from myoglobin [26]. The reliability of the NIRO-300 in measuring SO_2 has been assessed both *in vitro* on tissue-like phantoms, and *in vivo* [8,29]. The NIRO-300 optical probes (each consisting of a source and a detector at 4.5 cm apart) were kept at a constant distance and geometry by a rigid rubber shell which in turn was firmly attached by a double-sided adhesive sheet to the skin covering the major head of the two muscle groups. One optical probe was positioned 10 – 12 cm above the knee, parallel to the major axis of the vastus lateralis muscle. The other probe was positioned 5 – 6 cm from the acromion parallel to the major axis of the trapezius muscle. An elastic band (Tensoplast, Smith+Nephew, MediLimited, Hull, UK) was also used to further secure the probes. The margins of the rubber shells were marked in order to facilitate their repositioning.

Muscle masses

In order to assess the relative contribution of upper and lower body muscle masses of rowers to the active work, the subject's body composition was evaluated for each body part. Fat mass (FM), soft fat free tissue (SFFT), and bone mineral content (BMC) were measured with a dual energy X-ray absorptiometry (DXA) total body scanner (model DPX, software version 3.6; Lunar, Madison, WI, USA) that used a constant potential X-ray source at 12.5 fJ and a K-edge filter to achieve a congruent beam of stable dual energy content (40 and 70 keV) [12].

Oxygen uptake

Pulmonary ventilation (in BTPS), O_2 uptake (in STPD), and CO_2 output (in STPD) were continuously measured at the mouth on a breath-by-breath basis by a computerized system (Quark b^2, Cosmed, Rome, Italy), which was calibrated before each test according to the manufacturer's instructions, using gases of known concentration and a precision three-liter syringe. The system was also calibrated to calculate the transient lag time required by the gas sample to pass through the sampling line before being analyzed.

Heart rate

During all tests, subjects wore a heart rate (HR) transmitter (Polar, Electro, Kempele, Finland) and their HR was registered at every breath by the Quark b^2 software.

Data analysis

Blood lactate concentration

Blood lactate differences between exercise modes were analyzed for baseline concentration values and for accumulation values after constant intensity exercises. The latter was calculated as the difference between the peak value measured after the test and the baseline value ($\Delta[La]_b$). Blood lactate accumulation contribution to the total energy cost of exercise was also measured as follows: $[(\Delta[La]b \times 3) \times kg]$ for each minute of exercise [13], the result was calculated as percentage of the highest oxygen uptake value achieved during the constant intensity tests.

Surface electromyography

The sEMG data were divided for each stroke, the single strokes were time aligned into percentage points with 0% representing the catch position. Mean values over the 25 – 30 strokes executed by the subject in the last minute of exercise are reported as mean values ± 1 SD on separate graphs for each monitored muscle. The sEMG data were collected upon the sliding seat or handlebar range of movement (**Fig. 1**).

Local muscle oxyhemoglobin saturation

The decrease in SO_2 (A_{SO2}) was calculated as the difference between the average value of the last min of exercise and the average value over the last 2 min of resting baseline measurement.

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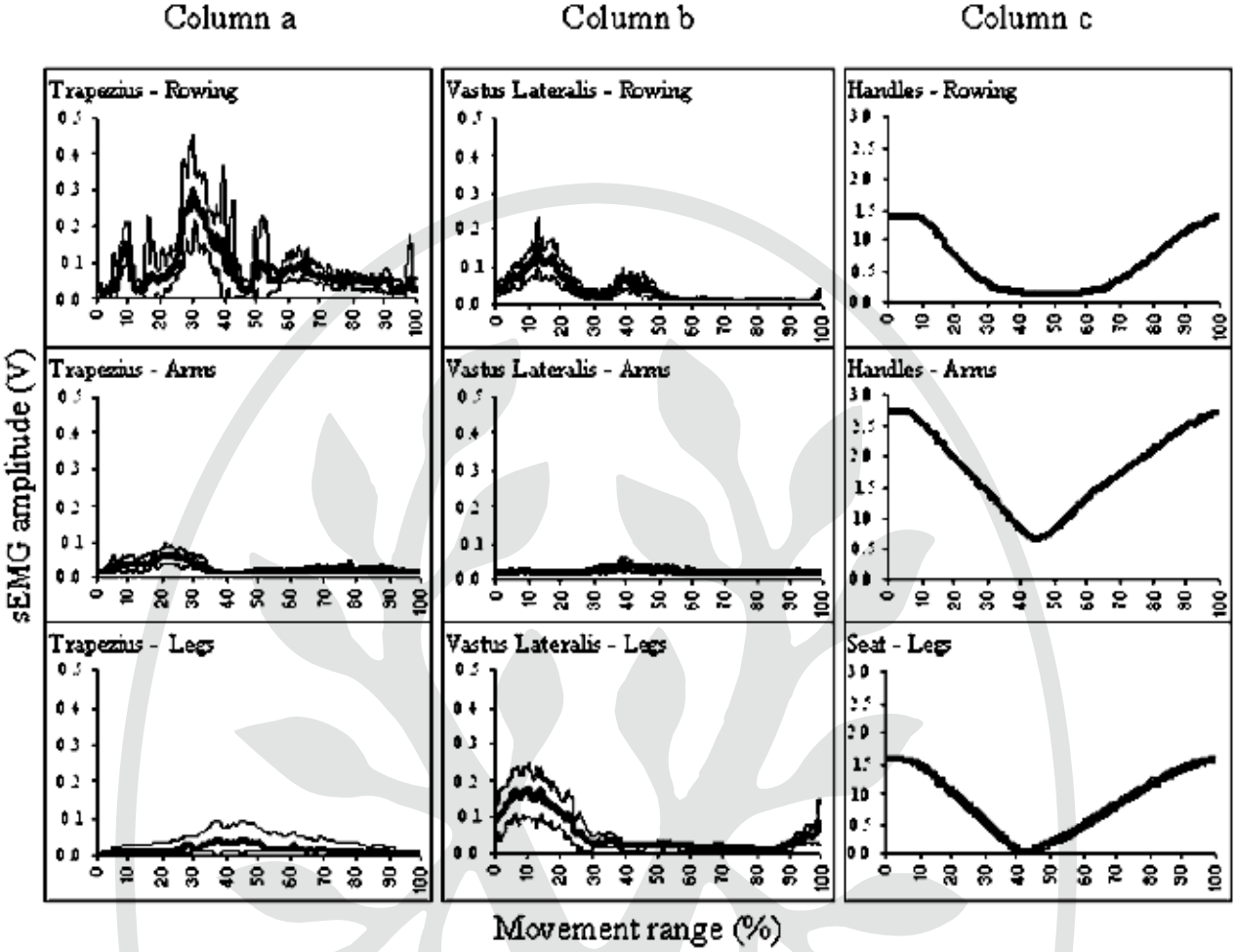

Fig. 1 a to **c** Surface electromyography registration of the pattern of activation during rowing, arms and legs exercise modalities (mean of the last minute of exercise, about 25 strokes, performed by 2 subjects) of the trapezius (Column **a**), vastus lateralis (Column **b**) muscles and of the sliding seat and handlebar (Column **c**) during the three exercise modes. The x axis of each graph represents a complete stroke, each start is in the forward position with the legs completely bended and the arms stretched (0%), each end is in the same position (100%).

Muscle masses

FM was calculated from the soft tissue attenuation ratio, which was defined as the ratio of beam attenuation at the lower energy relative to that at the higher energy. The percentage of fat mass relative to total body mass (%FM) and the fat free mass (FFM in kg) were calculated as:

$$\%FM = (FM/[FM + SFFT + BMC]) \cdot 100$$
$$FFM\ (kg) = (SFFT + BMC)\ (kg)$$

The reproducibility of the DXA instrument used in the present study has been previously reported for different body composition measurements [12]. From the SFFT value of the upper body part the percentage of weight of the viscera was subtracted in order to obtain a value as close as possible to the real muscle mass (MM). In agreement with the description of muscles involved in rowing [21], muscle masses were divided into the upper and lower body compartments, so that values corresponding to the primarily engaged muscle masses in rowing (whole body: MM_{pRow}), arms (upper body: MM_{pArms}) and legs (lower body: MM_{pLegs}) exercise modes were assessed. In the same way, the lower part of the body was considered as auxiliary in the arms, and the upper part of the body in the legs exercise mode, respectively.

Oxygen uptake kinetics

Since breath-by-breath $\dot{V}O_2$ data contain occasional breath values that result from swallowing, coughing, or premature ending of the breath for some other reason, data were first manually filtered to remove outlying breaths, defined as values deviating by more than three standard deviations [20]. To further analyze the character of the random $\dot{V}O_2$ fluctuations, the standard deviations between each breath were calculated during the last minute of the baseline registration and during the last minute of the test where peak $\dot{V}O_2$ values were reached [20]. $\dot{V}O_2$ kinetics were then mathematically modeled through a nonlinear regression technique, an iterative process ensured the sum of squared error was minimized. The mathematical model that best fitted our data consisted of three exponential terms described as follows [4, 5]:

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Table 1 Results of the parameters measured during the pretests

	Rowing	Arms	Legs
WL at pLT (W)	215.6 ± 47.2	136.67 ± 47.1*	99.7 ± 18.3**
WL at 70%Δ (W)	341.8 ± 50.1***	242.7 ± 68.8	157.7 ± 16.7
WL at $\dot{V}O_{2peak}$ (W)	395.9 ± 52.6***	288.1 ± 80.6	182.6 ± 18.1
WL at 70%Δ (%)	86.2 ± 1.7	84.2 ± 2.4	86.4 ± 2.2
$\dot{V}O_{2peak}$ (ml·min^{-1})	5095.9 ± 708.2	4505.3 ± 871.5	4057.4 ± 864.4**
$\dot{V}O_{2peak}$ (ml·kg^{-1}·min^{-1})	58.3 ± 5.3	51.4 ± 7.2	46.4 ± 8.1**

WL at pLT (W): workload corresponding to the power at lactate threshold in Watts; WL at 70%Δ (W): work-load at 70% of the difference between the power at $\dot{V}O_{2peak}$ and the power at lactate threshold in Watts; WL at $\dot{V}O_{2peak}$ (W): workload corresponding to the power at $\dot{V}O_{2peak}$ in Watts; WL at 70%Δ (%): workload at 70% of the difference between the power at $\dot{V}O_{2peak}$ and the power at lactate threshold in percentage of the power at $\dot{V}O_{2peak}$; $\dot{V}O_{2peak}$: peak $\dot{V}O_2$ value measured during the test. * $p < 0.05$ between rowing and arms; ** $p < 0.05$ between rowing and legs; *** $p < 0.05$ between all exercise modes

$$\dot{V}O_2(t) = \dot{V}O_2(b) + A_0\,(1 - e^{-t - TD0/\tau0}) + A_1\,(1 - e^{-(t - TD1)/\tau1}) + A_2\,(1 - e^{-(t - TD2)/\tau2}) \quad (1)$$

where $\dot{V}O_2(b)$ is the average value over the two min of resting baseline measurement (ml·min^{-1}); A_0, A_1 and A_2 are the asymptotic amplitudes for the exponential terms (ml·min^{-1}); τ_0, τ_1 and τ_2 are the time constants (s); and TD_0, TD_1 and TD_2 are the time delays (s). The phase one term was terminated at the start of phase two (TD_1) and was assigned the value for that time ($A_{0'}$):

$$A_{0'} = A_0\,(1\text{-}e^{-TD1/\tau0}) \quad (2)$$

$\dot{V}O_2$ at the end of phase one ($A_{0'}$) and the amplitude of phase two (A_1) were summed to calculate the amplitude of the fast primary component ($A_{1'}$). The amplitude of the fast primary component ($A_{1'}$) and the amplitude of the slow component (A_2) were summed together to obtain the gain of $\dot{V}O_2$ at the end of exercise ($\dot{V}O_{2net}$) and then added to the baseline $\dot{V}O_2$ value to calculate the highest oxygen uptake value achieved during the test ($\dot{V}O_{2tot}$).

Slow component relative to primarily engaged muscle mass

Since the rowing exercise modality requires the involvement of almost all muscles in the body [31], the slow component amplitude measured in ml·min^{-1} during this exercise mode (A_{2Row}) divided per kg of whole body muscle mass (MM_{wb}) was considered as the reference value for the $\dot{V}O_2$ slow component produced by each kilogram of primarily engaged muscle mass (A_{2pRow}):

$$A_{2Row}/\,MM_{wb} = A_{2pRow}$$

This value was multiplied by the kilograms of the primarily engaged muscle masses of the upper (MM_{pArms}) and the lower (MM_{pLegs}) part of the body separately, in order to obtain the $\dot{V}O_2$ slow component value deriving from the contraction of the primarily engaged muscles in the arms (A_{2pArms}) and legs (A_{2pLegs}) exercise modes, respectively.

$$A_{2pRow} \cdot MM_{pArms} = A_{2pArms}$$
$$A_{2pRow} \cdot MM_{pLegs} = A_{2pLegs}$$

Slow component relative to auxiliary muscle mass

The value calculated as the $\dot{V}O_2$ slow component deriving from the primarily engaged muscle masses was subtracted from the total A_2 measured in the arms (A_{2Arms}) and in the legs (A_{2Legs}) tests, in order to obtain the part of the $\dot{V}O_2$ slow component that should be generated from the auxiliary muscles (A_{2aArms} and A_{2aLegs}):

$$A_{2Arms} - A_{2pArms} = A_{2aArms}$$
$$A_{2Legs} - A_{2pLegs} = A_{2aLegs}$$

Statistical analysis

Once normal distribution of data was ensured, differences between the rowing, arms and legs exercise modes were evaluated by means of a one-way analysis of variance (ANOVA). Tukey's post hoc analysis was carried out when appropriate. Differences between two exercise modes were evaluated by the Student's *t*-test. The level of significance was set at $p < 0.05$. Results are reported as means ± SD.

Results

Pretests

Values measured during the pre-tests are reported in **Table 1**. The workload corresponding to 70%Δ was always statistically different between exercise modes ($p < 0.0001$), with the lowest values reported for legs and the highest values for rowing. However, when the workload at 70%Δ was calculated relative to the specific workload at $\dot{V}O_{2peak}$, it no longer showed significant differences between exercise modes ($p = 0.56$).

Blood lactate concentration

Blood lactate concentration measurements before and after the constant intensity tests showed no differences between exercise modes either for baseline $[La]_b$ values ($p = 0.12$), or for $\Delta[La]_b$ ($p = 0.40$). There were also no differences ($p = 0.95$) found in the percentage contribution of $\Delta[La]_b$ to total energy cost resulting of 2.4 ± 0.8%, 2.4 ± 0.8%, 2.5 ± 0.5%, for rowing, arms and legs, respectively.

Surface electromyography

The sEMG clarified the extent and the active involvement of the trapezius and vastus lateralis muscles in the three exercise modes (**Fig. 1**). During rowing, both muscles were markedly active during the catch phase with a sEMG peak at 30% of the stroke for the trapezius and at 15% of the stroke for the vastus lateralis. The trapezius muscle resulted active throughout the entire stroke, while the vastus lateralis muscle was almost silent

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between 60% and 90% of the stroke. During the arms and legs exercise modes, the amplitude of the sEMG signal recorded on the trapezius muscle was much lower than during rowing. Vastus lateralis was 3 times less activated in arms than in rowing and slightly more activated during legs than during rowing. During arms and legs exercises, the pattern of activation of both muscles differed from that of rowing, showing an earlier or later peak of activation, as reported in **Fig. 1**.

Local muscle oxyhemoglobin saturation

SO_2 measured both in the vastus lateralis and the trapezius muscles, after an initial drop (about 30 s after the onset of the exercise), slightly decreased up to the end of the exercise. The A_{SO2} was more pronounced for the vastus lateralis muscle than the trapezius during the rowing and legs exercise modes, whilst during the arms exercise mode a more consistent decrease was observed in the trapezius muscle (**Fig. 2**). Indeed, the A_{SO2} of the vastus lateralis muscle resulted significantly lower during the arms exercise mode (– 11.1 ± 4.6%) as compared to both the rowing (– 23.1 ± 5.3%; p = 0.001) and the legs exercise modes (– 20.5 ± 7.6%; p = 0.009). The A_{SO2} of the trapezius muscle during the legs exercise mode (– 11.4 ± 6.7%) was significantly lower than during both the rowing (– 22.2 ± 8.9%; p = 0.02) and the arms exercise mode (– 23.8 ± 9.0%; p = 0.01). When the trapezius and the vastus lateralis muscles were utilized as auxiliary muscle masses, they showed no significant differences between A_{SO2} values (p = 0.94). The same result was found when these muscle masses were acting as primarily engaged in the arms and legs exercise modes (p = 0.43). No significant difference (p = 0.087) was found between both muscles engaged in the four dynamic conditions, rowing and arms for the trapezius and rowing and legs for the vastus lateralis.

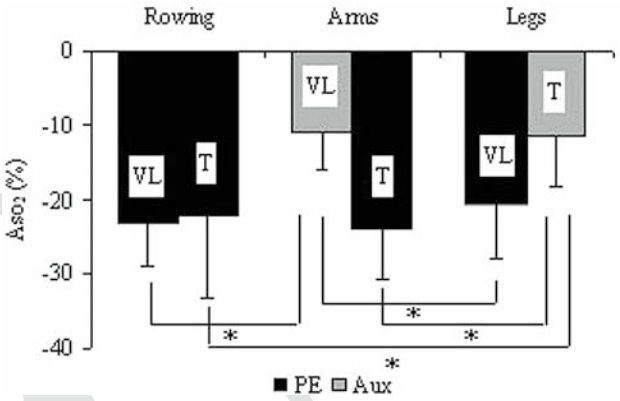

Fig. 2 Local muscle oxyhemoglobin saturation (A_{SO2}) of the trapezius (T) and vastus lateralis (VL) muscles when acting as primarily engaged (PE) or auxiliary (Aux) muscles during rowing, arms and legs exercise modes.
* p < 0.05.

Muscle masses

The muscle masses of the participants were 53.3 ± 5.1 kg for the whole body, 27.0 ± 3.4 kg for the upper part and 26.2 ± 1.7 kg for the lower part of the body.

Oxygen uptake kinetics

Standard deviation of the $\dot{V}O_2$ breath-by-breath registration at rest (SD_b) and at peak $\dot{V}O_2$ (SD_p) are given in **Table 2** for each subject for the three exercise modalities, together with the value of $\dot{V}O_{2net}$ and the ratio $SD_b/\dot{V}O_{2net}$ and $SD_p/\dot{V}O_{2net}$. In agreement with Lamarra et al. [20], these values show that there is no sta-

Table 2 Standard deviations of breath-by-breath fluctuation in $\dot{V}O_2$

Subjects	DS_b	DS_p	$\dot{V}O_{2net}$	$DS_b/\dot{V}O_{2net}$	$DS_p/\dot{V}O_{2net}$
Rowing	226.45	355.76	4264.7	0.053	0.083
1	116.71	208.27	4347.5	0.027	0.048
2	229.66	227.48	3806.1	0.060	0.060
3	446.5	407.55	5150.6	0.087	0.079
4	264.16	202.64	4352.3	0.061	0.047
5	405.14	415.24	4233.4	0.096	0.098
6	235.85	261.09	5037.6	0.047	0.052
7					
Arms	230.77	333.04	3629.9	0.064	0.092
1	389.59	361.51	3767.6	0.103	0.096
2	285.35	348.00	2716.8	0.105	0.128
3	581.21	541.15	4378.8	0.133	0.124
4	303.75	286.88	3756.4	0.081	0.076
5	330.29	316.47	3624.2	0.091	0.087
6	275.03	269.89	5068.2	0.054	0.053
7					
Legs	355.81	234.95	3212.3	0.111	0.073
1	280.89	253.26	3152.6	0.089	0.080
2	295.34	332.37	3049.0	0.097	0.109
3	339.55	334.12	3288.0	0.103	0.102
4	177.47	195.04	4017.2	0.044	0.049
5	312.73	319.14	3853.1	0.081	0.083
6	194.12	173.05	4021.0	0.048	0.043
7					

SD_b = standard deviation of the $\dot{V}O_2$ breath-by-breath registration at rest; SD_p = standard deviation of the $\dot{V}O_2$ breath-by-breath registration at peak $\dot{V}O_2$; $\dot{V}O_{2net}$ = net gain of $\dot{V}O_2$ at the end of exercise

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Table 3 Values measured during the constant intensity tests

	Rowing	Arms	Legs
$\dot{V}O_2$ (b) (ml·min^{-1})	603.6 ± 63.0	585.5 ± 156.6	464.6 ± 86.1
TD_0 (s)	1.0 ± 0.8	1.1 ± 0.9	1.7 ± 1.3
τ_0 (s)	8.6 ± 5.3	6.7 ± 2.9	11.9 ± 7.8
A_0 (ml·min^{-1})	669.8 ± 223.8	816.9 ± 168.1	902.3 ± 314.5
TD_1 (s)	13.4 ± 2.0	13.0 ± 5.8	9.7 ± 5.3
τ_1 (s)	23.2 ± 5.1	24.5 ± 8.1	29.9 ± 4.6
A_1 (ml·min^{-1})	3442.3 ± 576.2	2236.3 ± 435.2*	1915.3 ± 504.2**
TD_2 (s)	167.9 ± 108.6	175.7 ± 60.0	162.9 ± 20.2
τ_2 (s)	109.6 ± 94.2	175.4 ± 61.5	190.6 ± 71.6
A_2 (ml·min^{-1})	343.9 ± 232.2	795.6 ± 405.6*	695.8 ± 292.8
$\dot{V}O_{2tot}$ (ml·min^{-1})	5059.6 ± 527.0	4434.4 ± 854.0***	3978.0 ± 450.7**
Baseline $[La]_b$ (mM)	1.3 ± 0.8	1.3 ± 0.5	1.9 ± 0.4
$\Delta[La]_b$ (mM)	6.1 ± 1.8	5.2 ± 2.1	4.9 ± 0.5

$\dot{V}O_2$ (b): average value over 2 min of resting baseline measurement; MRT: mean response time of the fast phase; A_1: asymptotic amplitude of the primary exponential term (the fast phase); A_2: asymptotic amplitude of the second exponential term (the slow component); τ_2: time constant of the slow component; TD_2: time delay of the slow component; Baseline $[La]_b$: the lactate value measured before starting the test; $\Delta[La]_b$: the lactate accumulated during the test. * $p < 0.05$ between rowing and arms; ** $p < 0.05$ between rowing and legs; *** $p < 0.05$ between arms and legs

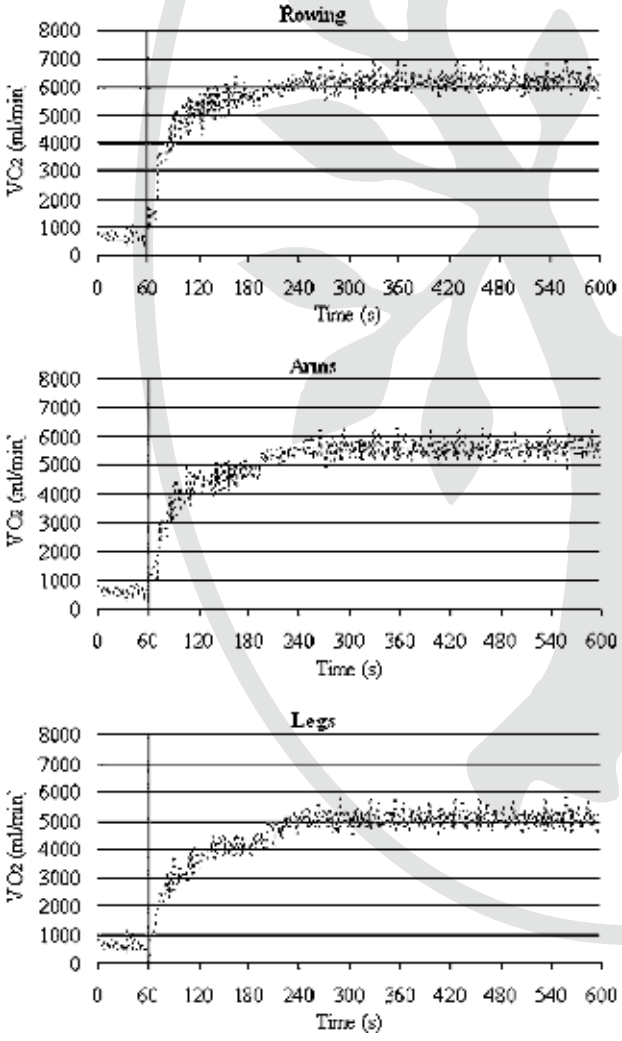

Fig. 3 An example of the kinetics from one subject for the three exercise modalities.

tistically significant difference between the noise magnitude at rest and at $\dot{V}O_{2peak}$ values, which is supposed to be a significant result to ensure the confidence with which the underlying physiological behavior can be discerned.

Results of the $\dot{V}O_2$ kinetics analysis are reported in **Table 3**. In **Fig. 3** an example of the $\dot{V}O_2$ kinetics from one subject is reported for all exercise modalities. The mathematical model of oxygen uptake response by three exponential terms resulted in best fitting curves with a mean standard error of 38.9 ± 14.5 ml·min^{-1} for rowing, 39.4 ± 5.2 ml·min^{-1} for arms and 34.4 ± 13.6 ml·min^{-1} for legs.

The $\dot{V}O_2$ slow component amplitude (A_2) in absolute values resulted in a statistical difference between the three exercise modes ($p = 0.04$), rowing being the lowest and arms the highest. When the amplitude of the $\dot{V}O_2$ slow component was calculated relatively to the highest $\dot{V}O_2$ response measured in the constant intensity test (baseline + A_1 + A_2 = $\dot{V}O_{2tot}$) it was significantly lower for rowing ($p = 0.007$), while no difference was found between arms and legs exercise modes ($p = 0.98$; **Fig. 4**).

Slow component relative to primarily engaged muscle mass

The amplitude of the $\dot{V}O_2$ slow component divided through the kilograms of the pertinent MM_p corresponded to 6.8 ± 4.9 ml·kg^{-1}·min^{-1} for the rowing exercise mode:

$$A_{2Row}/MM_{wb} = A_2/MM_{Row}\ 343.9\ (232.2)/53.3\ (5.1) = 6.8\ (4.9)$$

The value of 6.8 ml·kg^{-1}·min^{-1} multiplied by the kilograms of the MM_p separately for the upper and the lower part of the body, provided the $\dot{V}O_2$ slow component value that should derive from the primary contractions only in the arms (A_{2pArms}) and legs (A_{2pLegs}) exercise modes, respectively:

$$A_2/MM_{Row} \times MM_{pArms} = A_{2pArms}\ 6.8\ (4.9) \times 27.0\ (3.4) = 172.1\ (114.3)$$

$$A_2/MM_{Row} \times MM_{pLegs} = A_{2pLegs}\ 6.8\ (4.9) \times 26.2\ (1.7) = 171.9\ (118.2)$$

A_{2pArms} was not significantly different from A_{2pLegs} ($p = 0.97$).

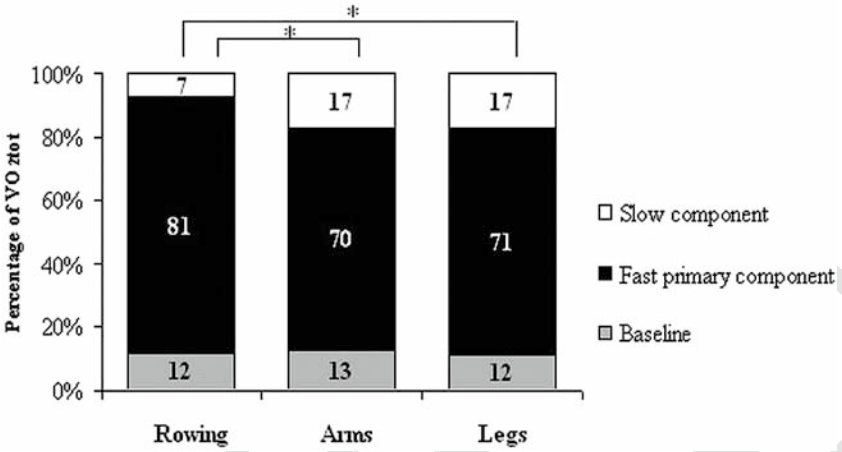

Fig. 4 Amplitude of the baseline, fast primary component ($A_{1'}$) and slow component (A_2) of oxygen uptake kinetics calculated relatively to the highest oxygen uptake response measured in the constant intensity test (baseline + $A_{1'}$ + A_2 = $\dot{V}O_{2tot}$) during rowing, arms and legs exercise modes.
* $p < 0.05$.

Slow component relative to auxiliary muscle mass

The part of the $\dot{V}O_2$ slow component that should be generated from the auxiliary muscles (A_{2aArms} and A_{2aLegs}) was calculated subtracting the $\dot{V}O_2$ slow component deriving from the primarily engaged muscle masses (A_{2pArms} and A_{2pLegs}) from the A_2 measured in the arms (A_{2Arms}) and legs (A_{2Legs}) exercise modes:

$A_{2Arms} - A_{2pArms} = A_{2aArms}$ 795.6 (405.6) – 172.1 (114.3) = 623.6 (487.2)

$A_{2Legs} - A_{2pLegs} = A_{2aLegs}$ 695.8 (292.8) – 171.9 (118.2) = 523.9 (348.6)

A_{2aArms} was not significantly different from A_{2aLegs} ($p = 0.65$).

Discussion

The lack of difference in the p70%Δ expressed relatively to the specific workload at $\dot{V}O_{2peak}$ ensured that the workload was comparable for all three exercise modes. Consistently, no differences were shown for $\Delta[La]_b$, both in absolute value and as percentage of $\dot{V}O_{2tot}$, between exercise modes in the constant intensity tests. The homogeneous distribution of muscle masses between the upper and lower part of the body of rowers allowed for the comparison of different biomechanical exercises performed at the same relative intensity.

Oxygen uptake kinetics

The lower slow component amplitude measured in absolute values and in values relative to the highest $\dot{V}O_{2tot}$ for the rowing exercise mode with respect to both arms and legs modes, reinforces the hypothesis that the auxiliary muscle involved in the latter two modes of exercise contributes to the increasing energetic cost due to the $\dot{V}O_2$ slow component. In support of this suggestion, a previous study demonstrated that the rate of hemoglobin desaturation in the arms musculature was significantly correlated to the magnitude of the $\dot{V}O_2$ slow component observed in high-intensity cycle exercise [23]. This result is in agreement with a study designed to delete or at least decrease extra work needed by the arms and trunk to support the athlete on the ergometer and the consequent extra $\dot{V}O_2$ due to the handgrip on the handlebars. To reduce the isometric effort of the upper body, a very light arm cranking exercise was added to a severe leg cycling exercise; a significant decrease of the amplitude of the $\dot{V}O_2$ slow component between the severe leg cycling alone and the same leg cycling with the additional light arm cranking was found [6]. Consistently, it has been found that greater peak power values were achieved by the participants when they were allowed to cycle with the normal with-grip position, than in the absence of handlebar grip [3]. As a matter of fact, during high-intensity pedaling, leg extension would result in a vertical displacement of the center of mass of the whole body, if, by pulling upon the handlebars, the leg extension would not be directed to pushing down the pedal [3]. Thus, it seems clear that a muscular contribution has to be given by the upper body via the handlebar grip, in order to help to overcome the large resistive loads typically used during high-intensity leg cycle ergometry. More recently, Koga et al. [19] planned a research study comparing oxygen uptake kinetics during knee extension and cycle exercise. The authors decided to utilize the two-leg over one-leg knee extension in order to minimize the contribution of isometric contraction of muscles utilized for postural support to the larger metabolic rate due to the slow component.

Smith et al. [28], studying the slow component response to heavy-intensity arm-crank ergometry, explained the significantly greater slow component measured at low crank rate by a greater isometric contraction of the muscles of the trunk and legs.

Slow component relative to primarily engaged and auxiliary muscle mass

The amplitude of the $\dot{V}O_2$ slow component value deriving from the contraction of the primarily engaged muscle masses only resulted statistically higher for rowing than for both arms and legs, while no difference was found between the latter two. The lack of difference between arms and legs is likely to be due to the similarity of the muscle mass amount primarily engaged in each exercise mode.

The surprising result of the present work is that the part of the $\dot{V}O_2$ slow component that was calculated to be produced by the primarily engaged muscles is much smaller than the one considered to be generated from the auxiliary muscles.

In this respect, Roberts et al. [27] found no difference in the amplitude of the slow component during heavy cycling and rowing, either when expressed in absolute or in relative terms. To justify their results the authors suggested that, since the amplitude of the slow component was similar between the exercise modes, despite the utilization of a great muscle mass during rowing, it

is likely that the slow component expressed in terms of ml·kg muscle mass^{-1}·min^{-1} was actually lower during rowing. In this case, the contribution of the auxiliary/support muscles during cycling was not taken into account. If that would be the case, and the auxiliary muscles do not produce any of the slow component, the doubled slow component amplitude during arms and legs in comparison to rowing would be even more striking, and even more so when considering that the primarily engaged muscle mass is halved in the first two exercise modes.

A classical study performed during severe-intensity ergometer cycling stated that the analysis of the relationship between pulmonary $\dot{V}O_2$ and leg $\dot{V}O_2$ after the initial transient at the exercise onset until fatigue indicates that the exercising limbs generate ~86% of the $\dot{V}O_2$ slow component [25]. Subsequent work [24] confirmed that, for both the fast initial and the slow secondary components of the $\dot{V}O_2$ response to exercise, measurements made at the mouth reflect closely those occurring across the exercising muscles. It has also been reported [24] that the contribution to the slow component amplitude of support processes exterior to the exercising limbs is small for large muscle exercise in comparison with the increased $\dot{V}O_2$ commanded by the working limb muscles. Indeed our results showed that the amplitude of the $\dot{V}O_2$ slow component was larger during arms and legs exercise modes, during which about half of the body muscle masses were acting as primarily engaged in the exercise. In comparison, the rowing exercise mode, which involves a greater primarily engaged muscle mass, produced a much lower slow component amplitude. Consequently, from the results of the present work, it can be supposed that the role of the auxiliary muscles in assisting the performance of the athlete is of great importance, but also that their assistance requires an additional energetic cost. Even though at present we are unable to distinguish and partition the contribution to performance, and to energetic cost, coming from auxiliary muscles or from other organs, this additional cost of exercise coming from something other than the primarily engaged muscles should not be neglected when planning exercise training and testing. Improvement in athlete's performance is generally found on changes in structures and metabolic capacities of skeletal muscle fibers; improved metabolism in muscle fibers needs collaboration with several organs. Functional capacities of all organs and tissues concerned have to improve, and improvement also has to take place in integral coordination and control of activities of contributing systems, organs, tissues and cells.

Consequently, in a study comparing heavy rowing and cycle exercise, where the metabolic stress produced in the two exercises was equivalent, no significant difference was found in the amplitude of the slow component. In this context, the authors suggested that it should be considered that although the recruitment of a greater "active" muscle mass in rowing for equivalent relative work rates might have important cardiovascular consequences, a sharing out of the requisite force generation across more active muscle fibers could be beneficial in reducing the metabolic perturbation in the fibers [27]. In agreement, Astrand and Saltin [1] demonstrated that time to exhaustion was significantly extended when the same absolute work rate was shared between arm and legs compared to legs alone, despite there being a similar absolute oxygen uptake. Therefore, the auxiliary muscle contribution to performance and the sharing out effect should be carefully quantified for both exercise training and testing and in the evaluation of the efficiency of the athlete's movement.

Indeed, a limitation of the present study was the impossibility to perform a biomechanically identical movement when the exercise was performed with a body part immobilized with respect to the complete rowing exercise. At this regard, the signals recorded from the hand grips (rowing and arms) and from the sliding seat (legs) give evidence that, when the movement is performed separately by the upper or the lower part of the body, the movement range presents a peak between 40 and 50% of the range of movement, while during the rowing exercise the signal is smoother, probably due to the movement coordination between the upper and lower limbs.

In conclusion, our study demonstrated the contribution of auxiliary muscles masses to the $\dot{V}O_2$ slow component development and to the consequently increased energetic cost of exercise. However, some part of the $\dot{V}O_2$ slow component calculated as not coming from the muscles primarily engaged in the exercise could derive from systemic factors. Thus, further research is needed to distinguish the origin of the $\dot{V}O_2$ slow component between systemic and muscular compartments.

Acknowledgements

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Letter to the Editor

Letter to the Editor, "Clinical Significance of Cerebral Oxygenation During Exercise in Patients With Coronary Artery Disease"

To the Editor:

With great pleasure we read the article by Koike et al[1] This is an interesting study investigating, by non-invasive near infrared spectroscopy[2] the forehead cortical oxy-hemoglobin changes (ΔO_2Hb) during an incremental symptom-limited cycling exercise test in 344 cardiac patients, and comparing the data with indexes obtained from cardiopulmonary exercise testing. The ΔO_2Hb measured from rest to peak exercise was significantly lower in non-survivors than in survivors, suggesting that a decrease in cerebral O_2Hb during exercise predicts future cardiovascular events in patients with coronary artery disease.

Although the results are of interest, we believe that certain points concerning the presentation of the brain oxygenation data need to be addressed. For measuring brain oxygenation Koike et al[1] used a multi-distance spatially resolved tissue oximeter (NIRO-300, Hamamatsu Photonics, Hamamatsu, Japan)[3] without exploiting the offered advantage to quantify brain oxygenation directly as tissue O_2Hb saturation (tissue oxygenation index, TOI%). The TOI reflects the dynamic balance between oxygen supply and oxygen consumption and it is independent of the path length of the near-infrared photons in brain tissue[4,5] Near-infrared spatially resolved spectroscopy implies that the light intensity is measured at several different source-detector distances[4,5] Therefore, this non-invasive technique allows the measurement of the slope of light attenuation vs distance and provides a high signal-to-noise ratio, without being so sensitive to the optical coupling and to the presence of superficial tissue layers[3] The TOI is supposed to replicate cortical O_2Hb saturation[6] Using the NIRO-300 in the controlled environment of carotid endarterectomy, it has been demonstrated that TOI is sensitive to changes in hemispheric, intracerebral blood supply and is little affected by extracranial contamination[7] The TOI has also been shown to be independent of hemoglobin concentration, skull thickness, and the area of the cerebrospinal fluid layer underlying the optodes[8]

Koike et al[1] made their patho-physiological conclusions on the basis of the interpretation of ΔO_2Hb only and without considering the differential path length factor corrected for the age of the patients[9] Unfortunately, Koike et al[1] did not report changes in (1) TOI, (2) deoxy-hemoglobin (HHb) (measurable also by the NIRO-300), and (3) total Hb ($\Delta tHb = \Delta O_2Hb + \Delta HHb$), which are necessary for a correct interpretation of brain oxygenation changes. The ΔtHb, being strictly related to blood volume changes, can be considered an indirect measure of changes in local blood flow. Because ΔHHb is closely associated with changes in venous oxygen content and is less sensitive to ΔtHb changes than ΔO_2Hb changes, HHb changes are believed to be a sensitive measure of relative tissue de-oxygenation due to oxygen extraction only when tHb is stable. Therefore, speculations on the forehead oxygenation changes based only on the increase and decrease of O_2Hb during the exercise are not fully reliable. Considering the potential clinical relevance of their findings[1] we would suggest they expand the results to include the TOI data as correctly done in their other recent interesting clinical studies[10,11]

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Muscle reoxygenation difference between superficial and deep regions of the muscles during static knee extension

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Abstract The purpose of this study was to test the hypothesis that differences in vertical spatial difference in reoxygenation after exercise exists, reflecting heterogeneity of muscle oxygenation during exercise might be due to the difference in dominantly recruited muscle fiber type. Methods: Ten healthy female subjects performed 1 minute static knee extension exercise at low (30%) and high (60%) fraction of maximal voluntary contraction (MVC). Muscle oxygenation in the vastus lateralis (VL) was monitored using multi channel near-infrared spectroscopy. Half time reoxygenation (T1/2reoxy) after exercise was calculated from oxygenated hemoglobin in the eight channels which changed the distance between light source and detector distances at 2,3,4,5cm. Blood flow (BF) in the femoral artery was measured by Doppler ultrasound. Mean arterial blood pressure (BP) at the end of the each exercise was assessed by a Finometer device. Results: BF during exercise did not differ significantly during exercise at low and high intensity, whereas BP was elevated at high intensity. T1/2reoxy tended to be prolonged at high intensity. It would be due to a transition of muscle fiber recruitment from type I toward type II fiber dominance, and/or insufficient oxygen supply for increased demand in the muscle. T1/2reoxy in different light source and detector distances was not different among them. Conclusion: This study demonstrated that the reoxygenation in the superficial region did not differ from that in the deeper region, including superficial, even when exercise intensity was high.

1 Introduction

Recent studies indicated a spatial heterogeneity in lateral direction of deoxygenation and reoxygenation in a single muscle [6,7,9,10]. One of the studies demonstrated that plantar flexion resulted in more deoxygenation during exercise and an earlier reoxygenation during recovery in the distal portion compared with the

proximal portion in gastrocremius muscle [9]. Another study also reported that reoxygenation in VL after cycling exercise was progressively delayed from distal sites to proximal site at the same submaximal intensities [6]. Possible reasons for such regional differences in muscle oxygenation between the proximal and distal portion are differences in muscle fiber composition, intramuscular pressure, and capillary density and so on [9]. A previous study in human demonstrated that distribution of different fiber type varied within a muscle, with a predominance to type II fibers at surface and type I fibers in deeper regions of the muscle [11]. Based upon the non-uniformity of muscle fiber composition from superficial to deeper portions of muscle, we assumed that muscle reoxygenation should be different depending on the depth of the region studied in the muscle. Additionally the difference in intramuscular pressure between the superficial and deep regions [12] should be considered, because it results in the difference in oxygen delivery and therefore reoxygenation difference.

Recently, muscle oxygenation during exercise has been measured noninvasively by near-infrared spectroscopy (NIRS). Recovery time of muscle oxygenation following the completion of exercise is used as an index of deficits of oxygen delivery to the muscle in relation to oxygen demand of working muscle [1,2,4,8]. Therefore we supposed that surface regions of muscle have a prolonged recovery time of muscle oxygenation as compared with deeper regions. The purpose of this study was to test the hypothesis that vertical spatial difference in recovery time of muscle oxygenation exists, reflecting heterogeneity of muscle oxygenation during exercise is probably caused by non-uniform fiber composition distribution.

2 Methods

Ten healthy females [age: 22.0 ± 1.2 (means ± SD) yr, body height: 160.4 ± 4.6cm, body mass: 55.3 ± 5.7kg] participated in this study. The subjects were fully informed of the purpose, nature, and potential risks of the experiments and gave their written, informed consent to participate in this study. This study was approved by The Ethical Committee of the Japan Women's College of Physical Education.

Static knee extension was adopted in this study. Before the experiments, all subjects were familiarized with the exercise equipment and the protocol. Maximal voluntary contraction (MVC) of knee extension was measured on the right leg. The exercise was performed in upright position with the knee joint angle set at 90 degrees. The exercise comprised 1 minute static contraction at low (30%MVC) and high (60%MVC) intensities. The order of the contractions was random, and separated by at least 5 minutes.

Femoral arterial blood velocity in the right leg was measured by Doppler ultrasound method (Vivid7 pro, GE Yokokawa Medical Systems, Japan) with a

7.5MHz transducer. The systolic and diastolic diameters in the femoral arterial were also measured using B-mode ultrasonography. The mean diameter was calculated based on the relative time periods of the systolic (1/3) and the diastolic (2/3) phases of the cardiac cycle: ([systolic diameter value × 1/3] + [diastolic diameter value × 2/3]). Mean blood velocity (Vmean) was obtained from angle corrected, time averaged, and integrated velocity of whole consecutive cardiac cycles of Doppler signals within the approximately last 5 seconds of each exercise. Femoral artery blood flow (FBF) was calculated by multiplying the cross-sectional area (area = π × [diame-ter/2]2) (CSA) of the femoral artery with Vmean ; FBF (L/min) = Vmean (cm/sec) × CSA (mm2) × 6 × 10-4.

Mean arterial blood pressure (BP) was measured non-invasively by photoelectric plethysmogaraphy with Finometer (Finapres Medical Systems BV, Netherlands). The beat-to-beat values were averaged over the last 5 seconds of exercise at each intensity.

Muscle oxygenation in the VL was monitored by near infrared continuous wave spectroscopy (NIRS, OMM-3000, Shimadzu, Japan). The NIRS probe was placed over the thickest site of VL, and 3cm distal part from there. The distance light source and detector distances was set at 2, 3, 4, and 5 cm. Tissue thickness over this position was 8.6±0.6 mm for the subcutaneous adipose tissue, 20.7±0.9 mm for VL and 16.2±0.8 mm for Vastus intermedius (VI) muscle. The NIRS signals at wavelengths of 780, 805, 830nm were used for calculation of changes in the concentration of oxygenated hemoglobin (oxyHb), deoxygenated hemoglobin (deoxyHb), and total hemoglobin (totalHb). Half time reoxygenation (T1/2reoxy) was determined as the time required to reach the value halfway between the oxyHb level immediately after exercise and that at peak hyperemia during recovery.

Values are represented as means ± SE, unless indicated otherwise. Differences in BF, BP, and T1/2reoxy between the low and high intensities were analyzed using the t test for paired samples. One-way ANOVA for repeated measurements was used to compare T1/2reoxy for different light source detector distances. A p-value of less than 0.05 was considered statistically significant.

3 Results

FBF at 30%MVC (0.45±0.04 L/min) was not different from that at 60% MVC (0.50±0.06 L/min) (Fig. 1.).

BP was significantly higher at 60%MVC (95±3 mmHg) compared with 30%MVC (106±6 mmHg) ($p<0.05$) (Fig. 2.).

T1/2reoxy tended to be prolonged at 60%MVC as compared with 30%MVC ($p<0.10$). However there were no differences among T1/2reoxy values in different light source detector distances (Fig. 3.).

4 Discussion

The present study examined muscle reoxygenation from the superficial to deep region of the VL in static knee extension exercise at low and high intensities. Results showed that T1/2reoxy tended to be prolonged at the high-intensity exercise. This would be explained by a transition of muscle fiber recruitment from type I toward type II fiber dominance, and/or due to insufficient oxygen supply for increased demand in the muscle supposed from pre-sent result of BF. BF during exercise was constant, and means that the blood supply condition was not different between low and high intensities. This result on BF is supported by previous studies [3, 5]. The values of T1/2reoxy in this study were smaller than that in previous references [6, 8]. It might be due to different exercise. We used static one-legged knee extension exercise and they used cycle ergometer exercise. Dynamic cycle exercise should induce recruitment of larger muscle mass and increase oxygen demand of working muscle.

We could not find differences in T1/2reoxy among different light source and detector distances. Following three possible reasons are considered; the first is that recruited muscle fibers in this exercise are not different in proportion of types between superficial and deep regions of the muscle. The second is that wider light source and detector distance has included not only deep region information but also superficial information of muscle oxygenation. The third is that the heterogeneity of intramuscular pressure could affect on T1/2reoxy in the opposite direction to the heterogeneity of muscle fiber distribution. The question remains unresolved if heterogeneity of muscle fiber composition and blood flow distribution will cause different recovery time of muscle oxygenation between superficial and deep regions of the muscle.

In conclusion, this study demonstrated that recovery time of muscle oxygenation in deep and superficial regions did not differ from that in the region limited to the superficial one after exercise even at high intensity.

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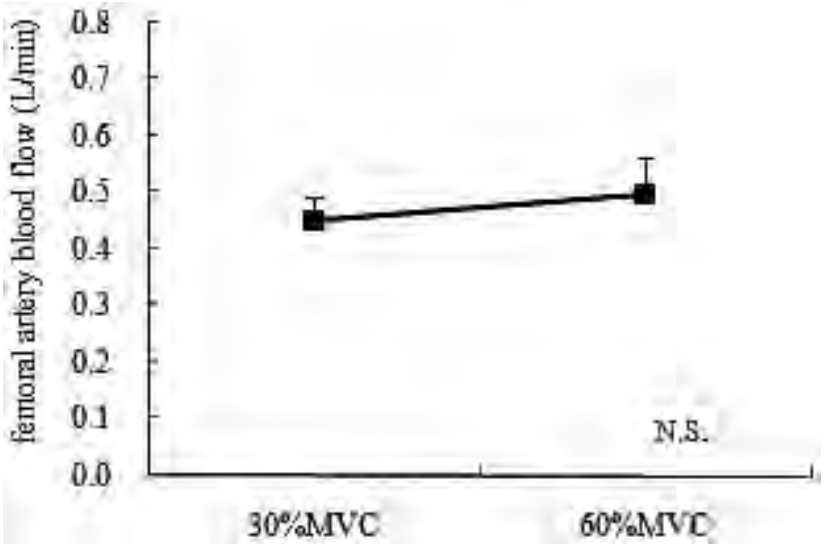

Fig. 1. Femoral artery blood flow (FBF) during knee extension exercise at low (30%MVC) and high (60%MVC) intensities. Values are mean±SE, n=9. NS.

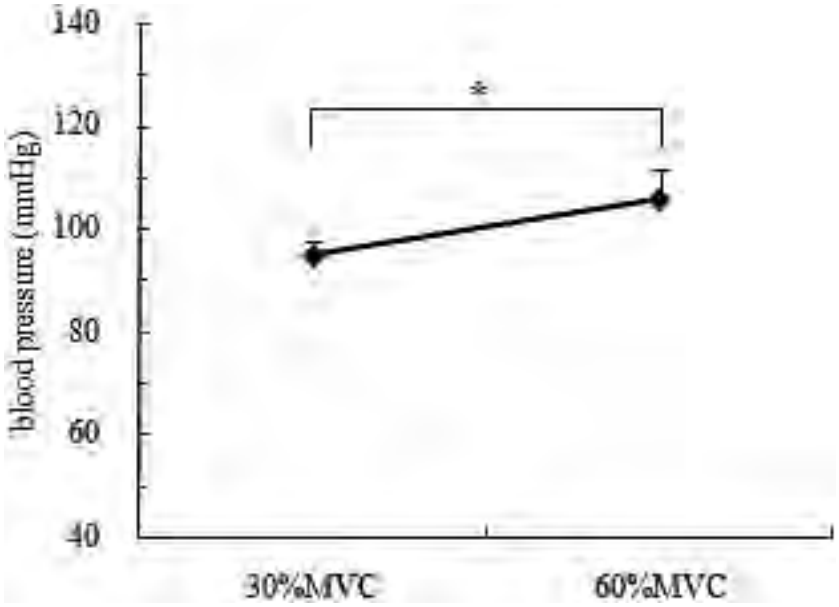

Fig. 2. Mean blood pressure (BP) during knee extension exercise at low (30%MVC) and high (60%MVC) intensities. Values are mean±SE, n=9. *Significant difference between intensities ($P<0.05$).

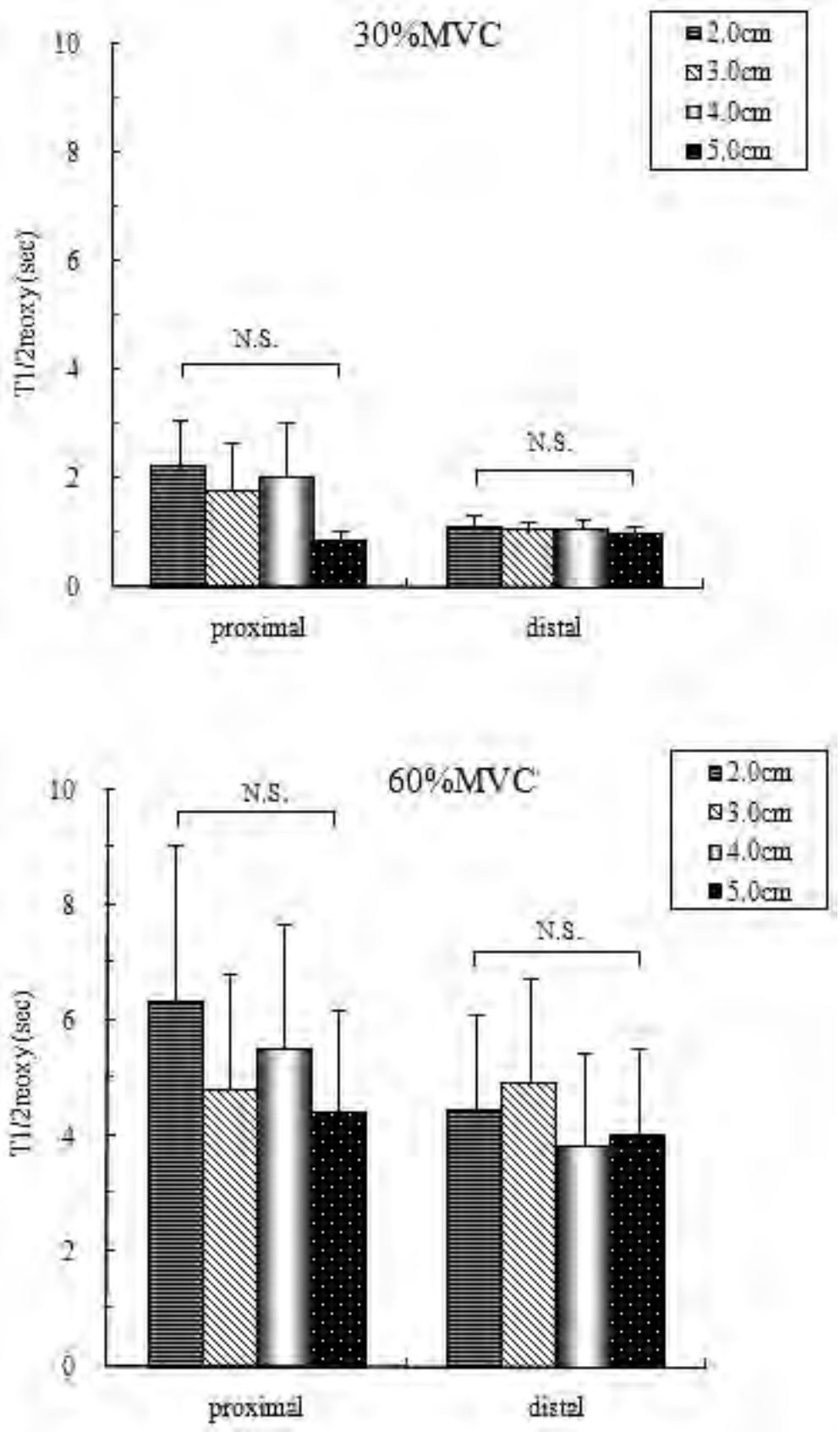

Fig. 3. Half time reoxygenation (T1/2reoxy) during knee extension exercise at low (30%MVC) and high (60%MVC) intensities in different light source detector distances. Values are mean±SE, n=10. P<0.1, 30%MVC vs. 60%MVC corresponding values.

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Blood flow and arterial vessel diameter change during graded handgrip exercise in dominant and non-dominant forearms of tennis players

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Abstract The training effect on exercise-induced maximal blood flow remains unclear. The purpose of this study was to clarify the difference of exercise-induced blood flow, blood flow velocity and vessel diameter of brachial artery in dominant and non-dominant forearms of tennis players during graded hand-grip exercise. Ten female tennis players aged 20.1±0.1 yrs. (mean±SD) performed 30-s static handgrip exercise in the supine position with either the dominant or non-dominant hand by increasing load at 30-s intervals until exhaustion. Brachial arterial blood flow velocity (Doppler ultrasound method) did not differ between both limbs, whereas the vessel diameter (2-D method) was significantly larger in the dominant limb during diastole both at baseline ($P<0.01$) and after exercise ($P<0.05$), but no difference was found during systole. As a result, the blood flow was significantly higher ($P<0.05$) in the dominant limb during post-exercise condition. Muscle thickness of the forearm muscles and maximal handgrip strength were significantly higher in the dominant limb. Thus, the effect of training on exercise-induced blood flow specific to the dominant limb was confirmed during post-exercise due to the enlarged vessel diameter during diastole of cardiac cycle. The dimensional change in the vasculature specific to the dominant side will be included in the training effects associated with the dimensional muscular changes in the dominant forearm.

1 Introduction

Maximal metabolic vasodilation capacity is enhanced due to training [2,3,14]. Cross-sectional study on blood flow in the dominant and non-dominant limbs of tennis players also indicated an increased blood flow in dominant limb used in

tennis [7,14]. However, it is unclear if these training effects are applicable to exercise-induced maximal blood flow, because the sympathetic vasoconstriction occurred during exercise and the blood flow during exercise did not reach a level of maximal metabolic vasodilation[9,16] .

Blood volume per unit time is determined by the cross-sectional area of vessel and blood flow velocity. Previous studies indicated that muscle vasculature was adjusted to training or disuse of the muscle [3,4,8,13]. Despite that structural adaptation of vasculature has been reported at baseline, a training effect on vascular dimension during exercise remains to be studied.

The purpose of this study was to clarify the effects of training on blood flow and structure of the conduit artery during static exercise (muscle action). For this purpose, the blood flow velocity and vessel diameter of the brachial artery were determined in dominant and non-dominant forearms of tennis players during and after each load of graded handgrip exercise.

2 Methods

Subjects; Ten female tennis players aged 20.1±0.1(mean±SD) years old participated in the study. They were recruited from the collegiate tennis team, which won 4th place in the national inter-collegiate tennis tournament that year. The study was approved by the Ethical Committee on Human Subjects Research at the Japan Women's College of Physical Education. All subjects provided written informed consent after being informed about all experimental procedures, the exercise protocol, and possible risks associated with participation in the study.

Experimental protocol and physiological measurements; Following 3-minute baseline measurements, the subject performed 30-s static handgrip exercise in a supine position with either the dominant (right side) or non-dominant hand on different days. The static handgrip exercise was repeated at 30-s intervals with increasing load by 2kgw until exhaustion. Total work index was calculated as a sum of each work load multiplied by duration. Brachial arterial blood flow velocity (V) and diameter (D) were obtained continuously using ultrasound Doppler and 2-D methods (GE, Vivid7 Pro) and determined for 10 (baseline), 5 (during exercise) or 2-3 cardiac cycles (immediate post-exercise) each at diastole (Dd) and systole (Ds). Brachial arterial blood flow was calculated as $V*\pi(D/2)2$ (D=2Dd/3+Ds/3). Blood pressure (BP) was measured on the contralateral finger on beat-by-beat basis throughout the experiment (Finapres model 2300, Ohmeda, USA). Maximal voluntary contraction (MVC) of forearm muscles, and radial and ulnar forearm flexor muscle thickness were measured (Aloka, SSD1000).

Data Analysis and Statistics; The group data were expressed as mean±SE, unless otherwise indicated. Differences among the means obtained from 7 loads and 2 limbs (dominant and non-dominant) were evaluated using two-way analysis of variance (ANOVA). When significant differences (major effect, interaction)

were observed, a *post hoc* comparison was performed using Tukey's HSD. A P-value less than 0.05 was accepted as significant.

3 Results

Muscle thickness of Rad and UL, MVC, highest load attained by each subject and total work index performed until exhaustion were significantly higher in the dominant limb.

The blood flow velocity during exercise and immediately after exercise increased significantly ($P<0.01$) with loads both in dominant and non-dominant limbs. No significant differences were found between both limbs. The diastolic and systolic vessel diameters, during exercise and immediate post-exercise, gradually increased with time and increasing loads. A significant major effect on diastolic diameter was obtained only for load during ($P<0.01$) and post ($P<0.05$) exercise. Interaction was significant ($P<0.01$) for the means of diastolic diameters, which were significantly larger in the dominant limb at baseline (dominant; 3.4±0.1, non-dominant; 3.0±0.1mm) and after exercise at the highest load (dominant; 3.5±0.1, non-dominant; 3.2±0.1mm) (Figure 1a). In contrast, systolic diameter did not differ either during exercise or post-exercise between both limbs (Figure 1b). The brachial arterial blood flow in both limbs increased linearly related to exercise load both during ($P<0.01$) exercise and post-exercise ($P<0.01$). Interaction was significant ($P<0.05$) and higher post-exercise blood flow was obtained in the dominant limb after exercise at the highest load ($P<0.05$) (Figure1c).

4 Discussion

The first finding of this study was that the lateral difference in blood flow in tennis players was detected post-exercise when muscle contraction was terminated, which is consistent with the study of Sinoway *et al.* [15] on tennis players. However, the blood flow during exercise did not differ between both arms in this study. Therefore, the exercise training will induce an increase in exercise-induced blood flow during post-exercise phase, (or relaxation phase of dynamic exercise) and metaboreceptor mediated vasodilation [7,14,15]. However, this functional adaptation would not increase blood flow during static muscle action, probably because an elevated intramuscular pressure due to muscle contraction [17] impedes a vasodilation in the contracting muscles.

Cross-sectional studies on vasculature demonstrated that diameters of the conduit artery were positively associated with the level of physical activity. Larger

vessel size was observed in trained people of various sports, limited to the trained region of the body [8, 13], whereas smaller dimension of vessel diameter was reported in sedentary and paraplegic subjects, and in healthy people after bed-rest or limb suspension [3, 4, 8,13]. Longitudinal study confirmed the vessel expansion due to training in various arteries [6, 11,12]. However, those studies measured the vessel diameters at baseline, and no studies, to our knowledge, compared dimensional adaptation during exercise. Furthermore, no study except the study of Schmidt-Trucksäss *et al.* [13], considered the vascular size fluctuation with cardiac cycle; systole or diastole. Our second new finding, therefore, was that the luminal vessel diameter of the brachial artery during systole did not change significantly between limbs, whereas the diameter during diastole was larger in the dominant limb. The latter finding is consistent with the study of Huonker *et al.* [8], who studied thoracic, abdominal, subclavian and common femoral arteries in trained athletes including professional tennis players, but not with the study of Schmidt-Trucksäss et al. [13]. They demonstrated that the vessel diameters were significantly larger in athletes for both systolic and diastolic phases. The discrepancy might be due to the difference of subjects compared in the respective studies; dominant vs. non-dominant (this study) limbs, or professional athletes vs. sedentary and paraplegic subjects [13].

The mechanism to explain an increased blood flow with training has not yet been completely elucidated, but structural remodeling of the vasculature might be one of the most potent mechanisms [6, 12]. As the muscle thickness of the dominant forearm was significantly larger compared to that of the non-dominant one in this study, the dimensional change in muscle due to training will be considered to influence vascular remodeling. Other underlying mechanisms for the increased blood flow with training will include a change in vasoactivity because of an increased flow-mediated dilation after training [1, 5]. Considered from the role of nitric oxide (NO) in exercise hyperemia [10], one potent mechanism will be an increase in NO production or sensitivity to NO. However, the contribution of NO to the effect of exercise training on vascular responses in human subjects remains undecided [7]. This study suggests that the training effect on NO-dependent vasodilation, if any, might be masked during muscle contraction.

In conclusion, larger brachial arterial vessel diameter and muscle thickness in tennis players will probably be included in training effects. However, the effect of training on exercise-induced blood flow specific to the dominant limb was not confirmed during exercise but was detected during post-exercise due to the enlarged vessel diameter during diastole of the cardiac cycle. The dimensional change in the vasculature specific to the dominant side will be included in the training effects associated with the dimensional muscular changes in the dominant forearm.

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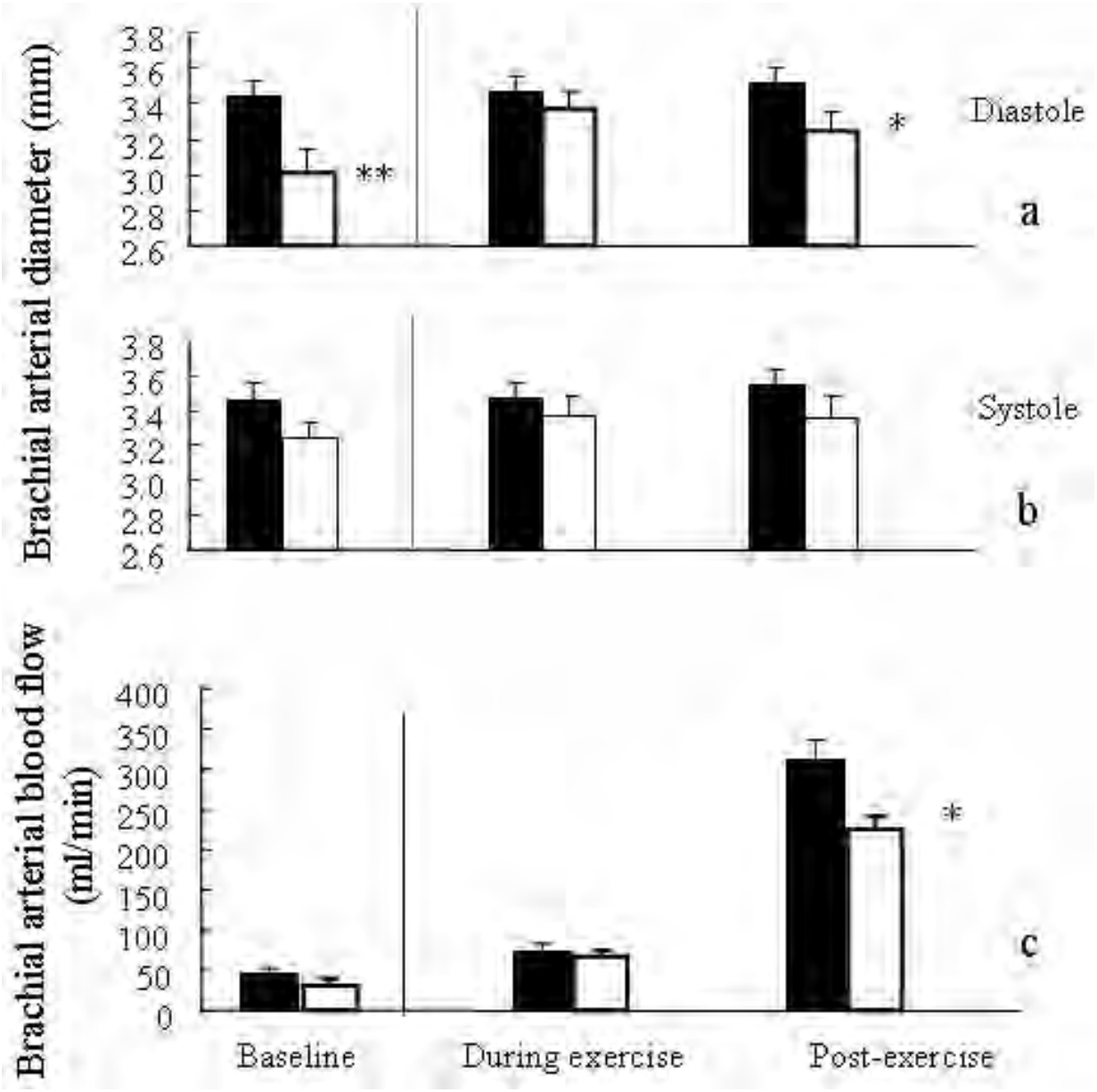

Figure 1 Diastolic (a), systolic (b) vessel diameter and brachial arterial blood flow (c) at baseline, during, and after exercise at the highest loads in dominant (■) and non-dominant (□) limbs.
*, **; P<0.05, P<0.001 between limbs.

Cerebrovascular response during heavy upper body exercise: effect of mode of ventilation on blood flow velocity in the middle cerebral artery

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Abstract Heavy resistance exercise may be associated with a small risk of cerebral aneurysm rupture, subarachnoid hemorrhage, and symptoms of dizziness or outright weight-lifters' blackout, which may be induced by a rapid change in the cerebral blood flow. We hypothesized that these changes during heavy exercise could be associated with the mode of ventilation. The purpose of the present study was to elucidate the effect of the mode of ventilation on cerebral blood flow response during heavy upper body exercise. Subjects performed 15-s static exercises at 80% maximum voluntary contraction (MVC) under different modes of ventilation. In this study, we observed that heavy exercise with breath holding induced marked and rapid changes in the cerebral blood flow velocity in the middle cerebral artery during and after exercise as compared with that with continued normal ventilation. We also observed that hyperventilation before exercise could largely contribute to a lower cerebral blood flow velocity during exercise and extending to the recovery phase. Our data suggested that even during heavy upper body exercise, the mode of ventilation is very important for maintaining cerebral circulation.

1 Introduction

Heavy resistance exercise is associated with a pronounced increase in the arterial pressure and cerebral blood flow, which may occasionally result in bleeding around the brain. On the other hand, symptoms of dizziness or outright weight lifters "black out" could be linked to decrease in the cerebral blood flow during and after heavy exercise. Despite the benefits of resistance exercise on skeletal morphology and function, heavy resistance exercise may be associated with a small

risk of rupture of cerebral aneurysm, subarachnoid hemorrhage, and weight lifters "black out" [2, 6, 7].

Change in the cerebral blood flow during heavy exercise could be associated with the mode of ventilation, including the forced expiration against a closed glottis (breath holding induced a Valsalva-like maneuver) and hypocapnia induced by hyperventilation before and during exercise [1, 6, 7, 10]. A previous study reported marked change in the mean cerebral blood flow velocity in the middle cerebral artery (MCA V_{mean}) during heavy two legged extension with concomitant Valsalva-like maneuver [7]. More recently, Romero and Cooke [10] demonstrated that hyperventilation before exercise exacerbates the reduction in MCA V_{mean} during leg-press resistance exercise. These studies suggested that during heavy exercise the associated mode of ventilation may be of deterministic importance for cerebral circulation. However, these investigations focus on cerebral blood flow regulation during lower-body exercise involving a large muscle mass. To date, there is no information regarding the effect of the mode of ventilation on the cerebral blood flow response during upper body heavy exercise involving a small muscle mass. In addition, the individual effects of breath holding during exercise and of hyperventilation before exercise on cerebral blood flow remain unclear.

Therefore, the purpose of the present study was to elucidate the effect of the mode of ventilation on cerebral blood flow response during heavy upper body exercise. We hypothesized that hypocapnia induced by hyperventilation before exercise and by breath holding during exercise may cause greater reduction in the cerebral blood flow as compared with that during continued normal ventilation.

2 Methods

Subjects A total of 10 male field athletes (7 shot putters and 3 hammer throwers; mean age ± SD: 21.2 ± 1.2 years) volunteered to participate in this study after providing informed consent to the protocol, as approved by the ethics committee of Japan Women's College of Physical Education.

Exercise and mode of ventilation In this study, single arm elbow flexion exercise was performed with the use of a multifunctional dynamometer device. The exercise load selected was 80% of the maximal voluntary contraction (MVC) force. After a 3-min resting period, the subjects performed 15-s static exercises at 80% MVC with the following 3 different modes of ventilation (in random order): 1) continued normal ventilation (EX), 2) exercise with concomitant breath holding (EX+BH), and 3) pre-exercise hyperventilation till an end tidal partial pressure of CO_2 (P_{ET} CO_2) of 3.5% was achieved (HV). In HV, after a 2-min rest, the subjects were instructed to perform voluntary hyperventilation for 1-min in order to

achieve a P_{ET} CO_2 of ~3.5% [10]. After the 1-min hyperventilation, the subjects performed 15-s static exercises with continued normal ventilation.

Measurement MCA V_{mean} measurement was performed with an ultrasound system (Vivid 7pro; GE Yokogawa Medical Systems) equipped with a 2.0 MHz sector transducer. The MCA V_{mean} was defined as the time-averaged mean velocity obtained in automatic calculation mode. Mean arterial pressure (MAP) was measured non-invasively by photoelectric plethysmography with Finometer (Finapres Medical Systems BV). Furthermore, we determined the stroke volume (SV), and cardiac output (CO), from the blood pressure wave form by using the Modelflow method. Respiratory parameters were determined with an online system for the breath-by-breath method. The ratio of MAP/ MCA V_{mean} was calculated as an index of cerebrovascular resistance (CVR).

Statistics To confirm whether the parameters had actually changed as a result of exercise as compared with the resting values, two-way analysis of variance (ANOVA) with repeated measurements and Dunnett's t-test were conducted.

3 Results

The MCA V_{mean} and CVR responses at rest, during, and after exercise are illustrated in Figure 1. In EX, MCA V_{mean} decreased (not significantly) from 36.8 to 34.9 cm·s^{-1} and significantly ($P < 0.05$) decreased further to 32.4 cm·s^{-1} at 1–5 s after the end of exercise. The CVR gradually increases at the onset of exercise, and returned to resting levels immediately after the end of exercise. The P_{ET} CO_2 rapidly decreased during exercise in EX.

In EX + BH, MCA V_{mean} dropped sharply to below the resting revel (from 38.2 to 31.9 cm·s^{-1}) with a subsequent overshoot to 43.4 cm·s^{-1} at 1–5 s after the end of exercise. The CVR significantly ($P < 0.05$) increased at the onset of exercise, and rapidly returned to resting levels immediately after the end of exercise. The CO significantly ($P < 0.01$) decreased until just after the end of exercise (from 9.2 to 5.6 l·min^{-1}), with a subsequent overshoot until 10 s after the end of exercise (to 10.4 ·min^{-1}).

Hyperventilation before exercise reduced the MCA V_{mean} from 35.2 cm·s^{-1} at rest to 28.4 cm·s^{-1} at 5 s before the start of exercise. In contrast to both the EX and EX+BH, the MCA V_{mean} gradually increased until the end of exercise (from 28.4 to 33.0 cm·s^{-1}) and subsequently decreased to 30.9 cm·s^{-1} at 1–5 s after the end of exercise. During hyperventilation, the CVR significantly ($P < 0.05$) increased and this increasing continued and ex-tending to during and after the end of exercise. Before exercise, P_{ET} CO_2 significantly ($P < 0.05$) decreased to 27.7 mmHg with hyperventilation and was 27.5 l/min immediately before the start of exercise. P_{ET}

CO_2 values during exercise were significantly ($P < 0.05$) lower than the resting values. After the end of exercise, $P_{ET}\,CO_2$ gradually returned to the baseline.

The results can be summarized as follows: (1.) the magnitude of reduction in the MCA V_{mean} during exercise was larger in EX+BH than in EX, (2.) EX+BH also caused a rapid overshoot of MCA V_{mean} after exercise, and (3.) in HV, the hypercapnia induced by hyperventilation before exercise produced a marked reduction in the MCA V_{mean} before and during exercise, and extending to after exercise.

4 Discussion

It is well known that $P_a\,CO_2$ is important for the regulation of cerebral blood flow and CVR [4, 9, 10]. We suggested that the decrease in MCA V_{mean} during and after the end of exercise in EX might be related to $P_a\,CO_2$, which may reflect $P_{ET}\,CO_2$. The time constant for MCA V_{mean} responses to a step decrease $P_{ET}\,CO_2$ is ~6 s, whereas the response to a step increase in CO_2 takes ~14 s [8]. This seems to suggest that the observed time delay between MCA V_{mean} and $P_{ET}\,CO_2$ may have contributed to the lowest MCA V_{mean} during the recovery period in the EX.

The expiratory strain during a Valsalva-like maneuver might reduce blood flow to the brain [6, 7]. Forced expiration against a closed glottis increases intrathoracic pressure and central venous pressures and marked reduces in SV and thus CO. Previous studies indicated that CO is an important determinant of cerebral blood flow during exercise [3, 5, 7, 9]. However, our data suggested relationship between CO and MCA V_{mean} was not simply under this situation. Furthermore, the rapid increase in the CVR at the onset of exercise may also contribute to the change in MCA V_{mean} and the increase in the CVR may be induced by sympathoexcitation due to heavy exercise and/or the reduction in CO and $P_a\,CO_2$. The increase in the CVR during EX+BH suggested vasoconstriction of the peripheral branches of the MCA. On the other hand, over shooting of the MCA V_{mean} immediately after the end of exercise may be induced by rapid decrease in CVR, with rapid recovery of CO and $P_a\,CO_2$.

In the HV trials, reduced MCA V_{mean} occurred in conjunction with increased CVR. This reduction in MCA V_{mean} before, during, and after exercise was attributable to the reduction in $P_a\,CO_2$. These results indicate that the increase in CVR was probably associated with vasoconstriction of the cerebral blood vessels.

In summary, our data suggested that even during upper body heavy exercise involving small muscle mass, the mode of ventilation was very important for maintaining cerebral circulation. We think that the combination of hyperventilation before heavy exercise and breath holding during exercise is the worst scenario from the perspective of cerebral circulation. It may be that continued normal ventilation during heavy upper body exercise may be safer, in that it helps to avoid rapid

changes in the cerebral blood flow and CVR that may in turn cause symptoms of dizziness or outright weight lifter's "black out" and intracranial hemorrhage [7].

5 Acknowledgement

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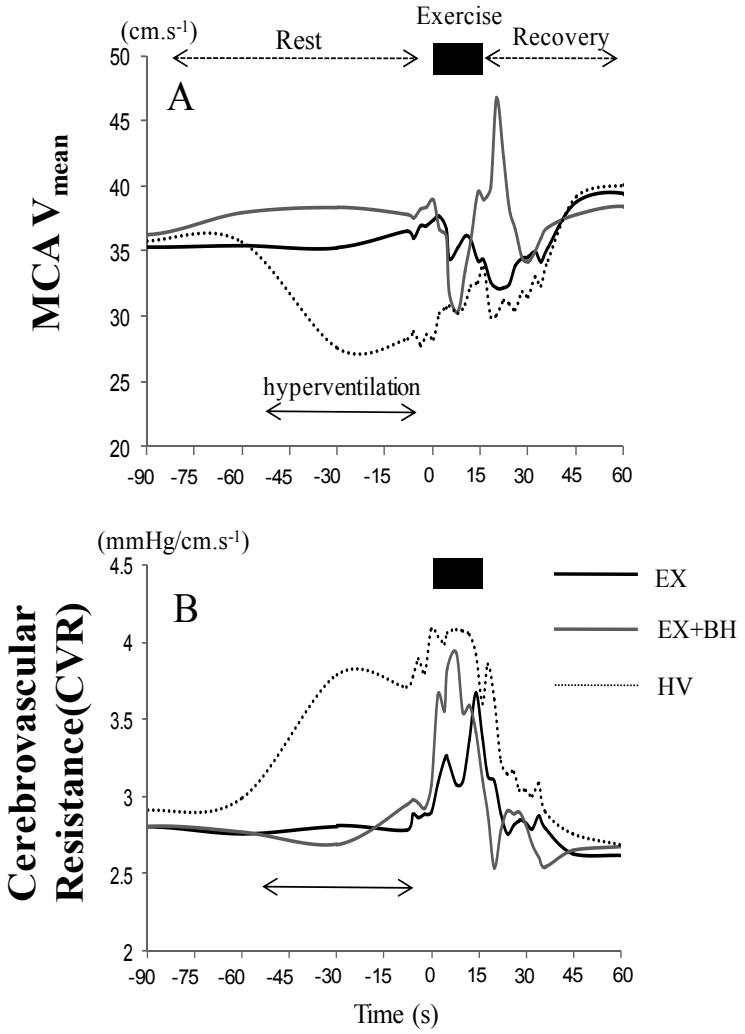

Fig. 1. Cerebrovascular responses at rest, during, and after heavy exercise. (A) MCA V_{mean} , Mean middle cerebral artery blood flow velocity and (B) CVR, Cerebrovascular resistance index.

学術フロンティア発足シンポジウム

日本女子体育大学体育学部附属基礎体力研究所開所15周年記念シンポジウム
－学術フロンティア推進事業「運動時の循環調節研究」の学術拠点形成を目指して－

日　　時：2004年10月23日（土）

基調講演：運動時の循環調節
－基礎体力研究所15年の成果と学術フロンティア「運動時の循環調節」共同研究プロジェクトの発足について－
加賀谷淳子（研究代表者；日本女子体育大学学長）

研究発表：学術フロンティア推進事業；運動時における循環調節機構の統合的解明
－スポーツによる健康・体力づくりプログラムの構築に向けて－
「運動時の腹部内臓の血流動態」　**定本　朋子**
「Effects of muscle exercise on prefrontal cortex oxygenation monitored by near infrared spectroscopy」　**Valentina Quaresima**
「Technical developments of near-infrared devices for studying oxygenation and hemodynamics in brain cortex and skeletal muscle」　**Marco Ferrari**
「運動時の腹部内臓の血流動態」　**斉藤　満**
「運動単位の動員状態からみた運動特性」　**加茂　美冬**
「運動時の心拍出量の変化と各種血管への血流分配」　**清水　靜代**
「心臓血管系患者の血流プロファイル」　**長田　卓也**

特別講演：Future perspectives in the study of circulatory regulation during exercise
Richard L. Hughson（University of Waterloo, Canada）

J. Exerc. Sci. 15：21—28, 2005

＜第15回基礎体力研究所研究フォーラム＞

基調講演

運動時の循環調節

基礎体力研究所15年の成果と学術フロンティア「運動時の循環調節」共同研究プロジェクトの発足

日本女子体育大学　加賀谷淳子

1. はじめに

日本女子体育大学体育学部附属基礎体力研究所が設置（1989年11月）されて以来15年が経過した．設立の趣旨と研究所への期待(宇土，前田，山川，1991）を踏まえて，「体力の基礎的研究，体力の維持・増進並びに競技力の向上に関する施策や方法を開発すること」を具体的目的として，4つの研究プロジェクトを掲げ，学内外の研究者と共同研究を進めてきた．研究所のコンセプトは「デパートメントストアではなく，専門店」を目指すことであった．また，「研究の成果を実践現場へ，実践現場で得た課題を実験室へ」をキーワードとし，基礎的研究によってヒトの身体運動のメカニズムを解明すること（プロジェクト1）と，そこで得たエビデンスを基に最終的にはスポーツや健康の実践現場の課題解決に貢献することであった．実践的課題のプロジェクトには，「子どもの身体特性に関する研究」（プロジェクト2），「中高年者のための運動処方に関する研究」（プロジェクト3）及び「女子競技選手の身体特性に関する研究」（プロジェクト4）がある．

開所5年間（1989-1994年）は，研究所の“体力”すなわち“研究能力”を高めるために努力し，その後の5年間（1995-2000年）は本研究所の独自性に特化した研究成果を上げることに全力を注いだ（**図1**）．この間の研究成果概要は開所10周年にあたって報告されている（加賀谷，2000）．その段階において，運動時の循環調節について基盤となる研究を10年間行ったことにより，研究所としての“体力”が応用的研究を実施できるレベルに向上したと感じられた．そこで，今後は応用的・実践的研究も推進する必要のあることが報告されている．

それから今日までの5年間（2001-2004年）は，それまでの研究成果を生かして，実践的研究を強化し，同時に学内競技選手のサポートにエネルギーを注いだ（紀要参照）．そして，あらたな5年のステップを踏み出そうとしていた2004年度に，文部科学省私立大学教育研究高度化推進事業学術フロンティア推進事業に本研究所のプロジェクトが採択された．

本稿では，開所15周年を迎えた基礎体力研究所の最近5年間の研究活動と今後5年間に取り組む予定の学術フロンティア共同研究プロジェクトについて報告する．

2. 実践的研究の促進

1）高齢者の生活機能維持に必要な身体運動に関する共同研究—科学技術振興調整費による高齢者プロジェクトへの参加—

21世紀の高齢社会において，身体活動の実施が高齢者の健康や生活機能維持に如何に効果的かについて確かな科学的根拠を示し，さらに実践できる提案をするという本プロジェクトは1999年から2004年まで，21世紀の幕開けを挟んで6年間続けられた．これは，筑波大学（代表；村上和雄元筑波大TARAセンター長）が

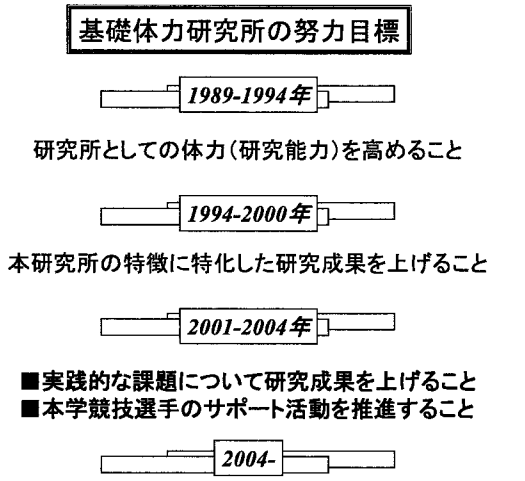

図1 基礎体力研究所の努力目標の年次推移

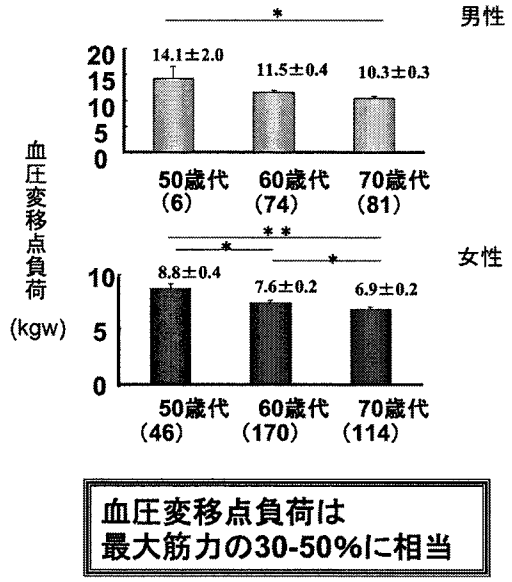

図2 高齢者の上肢作業能の加齢変化(加賀谷ら, 2003)

中心となり，多数の大学や研究機関が共同で取り組んだ大型研究であった．茨城県大洋村や埼玉県小鹿野町をフィールドとし，科技庁の振興調整費の補助を受けて行われた本プロジェクトは，後に，学術的枠内に留まらず，行政への政策提案や一般国民の運動にも大きな影響を与える成果をあげた．このプロジェクトにおいて，本研究所の研究チームが担当した課題「高齢者の上肢ワークキャパシティ」について研究成果をあげ得たことは研究所にとってエポックメーキングとなった．

本研究チームは，上肢運動時の血圧が急上昇する負荷の加齢変化を調べた．対象者（50-90歳の男女）は6年間で1,223名に達した．その結果，それが加齢と共に低下すること（図2），高い負荷での血圧上昇度は高齢者では大きいことが明らかになった．得られたデータに基づき血圧変移点負荷の性年齢別基準値を作成することができた．また，血圧変移点負荷の低下は，高齢者が低強度の規則的な身体活動を継続すると，抑制できることが明らかになった．これらの結果は，上肢の作業能は高齢者でも低下しないというこれまでの知見に反するものであり，精神活動と直結する上肢の運動の重要性と高齢期における上肢運動の意義を示すものであった．

加齢による血圧変移点負荷が低下する背景には，血管の器質的変化が上げられる．本研究所チームは上腕動脈，総頸動脈の血管径や血流速度および総頸動脈の内中膜複合体の加齢変化についても貴重なデータ（図3）を取得し，動脈硬化に関与する血管の器質的・機能的変化は身体運動の実施によって抑制できることを示すことができた．また，研究所兼担研究員であった赤羽多美子先生のアイディアから，高齢者向けの上肢運動プログラムの提供も行った（加賀谷，2003）．

2）高齢者の運動に関する地域や産業との連携

大洋村をフィールドとした研究は，大学近隣の人々にも注目されることとなり，三鷹市老人クラブ連合との共同事業が始まった．三鷹市における大規模な高齢者の健康増進講座へ，運動を科学する専門家の立場で協力して欲しいとの要請を受けたのは2002年のはじめであった．

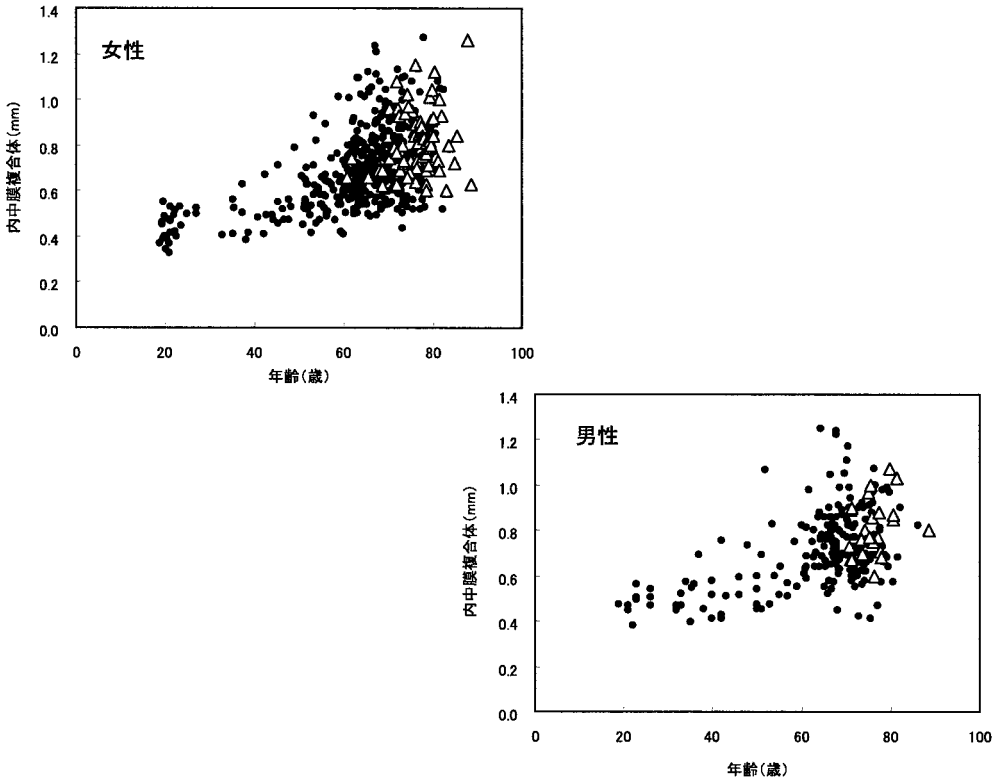

図3　総頸動脈の内中膜複合体にみられる加齢変化（清水ら）

そこで，「身体虚弱者・高齢者の運動懇談会」を学内に立ち上げ，この問題に関心を持つ教職員と研究所のスタッフが，1日100-200名の高齢者（後期高齢者を含む）に日常的な生活行動能力や健康度チェックを実施するという大変な仕事を始めることになった（**図4**）．本事業は老人クラブ連合（会長花岡氏）の担当者が体協や体育指導員と一緒に運営し，事前に医師によるヘルスチェックを受けて，救急救命士，看護師が見守る中で，細心の注意を払って測定が行われてきた．データは分析後，一人一人にフィードバックされて，生活に役立つようなアドバイスがなされている．三鷹市老人クラブ連合のこの事業に対して，健康増進施策を推進する三鷹市（清原市長）の関心が高く，本学が三鷹ネットワーク大学の立ち上げ準備当初からかかわるきっかけとなった．

さらに，この仕事は，烏山周辺に住む中年のスポーツ愛好者（科学研究費補助）や印刷会社で働く社員の健康度チェック等　5の仕事（総務庁補助）にも広がり，学内の先生方と共同して地域や産業の健康増進の一端に貢献できたと

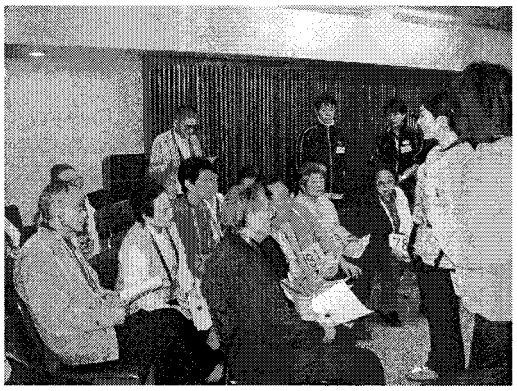

図4　三鷹市での高齢者健康増進事業実施風景
（測定について説明を受ける参加者たち）

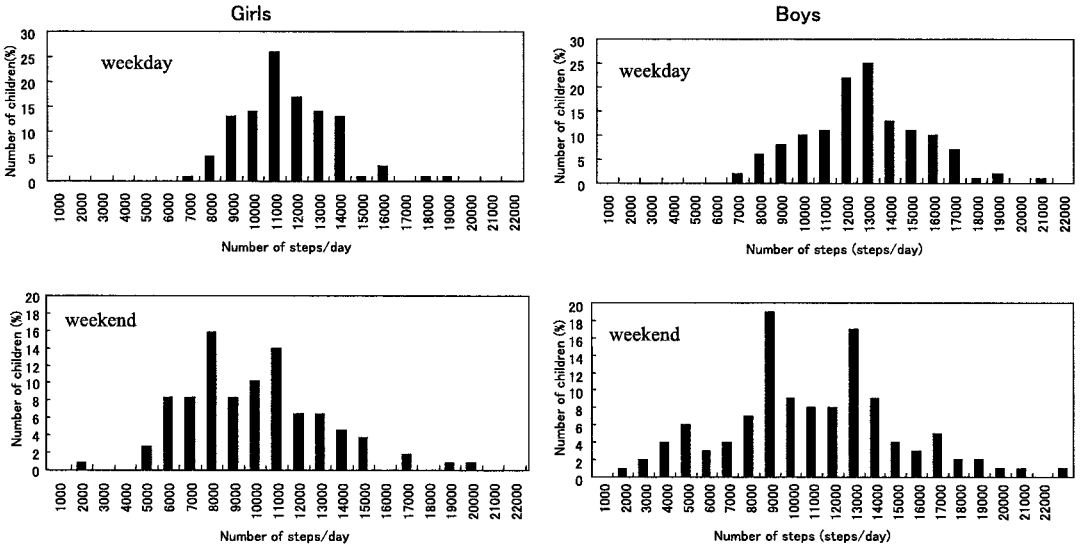

図5 幼児の歩数の分布（加賀谷ら）
平日（上）と休日（下）の分布を女児（左）と男児（右）で比較した．

思う．**図3**には，このようにして得られたデータも含まれている．研究所がこのようなプロジェクトの中で，中核的役割を果たすことができるようになったことは，研究所創設当時の前田充明理事長の「研究所は学内の先生方の研究拠点となるよう」との希望にも沿うものであった（前田，1991）．

3）子どもの健康と運動に関する共同研究

本研究所は開所当初から「子どもの遊びや日常的な身体活動」には関心をもって研究してきたが，研究が加速したのは厚生科学研究による共同研究（班長；村田光範　東京女子医科大学教授，当時）であった．本研究所が担当したのは，「子どもの身体活動量を測る」ということであり，観察法（タイムスタディ等），生理学的測定法（心拍数，酸素摂取量等），物理学的測定法（加速度，歩数等）について，幼児を含む子どもに適切な装置や方法の検討を行った．それぞれ長短あって，絶対的な方法はなく，目的にあわせて選ぶこと，できれば複数の方法を併用することが望ましいこととの結論であった．本研究所では，身体活動量の減少に伴う子どもの体力低下を阻止するために，子どもの身体活動量の目標値を設定することを目的としてきた．現段階では，**図5**のような歩数による結果を踏まえて，下記のような提案を行った（加賀谷ら，2003）．今後，生活環境，ライフスタイルの異なる子どもたちについて多数のデータ収集を行い，子どもの身体活動量の目標値を明確に示すことが必要である．

> 活動的な生活を目指した子どもの運動量の目標値（試案）
> 幼児から小学生　歩数　12000-14000歩/日
> 中学生　歩数　14000歩/日以上

一方，新体力テストの作成（文部科学省；研究代表者青木純一郎；順天堂大学教授）や子どもの体力低下予防に関する研究の推進（科研費：研究代表小林寛道；東京大学教授）プロジェクトにおいても，本研究所は，子どもの最大酸素摂取量や末梢血流，血管研究から貢献した（加賀谷ら，2003）．

しかし，子どもの身体活動の問題は，年々重要になっており，国をあげて取り組むべき課題であるとの認識が高まっている．今後も研究所が継続して取り組む課題である．

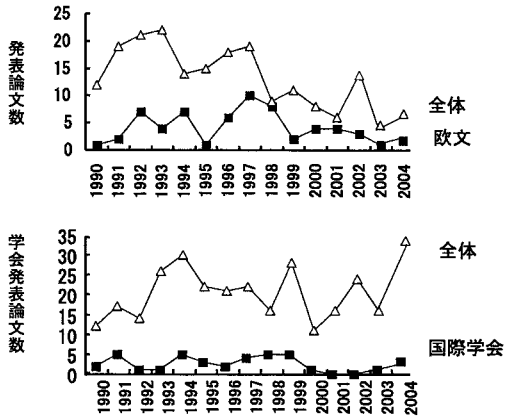

図6 研究成果の年次推移
発表論文数と学会発表数.

4) 本学競技選手の体力科学的サポート

本学に研究所を設立した目的のひとつに，本学競技選手の競技力向上に役立つ「科学的サポートを行う」ことがあった．当初，研究所スタッフとこの問題に関心をもって兼担研究員となった教員がその都度，努力してきたが，人的制約の中で，目標としたサポートは困難であった．幸い，学園・大学の理解が得られ，1999年11月から，技術職員（嘱託）が1名採用され，2000年から指定強化部の体力科学的サポートが開始された．これまで，バスケットボール部，新体操部，バレー部，陸上競技部等がそれぞれ独自の体力測定を要請し，選手強化を第一優先に考えた事業が展開されている．現在では定期的に体力測定を実施している運動部もあり，監督・コーチの側からは如何に研究所を利用するか，研究所スタッフからは如何に役立つデータを出すかについて智恵を出し合っている．国立スポーツ科学センターがオリンピック選手の活躍に科学の力を発揮したように，本学においても，本研究所の機能を発揮して，本学選手の競技力が飛躍的に向上する日がくることを願っている．

5) 研究所15年間の研究成果の推移

研究成果を論文数だけで評価することはできないが，それでも研究活動の一面を評価するものであることに異論はないと思う．そこで研究所発の研究成果を発表論文数で，研究活動の活発度を学会発表数から検討した（**図6**）．兼担研究員，客員研究員を含む研究所スタッフの数は年によって異なるが，ここでは総数で示した．

ここ5年間の学会発表数（全体）をみると，変動しながらもそれ以前と同レベルを保っている．それに対して，国際学会発表数，欧文・和文の論文発表数はいずれも漸減した．すなわち，この数年間の研究活動は，データ収集から学会発表までは以前通りであったものの，残念ながら，論文としての成果発表については満足できるレベルにはなかったことが示されている．その理由はいろいろあろうが，ひとつは，研究所の研究責任者である担当教員が短期間に3人も交代したことであり，筆者もその責任を感じている．もうひとつの理由は，長期間にわたるフィールドワーク（高齢者；6年，幼児・子ども；8年）を実施したことである．発表論文数の減少は必ずしも研究所スタッフの研究活動の低下によるものではなく開所10年を一区切りとして，この5年間はフィールドワークにエネルギーを注いだことが大きな原因であったろう．多くのスタッフを擁する研究所であれば，実験室研究とフィールドワークを併行することが可能であるが，本研究所のように極めて小さな規模の研究グループでは非常に困難な状況であった．本研究所では，兼任の研究所長の元に，兼任教員1名，専任助手1名，新たに増員された技術職員1名，兼任事務員1名が日常的な研究所活動の担い手である（学内の兼担研究員や学外からの客員研究員はそれぞれの研究を実施している）．したがって，大規模なフィールドワークの実施とデータ整理，データのフィードバック，研究報告書の作成等にスタッフ全員が多大な時間を費やした．この時期，研究所研究室に所属した大学院生および学部生の献身的な活動がなければ，この数年の研究所活動は成り立たなかったと思う．共同研究に参加して得たものは極めて大きかったが，一方，論

文作成にかける時間が激減したのも事実である．研究の現場担当者として，結果(学術論文)が不満足であることに自責の念にかられつつ，そこに透けて見える研究所若手スタッフの日夜の努力がいかに大きかったかを，感謝を込めてここに報告しておきたい．

しかし，このような状況の中で，研究所若手研究者が学会賞を受賞したことは，研究の質を保証された感があって喜びは大きかった．受賞論文と受賞者を下記に記す．

清水静代（受賞時：助手），本間幸子，加賀谷淳子：2002年度日本体力医学会賞
片側および両側掌握運動に対する心拍出量と活動体肢血流量の応答．体力科学50（5）：633-642, 2001.

木村有里（受賞時：技術職員）：2002年度東京体育学会賞
主働筋および拮抗筋の筋形状と筋酸素動態の変化が急速反復肘運動の持続に及ぼす影響．木村有里，村岡慈歩，加賀谷淳子，日本体育学会東京支部第30回記念大会．東京，2003. 3.

加賀谷淳子：平成14年度　財団法人中富健康科学振興財団「健康科学振興賞」
日本体育学会推薦

大森芙美子（受賞時；技術職員）：2005年，第8回アジアスポーツ医学会優秀論文賞
Blood flow after contraction of short duration reaches its peak by 3rd cardiac cycle.
Ohmori, F., Shimizu, S., Hamaoka, T., and Kagaya, A. Tokyo, 2005. 5

3. 学術フロンティア推進事業の立ち上げ―さらなる飛躍を目指して―

本学は，「確かな専門性と豊かな教養を持つ人材」養成を目的としているが，確かな専門性を保証するひとつとして，「科学的理解」を重視してきた．本研究所は，そのための学内拠点となることが開所当時の設置者の考えであった（前田，1991，山川，1991）．開所10年の歴史を経過し，より一層の発展を目指すには，施設設備はもとより人材確保の上でも，限界になっていた．そこで，私立大学学術研究高度化推進事業(学術フロンティア)へ申請することとなった．本事業は「優れた研究実績を上げ，将来の研究発展が期待される卓越した研究組織を＜学術フロンティア拠点＞に選定し，内外の研究機関との共同研究に必要な研究施設，研究装置・設備の整備に対し，重点的かつ総合的な支援を行う」として文部科学省が平成9年度に創設したものである．本学は，基礎体力研究所を中心に，国内3大学，国外1大学の研究者と協力してプロジェクト申請を行い，「運動時における循環調節機構の統合的解明―スポーツによる健康・体力づくりプログラムの構築に向けて―」というテーマの研究プロジェクトが採択された．プロジェクト申請時（2004年）の研究者は以下の8名であった．

加賀谷淳子（研究代表者）
（日本女子体育大学・学長・教授）
定本　朋子（日本女子体育大学・教授）
加茂　美冬（日本女子体育大学・講師）
斉藤　　満（豊田工業大学・教授）
清水　静代（日本女子体育大学助手）
長田　卓也（東京医科大学・助手）
Marco Ferrari
（University of L'Aquila, Italy）
Valentina Quaresima
（University of L'Aquila, Italy）

2005年には学術フロンティア支援スタッフとしてポスドクの岩館雅子が加わり，さらに清水の慶應義塾大学への転出による後任助手佐藤耕平も参加して10名の研究者によって研究が進められている．

本研究プロジェクトを文部科学省私立大学教育研究高度化推進事業学術フロンティアに申請し，採択された背景と基盤は**図7**に示す通りである．第一は，21世紀には個性輝く大学が求められており，本学も21世紀に輝く体育大学を目指して「科学的根拠に基づく運動指導の

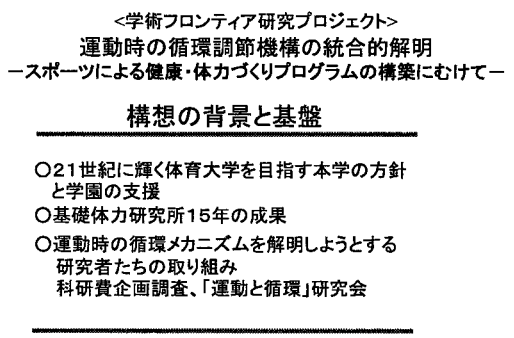

図7 学術フロンティア立ち上げの背景と基盤

できる人材養成」を重要視していることである．その大学の方針とそれに対する学園の支援の姿勢が，本プロジェクトが生まれる強力な基盤であった．一方，本プロジェクトが生まれた研究基盤は，基礎体力研究所を中心とした本学における研究成果の蓄積であった．さらに，運動時の循環メカニズムを解明しようとする国内・国外の研究者達の取組がある．国内においては，「運動と循環」研究会の継続的な活動やそこから発展した科学研究費企画調査による問題分析があった．

本研究所は，極めて小さな研究組織である．そこで，スタート当初から焦点を絞った研究をする「専門店」を目指してきた．専門店の内容は，運動の持続的遂行に重要であり，かつヒトの命に直結する「運動時の循環動態」に焦点を絞った研究であった．研究所の基礎的研究のプロジェクト「運動に対する身体の適応機序に関する生理学的研究」はこれに相当する．このプロジェクトでは，運動時の酸素供給系と消費系の運動への適合の仕組みを，心臓からの血液拍出と末梢血流，骨格筋間あるいは他の組織・臓器との血流分配，組織での酸素供給-利用のバランス，骨格筋の形状特性と筋内循環等について研究を進められた．そして，循環系に関与する複雑な要因を総合的に観察し，それらを統合して仕組みを考える研究の重要性が指摘された．また，科学研究費の補助を得て実施したこの分野の研究者たちとの企画調査においても同様の指摘がなされ，共同研究推進の重要性が強調された．今回，文部科学省学術フロンティア推進事業への構想が採択されたことにより，日本女子体育大学基礎体力研究所を学術拠点として整備し，循環関係に特化した先進的な研究を，一段を進める共同研究プロジェクトが発足することとなった．ここにあらためて関係各位に謝意を表する次第である．

本研究プロジェクトのゴールは，科学的 evidence を蓄積し，安全で効果的な運動のあり方を循環系指標から提案し，健康・体力の維持増進ための運動プログラムの開発に役立てることである．その前提となるのは，運動によって平衡を破られた循環システムをどのようにして調整するかを明らかにすることである．推進事業に採択されたことの責任を自覚し，学術的成果とその社会への還元を目指して，プロジェクト研究をすすめたい．

4. おわりに

15年の節目において，研究所の牽引者となる兼任教員は，スポーツ医学の赤間高雄助教授（当時）に変わり，さらに今日は，運動生理学の定本朋子教授へとバトンが渡された．また，研究所設立にあたって検討会委員として尽力された高橋和之教授が現所長である．研究所は今，新しい研究リーダを中心に若手研究者が活躍しており，研究所のさらなる飛躍の予感で満ちている．

開所以来15年間，研究所の活動をサポートして下さった学校法人二階堂学園と日本女子体育大学に謝意を表する．また，研究所の発展にご尽力下さった歴代所長はじめ，学生・院生を含む研究所関係者やご支援下さった学内外の皆様に感謝申し上げ，今後も学術フロンティア共同研究を推進する本研究所に対してご理解とご支援をお願いする次第である．

J. Exerc. Sci. 15 : 29—32, 2005

＜第 15 回基礎体力研究所研究フォーラム＞

特別講演

Future perspectives in the study of circulatory regulation during exercise

Professor, University of Waterloo Richard L. Hughson

Abstract

The matching of blood flow to the metabolic demand of skeletal muscle during physical activity is accomplished by the complex interplay of multiple feed forward and feedback mechanisms that are often redundant and compensatory. Therefore, the metabolite-induced vasodilation is modified by neural, hormonal(endocrine, paracrine and autocrine), local and physical factors. Ultrasound Doppler and imaging technologies have allowed researchers to explore the dynamic characteristics of blood flow regulation under conditions of dynamic and static muscle activity as well as in response to release from circulatory occlusion. At the onset of moderate intensity rhythmic contractions blood flow increases with two distinct phases. The first phase has been attributed in large part to the actions of the muscle pump with some vasodilation contributing to the increased flow. This first phase can be considered as primarily feed forward regulation from the perspective of delivery of oxygen to muscles that will soon have an elevated demand for aerobic energy supply. During the second phase blood flow adapts to meet the energy demand and there is normally a strong linear relationship between absolute blood flow and muscle oxygen consumption. This second phase of blood flow increase is regarded as being primarily under control of feedback regulation and research has examined the relationships between the change in blood flow and various vasodilator metabolites. In contrast to the concept of feedback regulation by local metabolites, recent research has shown that vasoactive compounds such as nitric oxide and prostaglandins play independent and additive roles in establishing blood flow during exercise that might be feedback or feed forward. However, additional studies are required to determine if these compounds actually have a role in establishing blood flow during exercise or if they simply permit blood flow to meet the metabolic demands. The link between blood flow and metabolism at the onset of exercise can be explored under conditions that manipulate flow such as acute elevation of mean arterial blood pressure by changes in body position or activation of the muscle chemoreflex response. It has been demonstrated that each of these models can modify muscle blood flow and cause changes in the rate of increase in muscle oxygen uptake. Blood vessel function is currently being explored during the reactive hyperemia that

follows a period of muscle ischemia. Evidence suggests that nitric oxide released in response to elevated shear stress stimulation of the endothelial cells has an important role in flow-mediated dilation. Further, factors such as chronic hypertension or elevated blood lipids might impair the response due to changes in the oxidant-antioxidant balance that alters the bioavailability of nitric oxide from the endothelial cell. However, experiments from our laboratory found contradictory results. We found that acute hyperlipidemia did not alter the flow-mediated dilation response in young and older subjects, and that acute elevations in sympathetic nerve activity achieved by muscle chemoreflex activation, lower body negative pressure, cold pressor test and mental arithmetic did not have consistent effects. Thus, future research is required to determine what links exist between sympathetic activation or elevated blood lipids and endothelium-mediated dilation of conduit and resistance arteries and arterioles.

日本女子体育大学体育学部附属基礎体力研究所開所15周年記念シンポジウム「学術フロンティア推進事業―『運動時の循環調節研究』の学術拠点を目指して―」において，運動時の呼吸循環調節研究の第一人者であるHughson教授（カナダのウォータールー大学）に特別講演をしていただいた．講演前に頂いた英文抄録は上記のとおりである．以下に，当日の講演内容をまとめた．

講演に先立ち，座長である加賀谷淳子先生から，Hughson博士が運動時の酸素動態（O_2 Kinetics）研究の専門家であり，また酸素の立ち上がりの決定に血流が深く関係することから，運動時の呼吸循環調節について研究成果を次々に公表されていること，Hughson博士の研究グループからは優れた研究者が輩出されていることなどの紹介があった．また博士自身がランナーであり，かつて福岡国際マラソンで10位に入るという経歴を持っておられること，そして指導した学生も国際マラソン等で好成績をおさめている，といった側面も紹介された．

Hughson教授は，交感神経活動による血流調節の重要性と活動筋の筋量の影響について報告した斉藤先生（豊田工業大学）と加賀谷先生の共著論文（Acta Physiol Scand, 1992）に触発されたことなどを話された後，次のような内容の講演をされた．

Ⅰ．運動開始時の酸素供給を決める血流調節について

一定負荷に対する酸素摂取量は指数関数的応答を示して定常状態にいたるが，その立ち上がりが運動パフォーマンスに深く関係していること，さらに酸素摂取量の立ち上がりはエネルギー代謝および呼吸循環調節機能といった身体諸機能を反映する指標であることから，運動生理学の課題として非常に重要であるといった主旨の話をまずされた．続いてO_2の立ち上がりを決める主要因が活動筋の血流であることから，筋血流の調節の検討が次に重要になることを話された．この血流調節の重要性を説明するために，酸素摂取量と筋血流量のレスポンスタイムが1対1で対応するという実験結果をスライドで示された．

続いて，筋血流が運動時にどのように調節されるのか，という話題に移り，①プロスタグランディンと一酸化窒素による調節，②動脈血圧の影響，③運動に伴う代謝物質に関わる因子による調節，といったトピックスを紹介された．

最初に，プロスタグランディン（PG）や一酸化窒素（NO）の調節についての話があった．現在，PGとNOが運動時の血流増大の説明因子であるという見解と逆に説明因子ではないという見解があるが，Hughson教授のグループでは，「PGとNOが各々単独では運動時血流

を増大させる因子とはならない」と考えていることを説明された．そしておそらくPGとNOは共に存在した時にはじめて血管拡張作用を示し，筋血流の増大をもたらすのだろうということも指摘された．

次に，巧みな実験により，動脈血圧(潅流圧)が血流を変化させることについて話された．その実験とは，循環調節の研究者であれば誰もが良く知っている運動後の筋を虚血し昇圧反応を生起させる実験手法である．筋代謝受容器反射の研究に不可欠な方法を活用して動脈血圧を上げると，筋の血流がみごとに上昇するという実験成果を示された．

さらに，高強度の運動(たとえば自転車作業)を2回連続させると，2回目の運動時の酸素摂取量が1回目より早く立ち上がり，また脚筋血流量の立ち上がりも早くなるという結果について話された．この2回目の立ち上がりを早くさせる要因を検討した結果，運動時の代謝産物であるカリウムイオン(K^+)，水素イオン(H^+)，アデノシンの間質液中濃度が2回目の運動時に大きく増加することを見出し，これらの因子が関与するのだろうと説明された．つまり，上記の代謝物質が筋中に放出されると，血管拡張を起こし，筋血流を増加させることになり，筋酸素摂取量の立ち上がりを早くさせることに繋がるということである．

Ⅱ．循環調節を決定するその他の要因

続いての話題は，動脈血管の拡張機能を示す血流依存性血管拡長作用（FMD）についてであった．まずFMDの計測方法について話された．

血管最内壁に存在する内皮細胞が，血流速度の機械的刺激（ズリ応力，シェアーストレス）により血管を拡長させる物質（たとえばNO）を出すことが知られている．またこの血管内皮細胞の働きが全身の血圧調節にも深く関わることから，さまざまな研究者がFMDを検討しているといえる．FMD測定によく用いられる手法は，上腕の動脈血流阻止後に圧を開放し，それにより一挙に増した血流速度がシェアストレスとなって，どの程度血管径を拡張させるのかを超音波法により測定するという方法である．この方法の中で，これまで加圧カフと超音波プローブの位置について，あまり注意が払われてこなかったと思うが，Hughson教授らのグループがこれらの位置がデータを大きく変えることを，明確に示したということである．カフの位置がFMDを大きく変動させる結果を見ながら，一定した方法・再現性のある方法を疎かにしてはならないと今更ながら考えさせられた．また教授はFMDが血流速度のピーク値によって決まること，血管径の計測値は実測値ではなく近似値を用いていることなども説明された．

次に，FMDの測定を用いて「食事が血管内皮機能に及ぼす影響」についての話をされた．高脂肪食（脂質48%，糖質36%，タンパク質16%，総カロリー1077kcal）あるいは低脂肪食（脂質2%，糖質86%，タンパク質12%，総カロリー1080kcal）を，約4週間とり続けるとFMDがどのように変化するかについて調べた実験であった．この研究の仮説は，高脂肪食を摂り続けると，他の研究でもいわれているように，血管内皮機能を低下させるということであったらしい．しかし実験の結果は，仮説どおりにはならず，高脂肪食をとってもFMDは低下しなかったそうである．教授の研究グループは，被験者群を変えて同様の実験を繰り返し追試したが，やはり仮説を支持するような結果は得られなかったことも話された．そして，なぜこのような結果になったのか，その理由は今後の検討課題ということであった．一方，トマトに多く含まれているというリコピン（抗酸化作用をもつ）を摂ると，明らかにFMDに相違がみられ，リコピン摂取はFMDの増大，つまり血管内皮機能を向上させる効果をもつという話をされた．こちらの方は仮説のとおりの結果ということであった．どちらも身近な話題であり，また新たなデータということでとても興味深く聴かせていただいた．

このような講演の最後に，Hughson教授は

これまでの研究成果を踏まえて，未解決課題や矛盾点をこれからも明らかにしたいということを述べられた．そして，基礎体力研究所の学術フロンティアが成功することを期待している，また同時に日本の多くの友人や仲間の成功も祈っている，という言葉で講演を締めくくられた．

講演の後には，さまざまな質疑応答がなされ，学術フロンティア推進事業の最初の国際シンポジウムにふさわしい充実した内容の意見交換も行われた．

このような有意義な会議にしていただいたHughson教授と学内および学外から参加していただいた多数の研究者および大学院生の方々に，あらためてここに深く感謝の意を表したいと思います．

（文責：定本朋子）

日本女子体育大学附属基礎体力研究所
第17回研究フォーラム・学術フロンティア研究成果中間報告会

日　　時：2006年11月25日　13：30～16：40

会　　場：日本女子体育大学本館　E102

プログラム

13：30　　開会の挨拶　　**永島　惇正**（日本女子体育大学学長）

13：40～15：00　研究成果（中間）報告

座長　**中村　　泉**（日本女子体育大学教授）

「プロジェクト全体の説明」

定本　朋子（日本女子体育大学教授）

「中心循環と末梢循環のマッチングとミスマッチング」

清水　静代（慶應義塾大学体育研究所講師）

「骨格筋への血流配分と筋からの血液還流」　**加賀谷淳子**（日本女子体育大学名誉教授）

大森芙美子（鹿屋体育大学大学院）

「運動時の内臓器官および脳の血流動態とその調節機構」

定本　朋子（日本女子体育大学教授）

「運動時の筋交感神経活動からみた中枢指令および反射性制御の調節機構」

斉藤　　満（豊田工業大学教授）

「運動準備期のセントラルコマンドの働き」

岩館　雅子（学術フロンティアポスドク研究員）

「運動時の呼吸循環系変化に対する中枢性・末梢性の神経調節」

佐藤　耕平（日本女子体育大学助手）

「有疾患者における運動および筋虚血に対する血流調節プロファイル」

長田　卓也（東京医科大学講師）

15：00～15：30　コーヒーブレイク　〈研究成果ポスター発表〉

15：40～16：30　特別講演

司会　**高橋　和之**（日本女子体育大学基礎体力研究所所長）

「脳を正しく使おう」

金澤　一郎先生

（国立精神・神経センター総長，日本学術会議会長，宮内庁長官官房・皇室医務主管）

16：40　閉　会

日本女子体育大学附属基礎体力研究所
第17回研究フォーラム・学術フロンティア研究成果中間報告会

「運動時における循環調節の統合的解明
－スポーツによる健康・体力づくりプログラムの構築に向けて－」

学術フロンティア推進事業「運動時における循環調節の統合的解明－スポーツによる健康・体力づくりプログラムの構築に向けて－」は，日本女子体育大学附属基礎体力研究所を拠点として，国内外の研究者中心に（表1参照），平成16年度から実施されている事業である．平成18年度はその5年間にわたる研究期間の中間年にあたり，基礎体力研究第17回研究フォーラムを兼ねた，学術フィロンティア研究成果中間報告会を平成18年11月25日に開催した．

永島　惇正学長（日本女子体育大学）の開会挨拶では，私学助成学術フィロンティア推進事業の経緯と本学における学術的意義に対する期待の言葉が述べられた．また成果の中間報告会という節目にあたり，多忙にも関わらず，特別講演をしてくださる金澤一郎先生への感謝が述べられた．研究成果中間報告会では，中村　泉教授（日本女子体育大学スポーツ健康学科長）の司会により，プロジェクト全体の概要（図1）およびこれまでの主な研究成果が報告された．発表された報告の要旨は以下のとおりである．

また，当日の午前中に開催された本プロジェクトの「外部評価委員会」においても，以下の要旨を含む研究成果についての報告がなされ，評価を受けるとともに，多くの示唆と教示を頂いた．その外部評価委員としてご尽力をいただいた浅見　俊雄先生（東京大学名誉教授・元国立スポーツ科学センター長），松田　光生先生（筑波大学名誉教授，流通経済大学教授），田村　照子先生（文化女子大学大学院研究科長・教授）に心より感謝を申し上げる次第である．また研究成果中間報告会の開催，外部評価委員会の実施にあたりご支援をいただいた学校法人二階堂学園理事長ならびに教職員の皆さまに重ねて感謝申し上げる次第である．

本プロジェクトの概要

現代社会においては日常的な身体活動の機会が減少し，すべての人々にとって意図的運動の実施が極めて重要である．しかし，「動く」ことに対する身体適応のメカニズム，特に「安全性」確保に不可欠であり，かつ多数の因子が複雑に作用する運動時の循環調節機序は十分明らかにされているわけではない．そこで本プロジェクトでは，さまざまな特性を持つ運動時の循環調節機構を明らかにすると同時に，多様な特性を持つ健康人および有疾患者に適用して検証し，科学的根拠を持つ「安全で有効な運動プログラム」の構築に向けた提案を行うことを目的としている．本プロジェクトは科学的な新知見をもたらすと同時に，国の重要かつ喫緊の課題となっている国民の健康のための運動推進にも貢献するという大きな意義がある．

平成16～20年度にわたる5年間の研究期間のうち，最初の3年間（平成16～18年度）は，運動時の循環調節の研究基盤を確立するために，様々な運動様式（動的と静的運動），種々の運動強度と運動時間，身体各部位の運動を実施させて，循環の中心である心臓からの血液の拍出量（心拍出量）と身体各部位・臓器（活動筋，非活動筋，腹部内臓，脳など）への血流の分配，筋組織での酸素動態，血圧応答，交感神経活動の変化を測定し，循環調節に関与する生理学的因子の解明とその調節機構を実験的に明らかにする計画である．続く2年間（平成19～20年度）は，それらの調節機構が，発育や加齢に伴ってどのように変化するか，疾患の有無，競技者と非競技者との体力差，男女の相違といったさまざまな身体特性をもった対象者において明らかにする．最終的には，これらの成果を総合して，循環調節の観点から安全で有効なスポーツ運動プログラムについて提案する．

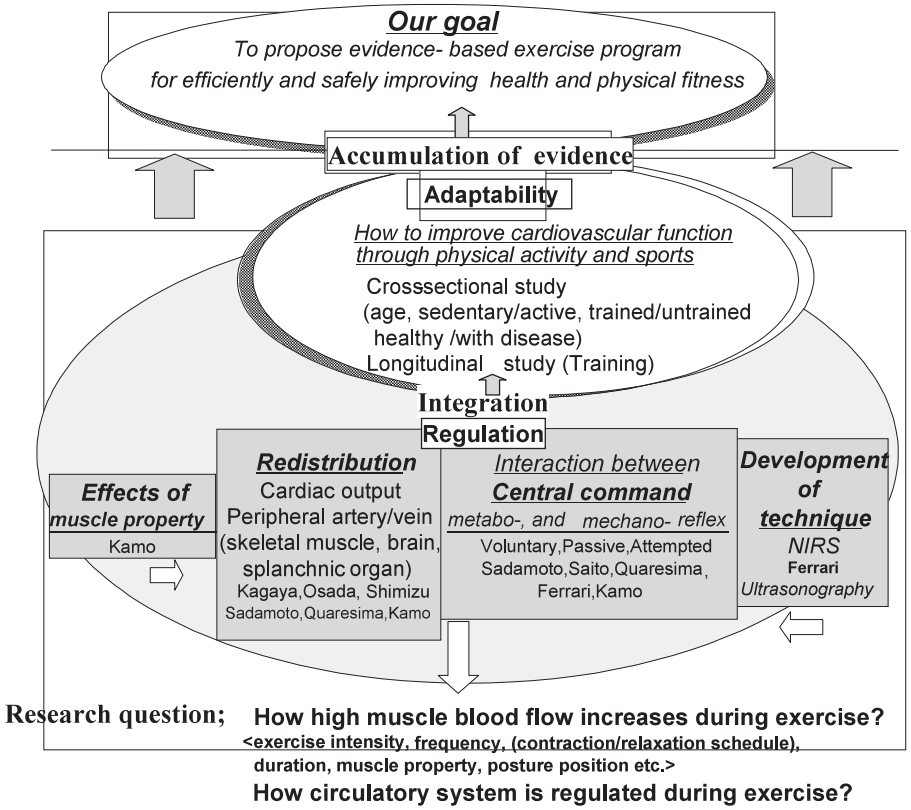

図1　本プロジェクトの研究デザイン

表1　プロジェクトの研究体制（平成18年現在）

研究者氏名	所属・職名	プロジェクトでの研究課題	プロジェクトでの役割
加賀谷淳子 研究代表者 (平成16～18年度)	日本女子体育大学 名誉教授	骨格筋への血流分配と筋からの血液還流	運動特性と骨格筋への血流分配への関係解明，研究全体の統括と推進.
定本　朋子	日本女子体育大学教授	運動時の内臓器官および脳の血流動態とその調節機構	非活動組織血流からみた運動時の循環調節の解明，研究の実施に関する統括と推進.
加茂　美冬	日本女子体育大学 助教授	運動様式，運動強度，運動時間および筋代謝からみたモーターユニットの動員特性	筋疲労発現，運動特性，筋代謝との相互連関の解明
清水　静代	慶應義塾大学体育研究所講師	運動時の心拍出量の変化と各種血管への血流分配	中心静脈と末梢循環のマッチングとミスマッチング
佐藤　耕平	日本女子体育大学助手	運動時の呼吸循環系変化に対する中枢性・末梢性の神経調節	呼吸循環応答に関わる調節因子の解明
岩館　雅子	学術フロンティア支援スタッフ，ポスドク研究員	運動準備期のセントラルコマンドの働き	セントラルコマンドと循環応答の対応関係の解明，各研究プロジェクト実施のための補助や調整
斉藤　　満	豊田工業大学教授	運動時の筋交感神経活動からみた中枢指令および反射性制御の調節機構	自律神経による運動時循環調節メカニズムの解明
長田　卓也	東京医科大学講師	有疾患者における運動および筋虚血に対する血流調節プロファイル	低体力者や有疾患者の循環調節メカニズムの解明と運動療法の基盤構築
Marco Ferrari	University of L'Aquila (Italy) 教授	脳循環・代謝測定用近赤外線分光法の開発	研究装置の開発
Valentina Quaresima	University of L'Aquila (Italy) 教授	近赤外線分光法による運動時の脳循環・代謝の変化	脳への血流分配にかかわる調節機構の解明

■ 研究成果（中間）要旨

骨格筋への血流分配と筋からの血液還流

加賀谷　淳子（日本女子体育大学）
大森芙　美子（鹿屋体育大学大学院）

Abstract

Re-distribution of blood flow to skeletal muscles was studied to clarify 1) an interaction between arterial and venous flow, 2) exercise time- and intensity-dependent blood flow changes to no-exercising limb, and 3) time course of changes in post-exercise blood flow. Three studies were conducted, The first study indicated that the brachial venous outflow due to muscle action accelerated brachial arterial blood flow when a prolonged handgrip exercise increased muscle blood volume. The second study observed blood flow and vascular conductance of non-exercising forearm and leg during handgrip exercise. Vascular conductance of non-exercising limb increased or decreased depending on exercise intensity, exercise duration, and the limb used and vessels studied. The third study was conducted to find the time course of blood flow changes immediately after exercise to find an optimal exercise interval (frequency). As a result, The largest occurrence of the cardiac cycle for peak blood flow after exercise was at the 3rd cardiac cycle in all contraction intervals and exercise intensities,

（1）活動中の骨格筋への血流供給は，筋内血液量や静脈血流出量によって修飾されると考えられてきたが，静脈血流量測定の困難さから，その仮説が実証されてはいなかった．本研究プロジェクトにおいて実施された掌握運動時の動静脈血流の研究から，時間経過に伴う両者の関係は必ずしも一致していないこと，筋ポンプ作用（筋収縮によって筋内から押し出される血液量）が動脈側に影響を与えるのは，運動開始直後の極く短時間と，運動持続後の筋内血管床が拡大する時期においてであることが明らかになった．

（2）筋活動中の非活動体肢血流量は，血管拡張作用によって減少するとする報告と，血圧依存で増加するとする報告があり，議論の対象となっている．すでに，アームクランキング（上肢回旋運動）とサイクリング運動では強度依存で増加すること，それは，血管に対するシアストレスによるものであることを示したが，本プロジェクトでは，掌握運動時の非活動上下肢の血管コンダクタンスは運動の強度だけでなく，持続時間にも依存した変化を示すこと及び部位特異性のあることを明らかにし，この論争に新たな知見を加えた．

（3）骨格筋への血流量が運動後，一過性に低下するのか，増加するのか，増加するとすれば時間はどれくらいかは明らかでなかった．本プロジェクトでは，下腿運動後の膝窩動脈血流量は運動後増加し，それは３心拍目に，最高値に達するとの新知見を得た（アジアスポーツ医学会賞受賞）．

運動時の内臓器官および脳の血流動態とその調節機構

定本　朋子（日本女子体育大学）

（1）内臓器官の血流動態とその調節機構

Abstract

Since visceral regions are consisted of functionally different organs such as kidneys and gastrointestinal tracts. It was hypothesized that blood flow regulation induced by the autonomic activation

during exercise is different among arteries supplying to specific organs. To verify the hypothesis. We studied blood flow responses in renal artery (RA) and the superior mesenteric artery (SMA) during static handgrip exercise and the postexercise muscle ischemia (PEMI). Ten healthy female volunteers performed a sustained static handgrip exercise at 30 % of maximum voluntary contraction for 2 min followed by a 6-min recovery period (control condition). Subjects also underwent the occlusion condition. In which arterial blood flow in the upper arm was arrested immediately after the handgrip exercise. Mean arterial blood pressure (Finapres), heart rate (ECG), and blood flow in RA (RABF) and SMA (SMABF) were measured by Doppler ultrasound technique. Vascular resistance in RA and SMA (RAVR and SMAVR) were calculated. During handgrip exercise, RAVR significantly increased and sustained at the higher level during PEMI in occlusion condition. Whereas RAVR in control condition returned to the resting level. On the contrary, SMAVR in both conditions slightly increased during exercise and returned to the resting level during PEMI. These results supported the hypothesis that blood flow regulation among different visceral organs is differential during exercise and PEMI. RA appeared to be more sensitive to exercise stimulus and the reflex signals arising from muscle metaboreceptors than SMA. The artery supplying to the digesting gastrointestinal tract such as SMA might be to some degree exempt from flow-reducing participation during exercise.

先行研究では「運動時には腹部内臓の血流減少が起こる」と一括されてきたが，本研究では，臓器によって運動時の内臓血流調節が異なるとの知見を得た．静的運動時（30％ MVC負荷）には腎動脈血流が低下し，腎の血管抵抗が著しく上昇した．一方，消化器官へ連絡する動脈（上腸間膜動脈）では，同一運動であっても腎動脈のような血流減少がみられず，血管抵抗の上昇も低いことが示された．このような腎動脈と上腸間膜動脈の血流反応の違いをもたらす要因として，筋代謝受容器反射（活動筋中に蓄積された代謝産物に由来する反射性制御）の働きが腎動脈と上腸間膜動脈では異なることが示された．腎動脈は上腸間膜動脈に比べ，筋代謝受容器反射による血管収縮作用を受けやすいことが示唆された．

(2) 運動時の脳血流動態とその調節

Abstract

To elucidate the cerebral blood flow responses to static exercise, we measured arterial blood flow responses in three sites of "the carotid artery root" and one site of "the vertebral artery root". Ten healthy female volunteers performed a 3-min sustained static handgrip exercise with ramp load increasing from 10% to 30% of maximum voluntary contraction followed by a 3-min postexercise muscle ischemia (PEMI). The blood flow (BF) in left common carotid artery (CCABF), the left internal carotid artery (ICABF), and the left vertebral artery (VABF) was measured by ultrasonography. Mean flow velocity in the left middle cerebral artery (MCAV) was also recorded. Mean arterial blood pressure (MAP; Finapres) and heart rate (HR; ECG). The vascular resistance (VR) was calculated from the ratio of MAP to the CCABF, ICABF, VABF, or MCAV. During static exercise the vascular resistance in all arteries increased from the resting level in parallel with the increase in MAP, but the magnitude of increase was greater in the "carotid artery root" than the "vertebral artery root". During PEMI, CCABF-VR, ICABF-VR, and MCA-VR were significantly higher than the resting level, whereas VABF-VR returned to the resting level. These data suggested that the static exercise produced greater vasoconstriction in the "carotid artery root" than the "vertebral artery root" and that the muscle metaboreflex played an important role in vasoconstriction in the "the carotid artery root" but not in the "vertebral artery root"

脳への血流は左右の内頸動脈経路（主に大脳皮質側頭葉，前頭葉，頭頂葉，島皮質へ潅流）と椎骨動脈経路（主に延髄，小脳，後頭葉へ潅流）の２経路により供給されるが，この２経路における運動時の血流動態およびその調節機構に相違があることが示された．内頸動脈経路では，血圧が上昇するような運動時には顕著な血管抵抗

の増大，つまり血管収縮作用がみられ，これにより流入血液を制限することが示唆された．一方，椎骨動脈経路では血管抵抗の増大が少なく，血流の制限が少ないことが示された．またこのような血管抵抗増大の要因として，頸動脈経路では筋代謝受容器反射が果たす役割が大きいが，椎骨動脈経路では筋代謝受容器反射の関与が殆どみられないことも示された．

運動時の筋交感神経活動からみた中枢指令および反射性制御の調節機構

斉藤　　満（豊田工業大学）

Abstract

This project attempted to investigate the effect of central command (CC) and peripheral reflex on regulation of exercise circulation. Since sympathetic nervous system has crucial role to regulate cardiovascular system, muscle sympathetic nerve activity (MSNA), which is modulated by CC and reflex input from periphery, was recorded during and following isometric handgrip. MSNA, blood pressure (BP) and perceived excretion as an index of CC increased gradually during exercise while inhibitory effect of baroreflex on MSNA decreased gradually until exercise end. However, during post exercise ischemia (PEI) its effect increased again compared with during exercise indicating that CC might influence baroreflex effect. In the second study, MSNA response during high intensity handgrip exercise and metaboreflex MSNA during PEI was compared between dominant (DA) and non-dominant arm (NDA) exercise. MSNA response during high intensity handgrip was the same in both arms, while metaboreflex MSNA response during PEI was greater in DA than in NDA. In addition, effect of four weeks resistance training of NDA on metaboreflex MSNA response was investigated and the response was still greater in DA compared to NDA exercise. These results demonstrate that no difference in CC between DA and NDA, but metaboreflex was different and the difference could not cancel with short-term resistance training.

運動時の圧反射調節にはセントラルコマンド（運動努力）が常時関わり，その強さに依存して変化することが示され，運動努力の重要性が確かめられた．利き腕と非利き腕をトレーニング，非トレーニング肢モデルとしてセントラルコマンドの効果を検討した結果，セントラルコマンドの左右差は認めなかったが，代謝受容器反射の差を認め，この結果に基づいて，代謝受容器反射がレジスタンストレーニングで解消できるかどうか検討した．その結果，短期間の高強度レジスタンストレーニングは最大筋力やパフォーマンスを向上させるが，MSNA反応の左右差を解消することはできず，代謝受容器反射への効果は認められなかった．したがって，代謝受容器反射に対する効果は４週以上のトレーニングが必要と考えられた．

運動様式，運動強度，運動時間および筋代謝からみたモーターユニットの動員特性

加茂　美冬（日本女子体育大学）

Abstract

The first new finding of this study was that a constant discharge rate of motor units does not maintain constant force development, and "rate coding" is considered to be necessary for keeping a constant force. This finding was based upon following experiments. The evoked force of muscle fibers was observed during repetitive electrical stimulation for 3min on m. vastus medialis. The stimulus frequency was 0.2 Hz, 10 HZ and 20 Hz. The changes in the evoked force did not represent a constant but

were complex at 10 Hz and 20 Hz stimulations. At 10 Hz the evoked force showed an initial transient increment, then an abrupt decrement followed by a gradual increase and then a gradual decrease. The initial transient peak did not appear at 20Hz stimulation. The magnitude of potentiation was not necessarily large at 20 Hz. The second finding of this study was that the mechanism to induce changes in AMP during muscle exertion was not explained by the previously proposed hypothesis, because a significant positive correlation coefficient was obtained between CV and AMP.

筋力は骨格筋の運動単位（motor unit）の振る舞いにより決定されている．本プロジェクトでは，随意的に一定張力を発揮し，それを維持する静的運動（関節角度が変化しない状態で筋力発揮をする運動様式）を多く用いている．また運動負荷をさまざまに変化させる運動様式も多用している．このような運動時の運動単位の特性について，まず一定筋力の保持時について次のような知見を得た．一定頻度の電気刺激により誘発張力は初期に増大するが，この初期における張力増大を抑えるように，運動単位の活動頻度（放電間隔）を延長させる仕組みがあることが明らかとなった．また随意筋力発揮時の運動単位活動電位の波形（振幅）が，一定筋力を維持した場合や強度を変化させた場合といった筋力発揮様式により異なることを運動単位活動電位の波形解析から明らかにした．そして筋力発揮様式により波形振幅を変化させる仕組みとして，従来の説明（Na^+-K^+ ポンプの増強）が当てはまらず，新たな説明が必要であることを指摘した．このような運動単位の活動変化は，筋線維間を走行する血管にも影響を与える重要因子であり，運動時の循環を考える上で貴重な知見である（第60回日本体力医学会学会賞受賞）．

有疾患者における運動および筋虚血に対する血流調節プロファイル

長田　卓也（東京医科大学）

Abstract

The present study examined the femoral arterial blood flow response in each leg during intermittent isometric knee extension at incremental exercise intensities in patients having peripheral vascular disease. Changes in blood flow during exercise tend to be higher in the more-affected leg (PVD side) than the control healthy leg. Hyperemic response in the working skeletal muscle may be different in both legs. It is speculated that peripheral vascular disease may influence the blood flow response in muscle contractions during a state of exercise.

閉塞性動脈硬化症保有者は，下肢動脈血管の動脈硬化による血行障害のために運動歩行時に間歇性跛行を認める．しかしながら，疾病下肢運動中の血流動態についての報告は少ない，そこで本研究では一過性運動時における血流動態を検討する事を目的とした．閉塞性動脈硬化症保有者を対象に，両下肢それぞれにおいて多段階負荷等尺性片側膝伸展運動中の下肢血行動態を検討した．安静時において，疾病下肢血流量は，その反対側である対照下肢と比較して少ない傾向を示した．しかしながら，運動強度に対する下肢血流増加は，対照下肢側に比べ疾病下肢側において大きい傾向が認められた．運動に伴う疾病側下肢血流反応は，対照下肢と比べ異なることが考えられ，末梢循環障害が安静時のみならず運動中の骨格筋循環に与える影響が示唆された．

中心循環と末梢循環のマッチングとミスマッチング

清水　靜代（慶應義塾大学）

Abstract

The purpose of this study was to determine cardiac output and active limb blood flow responses to knee extension exercises. Two physically active women performed knee extension exercises with the one-legged. Exercise intensities were 20%, 30% and 40% of the subjects' maximum voluntary contraction (MVC) and the exercise frequency was 50 contractions per minute. The 20% MVC exercise duration was 10 min, while the 30% and 50% MVC exercise conditions were performed to exhaustion. During exercise, stroke volume (SV) and heart rate (HR) were measured using Doppler ultrasound and electrocardiogram (ECG), respectively. Cardiac output (Qsys) was calculated as the product of SV and HR. Blood flow to the femoral (Qfa) was measured by Doppler ultrasound methods. The Qsys about increased 1.4-2.0 times, when Qsys and Qfa were compared in the change from the resting level. In contrast, Qfa during exercise were about 6-18 times. That it, compares the Qsys with Qfa did not changes from the resting level. In addition, during muscle contraction phase of knee extension exercise, the effect of muscle contraction and relaxation on blood flow differs between Qsys and Qfa.

循環の中枢である心臓の拍出量と末梢の血流量は互いに影響しあい，末梢循環のみで調節できる場合と，中心循環を増加させて調節する場合がある．したがって，中枢と末梢の循環を同時に測定し，両者の相互作用を明らかにすることは重要である．本研究は，活動筋量の相違，及び筋の活動期および活動休止期の大腿動脈血流量が，心拍出量とどのような関係にあるのかを明らかにすることを目的とした．その結果，いずれの強度においても心拍出量は，大腿動脈血流量と比較し安静時からの変化は少ないことが示された．また，大腿動脈血流量は筋活動時には抑制，筋活動休止期には亢進されるが，心拍出量は筋活動及び休止の影響を受けないことが示された．

運動時の呼吸循環系変化に対する中枢性・末梢性の神経調節

佐藤　耕平（日本女子体育大学）

Abstract

The purpose of the present study was to evaluate the role of central command and muscle mechanoreflex on the cardiorespiratory and cerebral blood flow responses at the onset of dynamic exercise. Eleven young women were studied during no-load voluntary exercise (central command/muscle mechanoreflex) and passive movement (muscle mechanoreflex). Voluntary exercise consisted of single arm elbow flexor-extensor exercise for 2-min with no-load. Passive movement was achieved using a motor-driven lever arm and performed with the same range of movement, angular velocity, and frequency as voluntary exercise. In the present study, the following results were obtained: 1) Middle cerebral artery blood velocity (V_{MCA}) and common carotid artery blood flow ($\dot{Q}_{CCA}$) increased significantly ($P < 0.05$) at the onset of voluntary exercise in parallel with increases in the circulatory responses such as heart rate (HR) and cardiac output (CO). 2) During passive movement, no changes in circulatory and cerebral blood flow responses were observed. These results suggested that central command, but not muscle mechanoreflex, may significantly contribute to the immediate increase in circulatory and cerebral blood flow responses at the onset of dynamic exercise. Moreover, it is possible that the increase in HR and CO at the onset of voluntary exercise may directly affect on cerebral

blood flow responses at the onset of voluntary exercise.

本研究課題では動的運動開始時における呼吸循環応答及び脳血流応答に対するセントラルコマンドと筋機械受容器反射の役割を検討する．被検者は11人の健康な女子大学生とし，2分間の安静後，無負荷での随意肘伸展屈曲運動（VOL）と，受動的にVOLと同じ動作を行なう受動的動作（PAS）をそれぞれ2分間行い，呼吸循環応答に加え，総頸動脈血流量，中大脳動脈血流速度を連続的に測定した．VOL開始時における総頸動脈血流量および中大脳動脈血流速度の増加は心拍数や心拍出量の増加と同期した．しかしながら，PAS開始時には毎分換気量といった呼吸応答に増加が見られたものの，循環応答及び脳血流応答には変化が認められなかった．この結果は，筋機械受容器反射由来の神経反射は主に呼吸系の応答に影響を与える可能性と，随意運動に伴うセントラルコマンド由来の心拍数，心拍出量の増加が脳血流応答に直接的に影響を与える可能性が示唆された．

運動準備期のセントラルコマンドの働き

岩館　雅子（日本女子体育大学基礎体力研究所ポスドク研究員）

Abstract

To study the relation between cardiovascular variables and the activation in the sensorimotor cortex (SM), we measured heart rate (HR), mean arterial blood pressure (MAP) and the oxygenation in SM area and in the forearm flexor muscles by near-infrared spectroscopy (NIRS) during preparatory phase of handgrip exercise. Eleven young healthy females participated in the three sessions with exercise task (ET), a load of 5%, 30%, or 80% of maximum voluntary contraction, and one session without exercise task (Con). In all sessions, subject was asked to count a number continuously from 1 to 50 in accordance with 1-Hz sound signal provided 10 sec before the number counting, and thereafter a 10-sec handgrip exercise was performed in ET but not in the Con. During the preparatory phase, the levels of oxyHb and totalHb in left SM area were higher in ET than those in Con. HR and oxyHb in the active muscle showed similar responses as seen in the oxyHb and totalHb in SM area in spite of different responses seen in mean arterial blood pressure and cardiac output. These results suggested there are a close linkage between the activation of cortical motor cortex and heart rate and the oxygenation in active muscle during preparatory phase.

循環調節におけるセントラルコマンド仮説によると，大脳皮質運動野の皮質活動は循環応答と対応した変化を生じている可能性が考えられるが，未だ不明な点が多い．本研究では，大脳皮質運動野周辺における脳酸素動態の変化が同部位の皮質活動を反映するのではないかと考え，運動準備期の脳酸素動態と循環応答の対応を検討した．その結果，脳の酸素化ヘモグロビンおよび総ヘモグロビン，心拍数，活動肢の酸素化ヘモグロビンは30％MVC強度以上の運動負荷において類似した反応を示した．このことから，運動準備期において運動関連領野に生じる皮質活動と心拍数および活動筋酸素動態は，比較的高い強度の運動時に対応した変化を生じるものと考えられた．

■特別講演

「脳を正しく使おう」

金澤　一郎　先生
（国立精神・神経センター総長，日本学術会議会長，
宮内庁長官官房・皇室医務主管）

第17回基礎体力研究所公開フォーラムでは，学術フロンティア推進事業「運動時における循環調節機構の統合的解明－スポーツによる健康・体力づくりのプログラムの構築に向けて－」の研究成果中間報告会の後に，金澤一郎先生をお迎えし，「脳を正しく使おう」という大変興味深い題目で特別講演をしていただいた．講演に先立って，高橋和之副学長（兼基礎体力研究所長）から金澤一郎先生の紹介が次のようにあった．

金澤一郎先生は，悠仁親王殿下が誕生された折に，笑顔で記者会見に臨まれた皇室医務主管としてメディアを通してご存知の方も多いが，先生は国立精神・神経センター総長，そして日本の科学者77万人を代表する第20期日本学術会議の会長でもあり，脳科学における臨床医・研究者でもあるという先生の経歴がまず紹介された．また金澤先生は，厚生労働省の医道審議会医道分科会長，特定疾患対策懇談会座長，難病財団企画委員会委員長といった数々の委員会において，専門家の立場から優れた指導力を発揮されているリーダーであることも紹介された．

当日の講演は，立見が出るくらい多人数であり，先生のユーモアとウィットに富んだ語り口により，そしてタイミングよく挿入されるジョークとクイズにより，会場全体が金澤先生を中心に一体となり，熱気に満ち溢れた講演となった．その講演の中で，先生はどの年代においても，脳に刺激を与え脳を上手く使うことの大切さについて，次のように繰り返し話された．

最初の話は，講演会場に学生が多いことに配慮されてれて，脳細胞の話から大脳皮質における左右の機能局在などであり，脳機能に関する基礎知識の初歩的なところから丁寧に説明された．また馴染みやすい例を挙げられて，さまざまな脳の不思議さについて概観された．たとえば，右脳の機能が日本人と西洋人で違うため，われわれ日本人は，秋の夜に鈴虫の声を聞くと「ああ，情緒があるな」と感慨深く思うが，西洋人には，単なる雑音にしか聞こえないということ等であった．

本題の話に移り，脳には巨大な学習機能と許容量があるが，そのような脳に幼児期から高齢者にいたるまで，適切に働きかけることの重要性を説明された．「雀百まで踊り忘れず」，「三つ子の魂百まで」という諺が示すように，乳幼児期の経験・学習がとりわけ重要であると話された．人間社会から阻害・隔離されて育てられた子どもは，知的機能，感情表現，発話機能，言語理解といった発育が不十分となり，人間生活に不可欠な脳機能が獲得できないということを，次のような実験例をもとに説明された．成人したサルでは脳の変性は起こらないが，幼児期のサルの左目を遮蔽した生活をさせると，左目からの情報が入らないため，脳の構造・機能に変性がおこるということであった．

一方，成人後の学習や経験の重要性についても話された．認知症にみられるように，加齢とともに脳機能低下という健康問題も生じるが，成人後であってもさまざまな学習や経験によって脳細胞の新生がみられ，シナプス間の伝達効率も良くなるといった「脳機能向上」を示す研究成果が，日本の研究者により明らかにされていることを紹介された．脳機能を脆弱化させないよう，何事にも無反応な生活を続けるのではなく，さまざまな興味をもって生活することが肝要であるということであった．

続いて，認知症の予防に関する話をされた．カナダの研究者による20年間の追跡研究によると，ボードゲームやトランプなどを頻繁に行っている高齢者と行なわない高齢者では，認知症発症率が違い，トランプやゲームを行うグループの方が，明らかに認知症発症率が低いということを話された．また，身体運動やダンスをしている

人の方がしない人よりも認知能力が高いので，身体運動やスポーツが脳の健康に重要な役割を果たすのではないかというコメントも付け加えられた．脳も筋肉と同じで，使わなければ鈍るといえ，いろいろな刺激を与え，脳を目覚めさせて活性化させ，柔軟な脳をつくる必要性があることを強調された．

このような加齢と脳機能認低下予防に関わる話題の中で，年齢が高くなっても低下しない能力があることについても触れられた．専門的用語では「Crystallized ability（結晶化された能力）」とよばれるそうであるが，物事をカテゴリーに分類して記憶する，あるいは物事の共通点を見つけて，それを一区切りにまとめるといった能力であると説明された．文化的・社会的な経験を通して身に付ける能力だそうである．若いうちはこの能力が育成されていないため，「木を見て森を見ない」ということがあるが，経験を積むことによって「木も見て森も見る」ということが可能になる，ということである．同様に，状況判断能力なども，年齢とともに醸成される能力であるということを追加された．

最後に，脳を正しく使うための実例として，「脳をやわらかくする体操」を，会場の参加者全員で実施してみることになった．先生が提示されるスライドの写真・絵を見ながら，私たちの脳がいかに錯覚し，また誤判断をするのかについて，クイズ形式で体験した．金澤先生の明快でユーモアたっぷりの説明に，会場では幾度と無く驚きの歓声と笑いが渦巻くことになり，はっと気づいた時には講演終了の時間となっていた．そして，講演終了後も次々と質問が続き，参加者全員が金澤査先生に魅了された，実に充実した時間であった．

このような素晴らしい講演会をしてくださった金澤一郎先生に，あらためて深く感謝を申し上げたいと思います．また学術フロンティア推進事業の研究成果の中間報告会を含めて，公開フォーラムに参加していただいた学内外多くの研究者および学生・大学院生の方々にも感謝の意を表します．

（文責　佐藤　耕平，定本　朋子）

日本女子体育大学附属基礎体力研究所　第19回公開研究フォーラム
学術フロンティア推進事業（平成16～20年度）
公開国際シンポジウム

運動時における循環調節機構の統合的解明
－スポーツによる健康・体力づくりのプログラム構築に向けて－

日　　時：2008年11月29日（土）　13時30分～17時10分
会　　場：日本女子体育大学本館　E101

プログラム

開　　会　13：30　　**高橋　和之**（日本女子体育大学学長）

Session 1　13：35～14：55　　座長　**加賀谷淳子**

学術フロンティア成果

「運動時の血流再配分ー運動特性と関連させてー」

加賀谷淳子（日本女子体育大学客員教授）

招待講演

Changes in vascular structure and function following exercise training

Daniel J. Green, Ph.D., Professor.
(Cardiovascular Physiology, School of Exercise and Sports Sciences,Liverpool John Moores University, Liverpool, U.K.)

講演要旨説明　**長田　卓也**（東京医科大学講師）

ポスター発表＆ブレイク　14：55～15：25　　座長　**西田ますみ**（日本女子体育大学教授）

Session 2　15：30～16：50　　座長　**定本　朋子**

学術フロンティア成果

「運動時の循環調節機構－神経調節を中心に－」

定本　朋子（日本女子体育大学教授）

招待講演

The role of central command in the cardiovascular regulation during exercise

Jon W. Williamson, Ph.D., Professor, Associate Dean.
(Health Care Sciences, UT Southwestern School of Health Professions,The University of Texas Southwestern Medical Center at Dallas, U.S.A.)

講演要旨説明　**笹原千穂子**（東海学園大学講師）
佐藤　耕平（日本女子体育大学助教）

Session 3　16：50～17：10　　座長　**定本　朋子**

学術フロンティア成果

「運動時の循環調節機構の統合的解明へ向けて」

斉藤　満（豊田工業大学・教授）

閉　会　　**定本　朋子**

■招待講演Ⅰ

CHANGES IN VASCULAR FUNCTION AND STRUCTURE FOLLOWING EXERCISE TRAINING

Daniel J Green
Research Institute for Sport and Exercise Sciences,
Liverpool John Moores University, UK;
School of Sport Science, Exercise and Health,
The University of Western Australia, Australia

Summary

This presentation will address questions such as:

- Does risk factor modification explain the risk reduction associated with exercise?
- What could account for the positive effects of exercise beyond traditional risk factors?
- How does exercise training affect the vascular wall?
- What is the relationship between change in artery function and structure with training?
- Are the benefits of exercise training evident at all levels of the arterial tree?
- Are changes in artery function and structure clinically relevant?
- Can we use information about the direct vascular effects of exercise to optimise interventions aimed at decreasing cardiovascular risk?

Exercise is associated with an approximate 30% benefit in terms of decreased cardiovascular (CV) risk (Thompson *et al*. 2003), a magnitude similar to that associated with antihypertensive and lipid lowering interventions. The impact of exercise on traditional cardiovascular risk factors is, however, relatively modest. Indeed, a recent analysis of 27,000 subjects reported that around 50% of the cardiovascular risk reduction associated with exercise cannot be explained by changes in CV risk factors (Mora *et al*. 2003). Clearly, other explanations for the cardioprotective benefits of exercise must exist.

Exercise is associated with acute changes in central haemodynamics, arterial blood pressure and flow. The vascular endothelium, which forms the interface between the circulating blood and the artery wall, produces numerous paracrine hormones (eg nitric oxide NO) which are anti-atherogenic. Endothelial dysfunction can be considered an early and integral manifestation of vascular disease (Green *et al*. 2004). An important physiological stimulus to endothelium-mediated vasodilation is arterial shear stress. Exercise exerts direct effects on the vasculature via the impact of repetitive increases in shear stress on the endothelium.

There is strong evidence that exercise training of small and large muscle groups is associated with improvement in endothelial function (Green *et al*. 2004), which can occur in the absence of changes in lipid levels (Green *et al*. 2003), blood pressure (Green *et al*. 2003; Higashi *et al*. 1999), glucose tolerance (Green *et al*. 2003) and BMI (Watts *et al*. 2004). The mechanisms responsible may involve shear stress-mediated increases NO-synthase protein expression/phosphorylation or impacts of exercise on oxidative

stress. Exercise training also induces changes in artery lumen diameter, arterial remodelling, which may contribute to decreased atherothrombotic risk (Dinenno *et al*. 2001; Green *et al*. 1996; Naylor *et al*. 2006). Studies of the relationship between changes in artery function and structure in humans are now emerging (Tinken *et al*. 2004), as is information relating to the impact of exercise training in microvessels (Black *et al*. 2008).

A direct effect of exercise on the vasculature therefore provides a plausible explanation for the reduction in cardiac events associated with exercise training. Since different forms of exercise are associated with distinct patterns of shear stress, it is likely that exercise prescription may be optimised if the direct effects of exercise on vascular shear stress are taken into consideration.

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招待講演講師略歴

Daniel J. Green, Ph.D., Professor.

Daniel J. Green氏は，身体活動がどのようにして心臓血管系疾患に対するリスクを軽減するかという視点から研究を進めれられている．氏の数多くの業績のなかでも，1993年にJournal of Applied Physiology誌に発表された“Modification of forearm resistance vessels by exercise training in young men”や，近年では2005年にJournal of Physiology誌に発表された“Comparison of forearm blood flow responses to incremental handgrip and cycle ergometer exercise: relative contribution of nitric oxide”は運動中の活動筋・非活動筋への血流を研究するものに大きな影響を与えた．また，これまでに国際誌に投稿された80編以上の論文を査読しており，運動中の循環調節に関する研究をリードしている研究者の一人である．

■招待講演 II

THE ROLE OF CENTRAL COMMAND IN THE CARDIOVASCULAR REGULATION DURING EXERCISE

Jon W. Williamson
Health Care Sciences,
UT Southwestern School of Health Professions,
The University of Texas, Southwestern Medical Center at Dallas, USA.

Summary

The goal of this talk is to provide an update of current concepts on the role of central command in humans with a particular emphasis on the regions of the brain that may be involved in cardiovascular regulation during exercise. Central modulation of the cardiovascular system via descending signals from the cerebral cortex has been well recognized for over a century, yet the specific regions of the human brain involved in this exercise-related response have remained speculative. The concept of central command during exercise has been classically defined as "a feed forward mechanism involving parallel activation of motor and cardiovascular centers". The primary focus of many central command-related investigations has involved the modulation of motor effort and the resulting alterations in cardiovascular responses. However, most researchers would concur that the magnitude of central command during exercise can be largely dictated by an individual's perception of effort during actual or even attempted physical exertion, independent of the actual work load or force production. This suggests that the magnitude of a central command mediated cardiovascular response during exercise can be independent of force production (e.g. imagined exercise) and dictated more by an individual's perception of effort. Therefore, we would propose the use of the term "central command" to imply a central neural mechanism that can function as a feedback system, responding to an individual's sense of effort, to elicit proportional changes in cardiovascular responses, which does not require a parallel motor activation to exert its influence. However, during actual exercise, neural networks involving both "motor" and "cardiovascular" systems would be activated, yet these individual networks have not been well defined. Studies investigating the functional anatomy of central command-induced changes in regional cerebral blood flow (rCBF) have identified a network of structures activated in the human brain. These regions include the insular cortex and anterior cingulate cortex or the medial prefrontal region, as well as thalamic regions. These findings are consistent with findings from studies in animals. The structures involved appear to be activated in response to an increased perception of effort during exercise when heart rate and blood pressure are elevated. The cardiovascular and hemodynamic adjustments to exercise are primarily mediated by alterations in parasympathetic and sympathetic neural activity. These exercise-induced changes in autonomic neural outflow are designed to help meet the metabolic demands of the exercising muscle. Central command appears to initiate autonomic adjustments during exercise which involve a resetting of the arterial baroreflex during exercise. More specifically, central command input appears to be responsible for the relocation of the operating point (pre-stimulus blood pressure) away from the centering point (point at which there is an equal depressor and pressor response to a given change in blood pressure) and closer to the threshold of the cardiac baroreflex stimulus response curve. This effect of central command on the operating point appears to be

mediated via vagal withdrawal associated with increases in exercise intensity. It has been shown to occur in order to allow the arterial baroreflex to adapt to and potentially modify the increases in blood pressure induced by activation of the exercise pressor reflex. A clear understanding of the role of central command and defining the regions involved in centrally-mediated cardiovascular modulation is of critical importance in furthering our understanding of this concept and may have important clinical implications related to various types of autonomic dysfunction (e.g. emotional syncope, white coat hypertension, etc.). Future investigations must be performed in humans to more clearly define the specific sites within these regions responsible for changes in autonomic function and how they interact to effectively modulate cardiovascular responses during exercise as well as during non-exercise conditions.

招待講演講師略歴

Jon W. Williamson, Ph.D., Professor Associate Dean.

Jon W. Williamson氏はこれまでCentral Commandが脳においてどのように発信されているかについて研究を進めてきた．氏の輝かしい研究業績の中でも2002年にJournal of Applied Physiology誌に発表された“Brain activation by central command during actual and imagined handgrip under hypnosis”や，2003年に同じくJournal of Applied Physiology誌に発表された“Evidence for central command activation of the human insular cortex during exercise”は，全身の血流調節という意味でのCentral Commandが脳のInsular cortexの活動に起因することを明らかにしたことで有名である．

「運動時の血流再配分－運動特性と関連させて－」

加賀谷淳子（日本女子体育大学）

運動は，活動する骨格筋への血流量を増加させると同時に，運動指令を出す脳，運動を支援する心臓や肺の筋への血液供給を適切に調節することが必要である．しかし，血液を循環させる心臓の拍出能力には限界があること，生命維持に必要な調節が不可欠であることなどから，これらの臓器への血流調節だけでなく，これ以外の臓器や組織への血流の再分配が必要になる．逆に言えば，運動時の各器官・組織への血流量変化は，それら調節の結果として起こったものであるので，それらを把握することは，その背後にある調節機構を解明する有力な手がかりになる．一方，循環経路の動脈側と静脈側をつなぐ間に介在する骨格筋の活動は，循環に対して物理的あるいは代謝性に干渉する．したがって骨格筋の活動特性が循環応答を修飾する極めて大きな要因である．そこで，本プロジェクトでは，運動特性と関連させながら，運動時の血流再分配を明らかにし，その背後にある循環機構の解明に役立てようとした．得られた成果の概要をまとめると以下の通りである．

1．骨格筋，脳，腹部内臓への血流分配

一般的に心拍出量は運動強度や活動筋量の増加に連動して変化するとされている．しかし，本プロジェクトでは，局所的な小筋群の運動の場合は，両者が必ずしも連動した変化を示さず，骨格筋の血流需要に対して末梢的な対応をすることもあることが示された[4]．

運動指令を出す脳への血流再分配を，内頸動脈と椎骨動脈の二つの経路から調べたところ，内頸動脈経路では静的および動的運動時に動脈血圧および心拍出量が著しく上昇しても，血流量の変化は見られないのに対して，椎骨動脈経路では運動による心拍出量の上昇に伴い血流量が増加することが明らかになった[6]．

活動筋への動脈血流は筋収縮時には阻害され，筋の弛緩期に増加する．一方，活動筋からの静脈血の流出は筋活動期に加速され，筋弛緩期には減速し，両者は，筋内圧の局所的変化により相互に関連しているが，一義的ではない[3]．また，筋の発揮張力が極めて低い場合であっても，ストレッチングのように筋線維が伸長すると，動脈側からの血流の逆行成分が増えて血流は減少し，ストレッチング終了後には動脈側での加速，それに連動した静脈側の流出増加が起こることがわかった[2]．

骨格筋の血流がどこまで増えるかについてはなお議論が続いている問題である．この問題は主として代謝性の血管拡張能を調べたものであったが，酸素運搬系としての血流量の役割と考えると，運動中にどこまで増加するかが重要になる．本プロジェクトでは運動時最高値がどれくらいに達するかを知る前提条件として，最高血流量に達する運動条件を明らかにしようとした．その結果，動的運動時筋弛緩期の血流量については，運動強度とテンポの増加に伴って増加し，両者の組み合わせによって運動時血流量が最高になるのではないかとの知見を得た[3]．また，活動筋での血流増加は酸素需要に応えて酸素輸送を高めるためであるが，閉塞性動脈硬化症保有者に多段階負荷運動を実施した結果では，安静時には患側での血流量が低いのに対して，運動時には患側の血流量が健側より増加して，虚血に伴う骨格筋酸素消費量を代償する現象が見られた[5]．運動の物理的特性と代謝性特性の両面から，酸素供給系としての血流動態を捉えることが重要であることが示された．

運動に直接関与しない臓器である腹部内臓への血流量は，運動時に骨格筋へ血流を優先的に分配するために減少するとされてきた．しかし，静的運動時の腎動脈と上腸間膜動脈の血流速度を調べると，腎動脈では血流速度減少が見られたが，上腸間膜動脈では顕著な変化は見られなかった．すなわち，運動時の腹部内臓器官への血流再分配は，一律の変化ではなく，本プロジェクトで調べた運動の範囲では，消化器官血流量は腎動脈血流量のように減少しないことが示された[6]．

2．運動の時間経過に伴う循環・代謝応答の変化

静的筋活動開始直後には筋内圧の上昇により，動脈側からの流入が低下し，静脈側からの血液流出は加速される[3]．また，運動開始初期（約30秒程度）の動的運動では，心拍出量の増加に先行して活動筋への血流量が急速に増

加するとされている．一方，運動開始初期の非活動肢の血流量変化をみると，強度依存で一過性の血流量の増加が見られ，それに続いて強度依存の血流減少が起こった（Yoshizawa *et al*. 2008）．すなわち，筋収縮開始と同時に起こる動静脈血流勾配の増加[3]等の作用によって，運動開始初期から活動筋での血流増加が素早く起こるものの，全身性の血管収縮作用は高まらずに，この時期には血流再分配は適切になされていないことが示唆される．非活動肢での血流量増加や，総末梢血管抵抗の減少により血圧が低下[1]はそれを支持する結果であると考えられる．

律動的な運動が持続すると，活動筋での血管拡張により動脈血流量の増加が起こり，筋血液量が増加する．そうなると，筋活動による静脈側の血液流出が続いて起こる動脈血流入量と密接な関係を保つようになることがわかっている[3]．

運動が終了すると，静的筋活動後は急激な血流増加が起こり，運動後の血流は約３拍目の心周期で最高値に達する（Ohmori *et al*. 2006）．この時期には静脈血流は安静時以下に減速し，動脈血流量が最高値に達し，筋の血管床への血液再充満が起こってから静脈血流が安静レベルに復帰した[3]．

運動後の筋の酸素化動態の回復の速さは運動中の筋の代謝を反映しているので，筋線維組成の異なる深部と浅部において回復の速さ（$T_{1/2}$）が異なるかどうかを検討したが有意な差は見られなかった[7]．

3．運動強度と血流再分配

運動プログラムを考える上で，運動強度は極めて重要な運動条件である．本プロジェクトでは運動強度を筋収縮強度と収縮頻度から検討した．筋収縮強度がある強度を超えると筋交感神経の亢進が起こる（Saito *et al*. 1986）ことが知られているが，その結果，強度変化に対する血圧上昇が顕著になる（Kagaya *et al*. 2001）．そこで，血圧上昇が高くなる負荷（血圧変移点負荷）を基準として強度をとらえ，本研究の血流再分配の成果をまとめた．

活動筋への血流量が運動負荷強度の増加に伴って増加し，頭打ちになるかどうかは議論のあるところである．本プロジェクトでは動的膝伸展運動・足底屈運動や間欠的な静的掌握運動において検討し，前者では頭打ちが観察され，後者では筋弛緩期血流が負荷の増加と共に増加するという結果を得た[1, 3]．動的・静的運動共に，運動後血流量に対する運動中血流量の比は，血圧変移点負荷とほぼ類似の負荷強度で急激に低下し，運動中の血流需要を満たす割合が低くなることが確認された[1]．また，強度が高くなると，運動持続に伴う筋の電気活動漸増の割合が高くなり，筋疲労耐性の低い筋が動員されるようになることが示唆されたが，その強度は血圧変移点と類似であった[1]．筋の酸素代謝をみると，運動中の活動肢筋酸素化動態が負荷強度に対して低負荷とは異なる対応をする[1]ようになるのは，血圧変移点負荷よりやや低い負荷からであった[3]．さらに，運動中の有酸素性エネルギー機構関与の度合いを，運動後の筋酸素動態（再酸素化時間$T_{1/2}$）からみると，強度に対して指数関数的な延長を示し，有意な延長を示すようになるのは血圧変移点よりさらに高い強度においてであった[7]．

次に，運動中，活動筋での変化を中心に身体の様々な変化を統合して感知する主観的筋疲労感覚（10段階）は，血圧変移点より低い負荷（38％MVC）から急上昇した．血圧変移点に対応する値は4.0であった[3]．

骨格筋への血流量が心臓の拍出量とどう対応するかをみると，局所的な運動（足底屈運動）では，活動筋への動脈血流量が低負荷から増加を開始し始めるが，心拍出量（中心循環）は中等度負荷にならないと増加しなかった[4]．すなわち，低負荷では，心拍出量の増加を伴わずに活動筋への血流再分配が起こり，強度が高くなると心拍出量を増加させて骨格筋への血流再分配を行っていることが明らかになった．

血圧が上昇するような強度の高い負荷では，脳への血液を供給するひとつの経路である椎骨動脈の血流増加が見られた．それに対して，腹部内臓においては腎動脈での血流減少が確認された[6]．

4．運動時の循環に対する重力の影響

本プロジェクトでは，循環系に対する重力の影響を，活動体肢の位置を変化させて検討した[3]．掌握運時の前腕を心臓より下にすると，筋活動中止期の血流量が有意に変化し，上腕動脈では増加，静脈では減少を示した．近赤外線分光法の総ヘモグロビン濃度変化からみた筋血液量は垂下で増加した．また，重力負荷を一定にして，血液貯留状態を変えた下肢の運動条件では，動脈静脈血流量には相違が見られず，30分程度では，貯留血液量レベルの差は影響しないことが示された．

上記知見の得られた研究課題

[1]「再分配」共同研究　[2]若手研究者受け入れ「ストレッチング」共同研究　[3]加賀谷担当個別課題　[4]奥山（清水）担当個別課題　[5]長田担当個別課題　[6]定本担当個別課題　[7]笹原（上田）担当個別課題

■学術フロンティア成果報告（Session 2）

「運動時の循環調節機構－神経調節を中心に－」

定本　朋子（日本女子体育大学）

1．運動発現に関わる仕組み

骨格筋の運動単位は神経系により運動指令が与えられることにより収縮する．筋に運動指令を直接伝えるのは運動神経であるが，脳や脊髄に実行したい運動を計画し，統合する中枢がある．このような運動に関わる脳・神経系の働きと運動単位の動員特性について理解することは，運動時の循環調節機構の統合的解明に不可欠である．本プロジェクトでは運動発現に関わる仕組みに関して，次のような成果を得ている．

Ferrariは機能的近赤外線分光法装置の開発に携わり，その装置を用いてQuaresimaと共同して前頭皮質の酸素化動態を検討している．その結果，力発揮を維持させること，そして正確で巧みな力発揮をするためには前頭前野の働きが重要な役割を担うことを明らかにしている．また澁谷は，運動指令を出す一次運動野の働きを調べ，運動時には一次運動野が左右半球間で相互連絡をもち，両側間の結合が生じることを示唆している．このような半球間結合は，対側一次運動野のみでは不十分な力発揮しか行えない場合に，それを補完する役割を担うと考えられている．さらに，加茂は，運動指令に基づいて生起する運動単位の活動参加および放電間隔変化と循環系応答の関係について検討している．その結果，一定筋力発揮時には運動単位の放電間隔時間の延長が観察されることを報告している．

2．運動時の循環調節－主にセントラルコマンドとの関わりから－

運動の準備および運動の発現とともに，循環応答も刻々と変動する．このような運動発現と循環応答を連結させる仕組みとして，活動筋からの反射性制御や圧受容器反射の働きが重要である．本プロジェクトでは，反射性制御については，メンバーが個別課題においてさまざまな検討を加えている．たとえば，斉藤は，利き腕と非利き腕における運動時の筋交感神経活動を各々調べ，利き腕運動後の筋虚血時における交感神経活動が非利き腕の場合よりも高いことを報告し，筋代謝受容器反射が利き腕運動時に高くなることを指摘している．定本は，腎動脈および上腸間膜動脈（主に消化器官へ連絡）の血流動態に対する筋虚血の影響を調べ，腎動脈血流量に比べ，上腸間膜動脈血流量が筋代謝受容器反射の影響を受けにくいことを報告している．さらに内因性反射である圧受容器反射と循環調節との関わりについても，個別課題において考察がなされている．

このような反射性制御に加えて，本プロジェクトでは高位中枢からの指令であるセントラルコマンドの働きに力点をおいた検討を行ってきた．セントラルコマンドの定義と解剖学的経路は未解決な部分が多いが，本プロジェクトでは，運動の準備，運動直前の予測制御，運動開始直後の制御，運動の意志や努力感・頑張り（主観的運動強度）に関わるセントラルコマンドという側面において，次のような知見を得ている．

岩館は運動準備期（約1分前から）の大脳皮質運動野周辺の脳酸素動態と心拍数，血圧および前腕屈筋の酸素動態を同時計測し，掌握運動の準備に関連した皮質活動と循環応答の対応性を検討した．その結果，運動準備のための大脳運動野周辺の活動と心拍数および前腕屈筋の酸素化ヘモグロビンの上昇が共に生起することを観察し，運動の準備に付随する皮質運動野周辺の活性と循環応答との対応関係を示唆した．定本と佐藤は，随意運動と受動運動に伴う頸動脈経路（総頸動脈，中大脳動脈: 主に大脳皮質への血液供給路）とおよび椎骨動脈経路（椎骨動脈，後大脳動脈: 主に脳幹，小脳，脊髄などへの血液供給路）の血流変化を比較した結果，随意運動の開始前には動作に先行する血管拡張が椎骨動脈経路に生じることを報告し，この経路が潅流する脳部位にはセントラルコマンドによる予測制御が働くことを示唆した．また，定本は，腎動脈および上腸間膜動脈（主に消化器官へ連絡）

の血流速度の応答についても同様の検討を行ったが，腎動脈および上腸間膜動脈には予測制御の影響が及ばないことを指摘した．さらに，血流分配に関する共同研究の成果から，佐藤は動的運動開始直後（30秒以内）の活動筋では急激な血管拡張が起こり，総末梢血管抵抗が減少するため，運動開始直後の平均血圧が一過性に低下することを報告した．そしてこの応答はセントラルコマンドおよび圧受容器反射による調節が関わると報告した．斉藤は，ハンドグリップ運動時の筋交感神経活動の記録から，筋疲労にいたるような運動持続時には筋代謝受容器反射の働きも重要であるが，運動の意志・頑張り（すなわちセントラルコマンド）が筋交感神経活動を上昇させ，それにより筋力が維持されることを明らかにした．さらに，短期間のハンドグリップレジスタンストレーニングがセントラルコマンドを増大させ，筋交感神経活動を亢進させることを示唆した．

運動時のセントラルコマンドに関する国内メンバーの共同研究において，次のような検討がなされた．一定負荷保持時の活動筋への振動刺激（バイブレーション）により，運動指令を低下させる実験条件を設定し，バイブレーションを伴わない通常の運動条件における循環応答を比較した．特に，前頭前野の酸素化動態，中大脳動脈血流速度，椎骨動脈血流量，腎動脈血流速度に及ぼす影響を中心に検討した．これらの実験の結果，セントラルコマンドの低下条件である「振動＋運動」条件では，振動刺激を伴わない通常の「運動」条件に比べ，筋疲労感覚と心拍数が低くなり，セントラルコマンドの低下に対応した変化が示された．同様に，セントラルコマンドの低下に対応した変化が椎骨動脈血流量の応答においても示された．しかし，前頭前野の酸素化動態，中大脳動脈血流速度，腎動脈血流速度の応答には，セントラルコマンドの低下に対応した変化はみられなかった．このような結果から，先行研究で示されている心臓および皮膚組織といった組織・器官に加えて，セントラルコマンドは椎骨動脈経路の脳血流調節にも働く可能性が示唆された．

■学術フロンティア成果報告（Session 3）

「運動時の循環調節機構の統合的解明へ向けて」

斉藤　　満（豊田工業大学）

1．循環調節機構解明の意義

スポーツを楽しむには必要な酸素を取り込み，活動筋は勿論酸素を必要とする部位に十分酸素を供給しなければならない．この役割は循環系が担い，その調節を誤ると楽しいスポーツも台無しとなる．このことは健康や体力にもあてはまる．たとえば健康を脅かす循環系疾患の多くは不適切な循環調節に起因することが少なくないし，体力の向上や低下も循環系機能と密接に関係することが明らかにされている．

循環系はポンプとしての心臓と血液を運ぶ血管系から構成され，構造的には極めて単純な系として捉えることができる．しかし，運動開始とともに活動筋は多量の血流を必要とするが非活動筋はほとんど必要としない．このとき両方へ同じように血流を配分していては活動筋に血液が十分行き渡らないだけでなく，無駄にもなる．また，血流調節のために血管を収縮しすぎると過剰な昇圧反応が生じ，心臓ポンプに負担をかけることになる．このように，どのような運動条件において適切な，あるいは不適切な循環調節が生じるか明らかにすることは，安全に運動を実行し，健康・体力の維持増進を目指す上で重要である．さらに，日常的に運動を続けることが循環調節機構にどのような影響を及ぼし，改善をもたらすのか明確にしておくことは運動プログラム構築にとって必須のことといえる．

2．運動時の循環調節機構解明と課題

運動時の循環調節が安静時と明確に異なることは，運動が意志に基づいて特定の筋を収縮し，ここに優先的に血流を配分することである．この調節は幾つもの調節系で構成され，統合的に実行されるが，系全体を一度に捉えることは出来ないため以下に示す観点から解析を進めた．

観点１：循環調節機構に与える‘運動の意志（セントラルコマンド)’の効果を的確に把握すること．本プロジェクトでは循環調節機構に及ぼすセントラルコマンドの影響を，交感神経活動反応と血圧及び脳血流反応を指標に，運動強度，時間，さらに末梢体性感覚受容器刺激を用いセントラルコマンドに外乱を与えた際の解析を行った．この成果から，‘運動の意志’が循環調節に大な影響を及ぼすことが明らかとなった．本研究では小筋群の静的運動での実験解析が多かったことから，次の課題は大筋群の動的運動で検証をすすめることである．

観点２：600余りあるからだの筋のうち特定の筋が運動に動員され，しかも発揮する力や様式，リズムも様々である．また，筋活動をミクロにみると単一筋内でも代謝や血管拡張に不均一がみられ，血液循環も時間的，空間的に大きく異なる．他方，中枢調節とは独立した筋活動に伴う代謝が血管拡張を引き起こし，さらに筋収縮にともなう筋ポンプ作用が活動筋血流を決定する重要な因子となる．これらの生理的，物理的因子を区分けしながら筋血流反応の解析をすすめた．この結果，運動の様式やテンポ，収縮強度，さらに脈管構造（疾病含む）や筋形状の違いにより血流反応が大きく変わることが明らかとなった．

観点３：酸素運搬に欠かせない血液を拍出する心臓，運動及び自律神経活動の指令中枢をもつ脳，体温調節器としての皮膚，さらに血液供給器官となる内臓のように運動発現には直接関与しないが重要である組織の血流と骨格筋血流がどのような仕組みで調節され，違いがみられるか明らかにすること．この調節の仕組みは交感神経による遠心性の全身調節と末梢における局所調節に大別される．ここでは，交感神経効果器としての血圧（血管）反応と局所の個別臓器血流の反応を指標に活動筋の代謝受容器反射，体性感覚受容器刺激（Ia 求心性神経刺激）時の脳，内臓器官，さらに骨格筋の血流変化から解析した．交感神経による血管収縮は臓器毎に異なるだけでな

く，例えば脳内への血流供給には部位差がみられ，運動と脳活動との連関を考える上での新しい成果が得られた．皮膚血流調節についての検討は今後の課題である．

観点４：ポンプとしての心臓，すなわち心拍出量と末梢循環調節の調和はスポーツパフォーマンスを考える上で重要なテーマである．運動に必要な血流は心臓ポンプに加えて筋ポンプによる静脈還流が重要な役目を果たしており，両者は車の両輪の関係にある．ここでは心拍出量と活動筋血流の相互関係が運動強度や運動テンポの影響を受けるか否かを検討した．その結果，両者の定量関係は常に一定であるとは限らないことが確かめられた．

観点５：継続的な運動は循環調節機構にどのような影響を及ぼすか確かめる．トレーニングに伴う運動時の交感神経活動反応から検討を試み，強い運動の意志は運動時の交感神経活動反応を高める効果をもつことを明らかにした．しかし，身体トレーニングは，有酸素運動，レジスタンス運動のように運動の特性や種類，運動強度・時間など組み合わせは無数にあり，さらに，運動実施者の特性や運動の目的を十分考慮した研究成果の蓄積が望まれよう．

3．今後に向けて

本プロジェクトでは運動時循環調節機構を統合的に捉えることを目的に，上記に示す多面的な循環応答解析をすすめ，多くの成果を生み出すことができた．今後はさらに実際的な運動，例えば全身運動での検証を加え，本研究で得られた多面的な成果を統合し，より安全で効果的な運動プログラム構築向けて努力を続ける．また，本プロジェクトでは，複雑な循環調節システムを多面的に捉えるために血流の連続測定法（ドップラー血流計），組織の酸素動態観察法（近赤外分光法），交感神経活動観察（微小神経電図法）などの新しい手法を導入して研究をすすめたが，さらに統合的な循環調節機構の解明を発展させるには循環に関わる血管拡張・収縮因子やホルモン，関連遺伝子解析など，最新の生化学的解析の導入が望まれる．特に，継続的な運動と循環調節機構の長期的適応の解明にとって重要である．

■学術フロンティア個別課題概要

骨格筋への血流分配と筋からの血液還流

加賀谷淳子（日本女子体育大学）

運動時活動筋への血流増加は，体循環システムの整合性を保ちながら，局所的な調節がなされた結果である．その調節は，遂行される運動の特性によって異なる．運動時の活動筋への血流量に関する報告は近年増えているが，運動特性との関係から調節機序を明らかにするには至っていない．特に，運動時に到達し得る血流量は，代謝性の最大血管拡張時に比べて抑制されていることが報告されているものの，最高血流量を得る運動条件については明らかにされていない．

本プロジェクトでは，運動中の骨格筋への血流増加が，どのような運動条件（運動強度・テンポなど）によって最高値に達するか，静脈からの血液流出（主として筋ポンプ作用）と動脈側からの血液供給がどのように関わっているかについて明らかにしようとした．

1．筋活動及び筋形状変化による動脈と静脈血流変化の関係

1）筋が短縮する時期の動脈血流量は一旦安静時より低下するが，この時期の静脈血流は加速される．筋活動が一定の張力を保っている間は，動静脈血流速度は一定値を保ち，筋収縮中止直後は，動脈血流量が顕著に増加し，その時期の静脈血流量は顕著に低下する．代謝性の血管拡張の関与が少ない短時間（5秒）の静的掌握運動で検討した結果，活動開始初期の静脈血流速度は，50，70％MVC強度で有意に高く，活動中止後の動脈血流速度と有意な相関関係のあることがわかった．運動後，動脈血流量は，徐々に高くなり，ほぼ3心周期で最高値に達する（Ohmori *et al*. 2006; Ohmori *et al*. 2007）が，この時期の静脈血流速度は安静時以下に低下し，復帰するのは血流量が最高値に達してからであった．
以上の運動条件下では，筋ポンプ作用が血流増加に効果的であることが示された．

2）筋活動が繰り返される動的運動の時間経過を追ってみると，運動開始直後（～20秒）は，動脈血流量が漸増するのに対し，静脈血流量は減少する．そして，時間経過につれて両者とも徐々に増加する．両者の関係は，運動開始時には動脈血の流入が静脈血流出に，運動が1分持続した時点では静脈血流の変化が動脈側の血流増加に影響していることが明らかになった．また，筋活動による静脈血流速度の変化が顕著になるのは，体肢が心臓レベルより下にある場合であり，筋ポンプ作用の影響は重力の影響で血液貯留が起こる状況下で顕著であることが確認された．

3）筋形状の変化は筋内血管形状を変化させる．筋が力を発揮しない下腿の受動的ストレッチングでは，ストレッチング中に膝窩動静脈血流速度がやや低下した．動脈血流速度の減少要因は，血流の順行成分の変化ではなく，ストレッチングによる逆行成分の増加によることが明らかになった．また，ストレッチングによる筋-腱複合体の伸長率が異なり，そのためストレッチングが筋血液量を減少させる筋と増加させる筋とがあることが示された．ストレッチング終了後には動脈血流の増加に続いて静脈血流速度の増加が起こり，動脈側依存で静脈血流の加速が起こることが明らかになった．
以上の結果から，筋活動時及び筋形状変化時の動静脈血流は相互に作用し合うことが示され，その運動条件（時間・強度）の具体例が得られた．

2．運動誘発性の血流量最高値発現の運動条件

運動強度の変化と循環パラメータとの関係は一次関数ではなく，血圧は急上昇する変移点があり，血流量

は，論議があるものの本研究で対象とした範囲ではレベリングオフを示す．血圧変移点強度付近では，主観的な筋疲労感覚の上昇，筋酸素動態の加速的変化がみられ，それ以上の強度から筋ポンプ作用による静脈流出が有意になる．そして，血流量が最高値に達する運動条件を運動頻度・強度から検討したが，最終結論を得るには至っていない．しかし，運動頻度，運動強度が高くなるほど血流量の増加が起こり，両者の組み合わせが，最高血流量を発現させる可能性が示唆されている．

3. 運動時の非活動肢の血流量の変化に関しては「増加」する，「減少」するなど，見解が分かれていた．本プロジェクトでは，アームクランキングと下肢サイクリング運動はどちらも，非活動肢の血流量を強度異存で増加させること （Tanaka *et al*. 2006），動的膝伸展時の対側の大腿動脈変化をみると運動開始直後は，一過性に強度依存の増加が起こるが，時間経過にしたがって，血流減少の起こることが明らにされた（Yoshizawa *et al*. 2008）．この結果は，運動開始直後（~30秒）は，活動筋以外の活動肢においても血流増加が起こり，筋交感神経の亢進が起って血管収縮が起こってくると非活動肢の血流量が減少し，血管拡張物質による血管拡張作用の高まる活動筋では血流増加が起こるという血流再分配がなされることを示したものである．これらの知見は，GreenらとHopmanらのグループによる論争に対して，運動時間，強度，活動体肢の位置などにより，非活動肢の血流量は増加，減少のどちらもあり得ることをコメントし，この論争に方向を示す重要な知見を得た （Kagaya *et al*. 2008）．

4. トレーニングによって代謝性血管拡張能が向上し，活動筋への血流量が増加するとの報告はいくつか見られるが，運動誘発性の血流最高値に効果があるか否かについての報告は少ない．また，それが血管径と血流速度のどちらに効果があるかは明らかにされていなかった．本プロジェクトでは，テニス選手の利き手と非利き手の血流量を比較し，筋活動中止期の血流量に差のあること，それは，血流速度の相違ではなく，拡張期の血管径の差によっていることが明らかにされた（Kagaya *et al*. 2008）．

運動時の心拍出量の変化と各種血管への血流分配
－中心循環と末梢循環のマッチングとミスマッチング－

奥山　静代（慶應義塾大学）

中心循環と末梢循環の関連について，血流速度から検討した研究はこれまでにみられていない．本プロジェクトにより，次のような知見が得られた．第一に，活動筋近位の末梢動脈における血流速度は筋の活動期に低く休止期には高いというように，筋活動による大きな変動が起きるが，中心動脈の血流速度は筋の活動期と休止期により大きな影響を受けないがことが示された．すなわち，筋活動は，中心循環ではなく末梢循環の変動を起こすことが示された．その結果，中心動脈および末梢動脈の血流速度の関係は筋の活動期と休止期で異なり，活動期では中心動脈血流速度が活動筋へ血液を供給する末梢動脈血流速度を上回り，休止期では逆に末梢動脈血流速度が中心動脈速度より早くなるという関係にあることが示された．第二に，運動強度に対する中心と末梢の循環応答が異なることが示された．運動負荷の増加とともに心拍出量と活動筋血流量が増加することは既に知られているが，両者が同期して生じるのかどうかは未解決な課題であった．本研究の結果において，末梢動脈血流量は低負荷運動時から増加し始めるが，心拍出量（中心循環）は中等度負荷にならないと増加しないことがわかった．このことから，運動時の中心循環と末梢循環は関連して変化するものの運動負荷強度によって両者の対応は異なることが示唆された．

有疾患者における運動および虚血に対する
血流調節プロファイル

長田　卓也（東京医科大学）

閉塞性動脈硬化症保有者は，下肢動脈血管の動脈硬化による血行障害のために運動歩行時に間歇性跛行を認める．そのためQuality of lifeの低下が問題とされている．閉塞性動脈硬化症は，下肢血行障害に関わる要因が関与するとされているが，疾病下肢における運動時の血流動態を検討した報告は少なく，不明な点が多い．そこで，本研究では閉塞性動脈硬化症保有者における一過性運動時の血流動態を検討することにした．両下肢（健側と患側）それぞれにおける多段階負荷等尺性片側膝伸展運動中の下肢血行動態を比較検討した．その結果，安静時において，患側の下肢血流量が反対側である健側下肢血流量よりが低い傾向がみられた．しかし，運動時の運動強度に対する血流増加反応をみると，患側において健側よりも大きな血流増加が観られることが明らかとなった，このような患側の血流増加は虚血に伴う骨格筋酸素消費量の代償や局所血管拡張を促す代謝産物の影響が推測される．このように末梢循環障害が安静時のみならず運動中の骨格筋循環に与える影響が示唆された．

筋の酸素代謝特性と運動時循環応答との連関

笹原（上田）千穂子（東海学園大学）

随意最大筋力（ＭＶＣ）の30～50％の運動強度で，筋放電量が増加し，筋疲労感覚も上がり，そして血圧が急

上昇する血圧変移点が出現すると報告されている（本プロジェクト「再分配共同研究」成果）．この変移点を境に有酸素系から無酸素系へとエネルギー供給機構のシフトが起こるのかどうかについて，筋再酸素化時間（運動後回復期に酸素動態が元に戻るまでの時間，この時間が延長すると筋の有酸素性代謝貢献が低いという関係性が示されている）の指標を用いて検討した．その結果，血圧変移点よりも高い70％MVC強度になるまで筋再酸素化時間は延長しないことが明らかとなった．したがって，活動筋では，血圧変移点を超えた高強度負荷に至るまで有酸素性代謝の貢献度が高く保たれていることが明らかとなった．また，深部では遅筋線維が多く，浅部では速筋線維が多いとい報告から，酸素化動態が筋の深さにより異なることが十分に仮定された．この点を筋再酸素化時間を用いて検討した結果，どの強度においても筋再酸素化時間は浅部と深部で差がみられなかった．筋の有酸素性代謝貢献度が深さによって相違ないことが明らかとなった．

運動時の内臓器官および脳の血流動態とその調節機構

定本　朋子（日本女子体育大学）

1. 運動時には活動筋への血流が増大すると同時に，腹部内臓器官への血流が減少するとされている．しかし，個々の器官への血流応答については十分な検討がされてはいない．本研究において，静的運動時および運動後筋虚血時における腎動脈と上腸間膜動脈（主に小腸へ連絡）における血流速度を比較検討した結果，同一負荷の運動に対する血流減少は，上腸間膜動脈よりも腎動脈の方が大きいことが示された．また多段階の動的運動時にも同様の結果を得た．さらに腎動脈の方が筋代謝受容器反射による血管収縮作用を受けやすいことも示された．これらの結果から，腹部内臓器官には，腎動脈のように運動刺激および反射性入力に顕著に反応する組織（器官）と上腸間膜動脈のように反応の低い組織（器官）があり，そのために，運動時の血流調節に関わる機構も組織間で異なると考えられた．
2. 脳へ連絡する血管は，左右の内頸動脈経路（主に大脳皮質側頭葉，前頭葉，頭頂葉，島皮質へ潅流）と椎骨動脈経路（主に延髄，小脳，後頭葉へ潅流）の２経路がある．内頸動脈血流量や中大脳動脈血流速度に関する研究は多いが，運動時の椎骨動脈経路の血流変化をみた研究はない．本研究では，静的および動的運動時における両経路の血流動態を比較検討した結果，運動に対する経路間の血流応答に次のような相違が示された．①内頸動脈経路では， 運動開始に先行した血管拡張（血流増加）はみられないが，椎骨動脈経路では見込み制御による顕著な血流増加がみられた．②運動時の動脈血圧および心拍出量の上昇に対して，内頸動脈経路では血管収縮が生じ，血液流入が制限されるが，椎骨動脈経路ではそのような血流制限が殆どみられなかった．③呼気終末二酸化炭素分圧の変化に対して，内頸動脈経路の血流量はそれに対応した変化を示すが，椎骨動脈経路ではその対応がみられなかった．④振動刺激操作によるセントラルコマンドの増減に対して，内頸動脈経路は対応した変化を示さないが，椎骨動脈経路ではセントラルコマンドの増減に応じた血流変化がみられた．このような相違は，自動調節や潅流部位の脳代謝に由来する調節および神経制御が経路間で異なることを示唆すると考えられた．

運動時の呼吸循環系変化に対する中枢性・末梢性の神経調節

佐藤　耕平（日本女子体育大学）

1．運動開始期の循環調節について

運動開始直後（30秒以内）には，酸素需要の増加に応えるために心拍数（HR）や心拍出量（CO）が急激に増加することが知られている．一方，活動筋では急激な血管拡張が起り，総末梢血管抵抗（TPR）が減少するため，運動開始直後の平均血圧（MAP）は一過性に低下する．このMAPの低下は，運動開始時の酸素供給においては不利であると考えられる．しかしながら，その後のCOの増加がTPRの減少を上回りMAPは回復・上昇を始め，活動筋での酸素供給に応えようとする．本研究では，このような運動開始期における循環調節と，運動強度の関連性について検討した．その結果，運動開始直後における一過性のMAP低下は，運動強度の増加に伴い抑制させることが明らかとなった．この結果は，運動強度に応じた開始期のHR・COの増加と，運動強度に依存しないTPRの減少によるものであり，この応答の調節因子はセントラルコマンドおよび圧受容器反射の作用であると考えられる．また，運動開始期におけるTPRは，活動肢での血管抵抗レベルを必ずしも反映しないことが明らかとなった．本研究より，運動開始期においても，運動強度の増加に応えるために，「システマティックな循環調節」が行われていることが示唆できる．

2．高強度運動開始時における脳血流調節と呼吸法の関連性について

運動実践の場面では，過換気を伴う運動や，逆に息こらえをしながら力発揮をすることは頻繁にみられることであり，時には意識を喪失するといった場面も起こりうる．安全で効果的な運動を考えるにあたり，このような運動時における呼吸法の違いがもたらす「限界に近い状況時」の脳血流変化を描記することは不可欠である．呼吸法と脳血流調節の観点から検討した先行研究は２本であり極く限られている．本研究では，アスリート（陸上投擲選手大学トップレベル）が，短時間の高強度レジスタンス運動を，通常呼吸（持続呼吸）で行った場合，呼吸を止めて行った場合，運動前に過呼吸を行った場合における脳血流反応を比較した．その結果，呼吸を止めた場合には運動開始時の脳血流減少が著しく，運動終了と同時に急激で過剰な血流増加（オーバーシュート）がおこる．過呼吸の場合においては，運動前から脳血流量は著しく低下し，その低下が運動終了後の回復期にまで持続することが明らかとなった．以上のように，トレーニング経験を積んだアスリートであっても，呼吸法によりレジスタンス運動時の脳血流反応が大きく変動する．このことから，意識喪失といった危険を回避するためにも，「呼吸のコントロールの重要性」が示された．

自律神経による運動時循環調節メカニズムの解明
－運動時の交感神経活動からみた中枢指令及び反射性制御の調節機構－

斉藤　　満（豊田工業大学）

運動を続けるためには活動筋に十分な血流が必要で，この調節には中枢指令と活動筋反射が重要な働きをする．この調節に対し「運動の意志・頑張り」や「レジスタンストレーニング」がどのような影響を与えるのか検討した．

1．運動の意志・頑張り

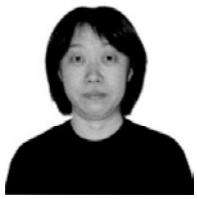
ハンドグリップ運動を用い，最大ハンドグリップの33％張力を疲労困憊まで維持する運動（Ex1）と，15秒間

の静的最大努力ハンドグリップ運動を15秒の休憩を挟んで左右10回繰り返す運動（Ex2）を行った．この時の心拍，血圧，筋交感神経活動，及び活動筋疲労感覚を測定した．Ex1では，活動筋疲労感覚の増強に比例して交感神経活動が高まった．この要因には筋疲労に伴う運動の意志・頑張り（中枢指令）の増強と運動時間とともに活動筋代謝産物が増加し筋からの反射を強めたことが考えられる．Ex2では，発揮筋力は運動回数とともに低下したが，交感神経活動は運動の1回目から有意に高まり，運動回数に関係なく10回目まで高い活動がみられた．発揮筋力が低下したにもかかわらず高い交感神経活動がみられた背景には筋反射より運動の意志・頑張り，すなわち中枢指令が大きく関係した可能性が考えられる．

2．レジスタンストレーニング

短期間のレジスタンストレーニングに伴う筋力向上には活動筋機能より中枢からの神経活動の増加が大きく関係するとされる．4週間のハンドグリップレジスタンストレーニングを行い，トレーニング前，後，及び停止4週後に，Ex1と同様のハンドグリップ運動と運動後阻血時の心拍，血圧，筋交感神経活動を観察した．疲労困憊時点の筋交感神経活動はトレーニング前及び停止4週後に比べてトレーニング後有意に高まった．しかし運動後阻血時の代謝受容器反射による筋交感神経活動増加の差は認められなかった．トレーニング前，後，及び停止4週後の心拍，血圧反応は疲労困憊時点，運動後阻血のいずれにおいても差は認められなかった．この結果から，短期間のレジスタンストレーニングは活動筋代謝受容器反射に影響しないが運動の疲労困憊時点では筋交感神経活動を増強することが明らかとなった．しかし，この適応反応はトレーニングを停止すると速やかに元に戻ることが明らかとなった．

運動様式，運動強度，運動時間および筋代謝からみたモーターユニットの動員特性（運動単位活動と循環系機能の相互関係）



加茂　美冬（日本女子体育大学）

運動は，時間的，空間的に様々な組み合わせで起こる運動単位活動を基礎として成り立っている．運動単位（Motor unit; MU）における筋線維群（筋単位）の収縮は，種々の血管拡張シグナルを発し血管を拡張させ血液循環を促進する．また，十分でない酸素供給はMU活動を変化させるなど，運動時の循環系機能とMU活動は密接に関わっていると考えられる．一定筋力を持続的に発揮するとき，MUは放電間隔すなわち活動する間隔を時間とともに延長させる．この延長は全ての筋力レベルにおいて共通して観察される特徴的な現象であることから，筋力調節および筋疲労発現に関して重要な役割を担っていることが示唆されている．本実験では，このMU活動様式に焦点を当て，合目的性および発現メカニズムを探ろうとした．

その結果，次のような知見を得た．MU放電間隔延長現象は骨格筋反復収縮初期の不完全強縮力増強に対して抑制効果をもつことを実験的に確かめ，さらに，低筋力発揮レベルではその効果は充分でないことを新たに見出した．また，放電間隔延長が必ずしも末梢感覚入力優位で生ずる現象とはいえない可能性を見出した．さらに，MUの動員（recruitment/decruitment）のみならず放電間隔変化（rate coding）と循環系応答の関係についても検討を加えることができた．

運動時における一次運動野の酸素化動態

澁谷　顕一（日本女子体育大学）

運動指令を出す一次運動野の働きを理解することは，運動時の循環調節の解明には不可欠である．活動肢と同側半球における一次運動野は，活動肢の運動を直接制御することはないと考えられてきた．つまり対側半球一次運動野の制御により行われていると考えられてきた．しかし，近年の研究では，左右半球間の一次運動野の相互作用が存在する可能性が示されている．本研究の近赤外線分光法を用いた脳酸素化動態の時系列的分析により，運動開始後の左半球の一次運動野と右半球一次運動野の酸素化動態に時間的差異が存在することが明らかとなり，運動開始後の左右半球間の一次運動野の相互作用形成の可能性が示された．このような両側半球間の結合は，対側半球の一次運動野だけでは力発揮が十分ではない場合に，それを補完するために同側半球一次運動野の活動が動員されると考えられる．また，トップアスリートと一般成人の一次運動野の活動比較から，疲労困憊に至る運動時に一次運動野の酸素化動態に明確な相違があることも示された．

脳循環・代謝測定用近赤外分光法の開発

Marco Ferrari
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His research activity has mainly been focused on the development and application of near infrared spectroscopy (NIRS) or imaging on different fields of medicine including sports medicine, cognitive neuroscience and psychiatry. In particular, his results have demonstrated the importance of reporting NIRS data for single subject/patient rather than as averaged data. Moreover, he 1) designed and realized specific probe holders for measuring oxygenation changes at cortical frontal lobe level of both hemispheres, and 2) developed/tested a software for data handling and statistical analysis. Research efforts were also made on the refinement of NIRS muscle measurements and data analysis.

本研究では，スポーツ医学や認知科学，精神医学を対象とした様々な医学分野へ近赤外線分光法（NIRS）およびその画像法を応用するために，主にそれらの開発を行ってきた．特に優れた点として，平均化されたデータよりも，個別の被験者・患者におけるNIRSデータを用いることの重要性を指示してきた．さらに，1）両半球の前頭皮質における酸素化測定のための特別なプローブホルダーを設計・実現化に注力し，2）NIRSによって得られたデータの抽出や，その統計的な解析を行うためのソフトウエアの開発・試行を行ってきた．研究に対する試みはNIRSによる筋酸素化測定と解析にも注がれてきた．

近赤外分光法による運動時の脳循環・代謝の変化

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Her research activity has mainly been focused on the study of the vascular and metabolic mechanism regulating the cerebral and muscular oxygenation and metabolism by using near infrared spectroscopy (NIRS) and functional NIRS with a multidisciplinary approach. In particular, her results want to give a contribution for: 1) understanding the mechanism of the muscle fatigue during exercise and the kinetics of the transition rest-exercise, and 2) supporting the hypothesis that prefrontal/frontal lobe plays a role in maintaining strength of the forearm muscles and ensuring a correct execution of motor tasks which require a fine motor control and coordination.

本研究では，学際的な視点を取り入れ，主に，心臓血管系と代謝は脳と筋の酸素化および代謝に影響を及ぼす心臓血管系および代謝機構を，近赤外線分光法（NIRS）と機能的NIRS（fNIRS）を用いて検証してきた．特に，1）運動中の筋疲労のメカニズムや安静から運動への移行期の酸素化動態のメカニズムの理解を進め，また，2）前腕筋の出力維持と，巧妙な運動の制御と協働を必要とする正確な動作遂行を可能なものとする上で，前頭前野・前頭野が重要な役割を果たすという仮説を支持する結果を発表してきた．

PROLONGED INTERMITTENT MAXIMAL HANDGRIP EXERCISE INDUCES LOSS IN MUSCLE FORCE AND PERSISTENT ACTIVATION OF FRONTAL CORTEX AS MEASURED BY FUNCTIONAL NEAR-INFRARED SPECTROSCOPY

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Introduction

Functional near-infrared spectroscopy (fNIRS) is a not harmful, non-invasive and safe optical technique allowing the simultaneous acquisition of oxygenated and deoxygenated hemoglobin concentration changes ($\Delta[O_2Hb]$ and $\Delta[HHb]$, respectively) from an array of optical fibers on the scalp to construct maps of cortical activity (Wolf *et al*. 2007). The hemodynamic response typically observed over an activated cortical area consists of a decrease in [HHb] accompanied by an increase in $[O_2Hb]$ of two or threefold of magnitude, resulting in an increased total hemoglobin concentration ($[tHb]=[O_2Hb] + [HHb]$). This hemodynamic pattern is representative of a localized increase in regional blood flow (rCBF).

The effect of fatiguing skeletal muscle exercise (involving small or large muscle groups) on brain, and in particular on ipsi- and contralateral frontal cortex (FC) has not been fully clarified (Liu *et al*. 2005). The aim of this study was to investigate by fNIRS the FC oxygenation response to a prolonged fatiguing rhythmic

handgrip exercise performed at the maximal voluntary contraction (MVC).

Methods

Twelve right-handed healthy volunteers completed two separate experimental sessions while lying supine.

I session: subject performed 5 MVCs (2-s contraction with a 120-s interval).

II session: two rhythmic handgrip exercises at MVC were executed, one exercise for each hand. The task consisted of a 5-min rhythmic exercise (100 MVCs, 2-s contraction at 100% MVC and 1-s relaxation) with the first hand. The same task was performed with the other hand 15-min after the end of the first one.

Handgrip force was measured by a digital handgrip analyzer. Heart rate (HR) was measured by a pulse oximeter. An 8-channel fNIRS system (NIRO-200 with multi-fiber adapter, Hamamatsu, Japan) was used to investigate the effects of this motor task on FC [O_2Hb] and [HHb] changes.

Results

A significant progressive decline (up to about 60%) of force was observed over the exercise duration. The so-called cortical activation of both FC areas (ipsi and contralateral) was observed in all subjects during rhythmic maximal handgrip exercise. The mismatched patterns of HR and [O_2Hb] changes suggest that the observed FC oxygenation changes were task related. The amplitude of [O_2Hb] changes was found greater in the FC ipsilateral to the exercising hand ($p < 0.001$).

Conclusions

Results confirm the previous ones obtained by functional Magnetic Resonance Imaging (Liu *et al*. 2005) and provide further evidence that FC plays a role in maintaining strength of the forearm muscles and ensuring a correct execution of motor tasks which require a fine motor control and coordination.

References

1. Wolf M, Ferrari M, Quaresima V: Progress of near-infrared spectroscopy and topography for brain and muscle clinical applications. J Biomed Opt, 12: 062104, 2007.
2. Liu JZ, Zhang L, Yao B, Sahgal V, Yue GH: Fatigue induces greater brain signal reduction during sustained than preparation phase of maximal voluntary contraction. Brain Res, 1057: 113-126, 2005.

日本女子体育大学附属基礎体力研究所
学術フロンティア推進事業（平成16～20年度）
最終研究成果報告会

運動時における循環調節機構の統合的解明
－スポーツによる健康・体力づくりのプログラム構築に向けて－

日　　時：2009年2月28日（土）　13時30分～17時10分
会　　場：日本女子体育大学本館　E101

プログラム

13：00　開会挨拶　　定本　朋子（日本女子体育大学教授/プロジェクトリーダー）

「本プロジェクトのねらい」　　加賀谷淳子（日本女子体育大学名誉教授）

13：05～14：15
Session 1　プログラム作成の基礎となる科学的エビデンス1－運動時の循環調節－
座長　　定本　朋子（日本女子体育大学教授）

「運動準備や想起に伴う脳活性」　　岩館　雅子（日本大学生産工学部助教）
「運動を持続させる大脳皮質の働き」　　澁谷　顕一（日本女子体育大学ポスドク研究員）
「運動時のモーターユニットの動員特性」　　加茂　美冬（日本女子体育大学准教授）
「活動筋代謝の有酸素性依存から無酸素性依存への変移」　　笹原千穂子（東海学園大学講師）
「筋活動による心拍出量の変化と血流分配」　　奥山　静代（慶應義塾大学講師）
「筋形状の変化が筋循環に与える影響」
大森芙美子（日本女子体育大学附属基礎体力研究所客員研究員）
「随意運動時の呼吸循環応答にみられるセントラルコマンドの働き」
佐藤　耕平（日本女子体育大学助教）

14：15～14：45　　質疑応答＆コーヒーブレイク

14：45～15：35
Session 2　プログラム作成の基礎となる科学的エビデンス2－発育，老化，疾患およびトレーニングによる循環系の変化－
座長　加茂　美冬（日本女子体育大学准教授）

「子どもの循環機能の発達」　　佐藤　耕平（日本女子体育大学助教）
「高齢者の左室重量と骨格筋量の関係」　　奥山　静代（慶應義塾大学講師）
「有疾患者における運動と虚血に対する末梢血流調節」　　長田　卓也（東京医科大学講師）

「身体トレーニングによる循環機能の向上」　斉藤　満（豊田工業大学教授）
質疑応答

15：35～16：00
Session 3　提案　－安全で効果的な運動プログラム構築に向けて－
座長　斉藤　　満（豊田工業大学教授）

「運動に対する循環応答からみた提案」　定本　朋子（日本女子体育大学教授）
質疑応答

16：10-17：10
特別講演
座長　加賀谷淳子（日本女子体育大学名誉教授）
長田　卓也（東京医科大学講師）
翻訳概略　佐藤　耕平（日本女子体育大学助教）

「Circulatory regulation during exercise」　Niels H. Secher
(Professor, The Copenhagen Muscle Research Center, Department of Anesthesia, Rigshospitalet, University of Copenhagen, Denmark.)

17：10　閉　会

■特別講演

Circulatory regulation during exercise

Niels H. Secher
Department of Anesthesia, The Copenhagen Muscle Research Center, Rigshospitalet,
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During exercise the circulation is challenged by the ability to balance a marked increases in vascular conductance as muscle blood flow increases with the ability to maintain arterial blood pressure. Central in the regulation of arterial pressure is the arterial baroreceptors, which regulated blood pressure beat to beat by controlling sympathetic nerve activity via integrating various signal in the nucleus tractus solitarius (NTS). The signals that NTS integrates include besides the influence from the arterial baroreceptors, neural influence from the working skeletal muscles (the muscle pressor reflex), influence from other parts of the brain (central command) probably dominated by signals from the cortex and the insula area, besides influence from variation in the central blood volume. In other words, the arterial baroreceptors may be viewed as the instrument that the NTS uses to control the set blood pressure.

In response to exercise these various neural influences reset the arterial baroreceptors to control an elevated heart rate and blood pressure and two strategies can be defined to defend the elevation in blood pressure. The ideal strategy is that the circulation is able to secure the increase in blood pressure by elevation of cardiac output. On the other hand, if the increase in cardiac output is not large enough to elevate blood pressure to the set level, then blood pressure is defended by peripheral vasoconstriction that primarily affects the splachnic blood flow and flow to the kidneys, but also affects skin blood flow, flow the working skeletal muscles and even to the brain. Such manifestations of restricted peripheral flow are important especially during whole body exercise, where the challenge to blood pressure control is the largest. Thus, during whole body exercise flow to the exercising muscles is lower than what is established when the investigated limb is working in isolation and the restriction in muscle blood flow is demonstrated to be by enhanced sympathetic activity. However, a restricted flow to both working skeletal muscles and to the brain manifests especially in diseases associated with a reduced ability to enhance cardiac output, i.e. with a failing heart.

A significant effect of endurance training is to elevate blood volume primarily by enhancing plasma volume. The likely mechanism involves that the central blood volume is reduced many hours after exercise because the muscle blood volume remains elevated in the recovery and hormonal variables restrain urine production, while thirst compensates for the reduced central blood volume. Also total hemoglobin increases may be in response to arterial desaturation during intense whole body exercise and may be also because of the reduced kidney blood flow. Whatever the mechanism, both the increase in plasma and red cell volume enhances preload to the heart and makes it possible for the heart to increase it output. Thus following training the cardiovascular response to upright exercise approaches that seen during supine exercise with attenuated heart rate and blood pressure responses.

While the training induced enlarged central blood volume readily explains heart rate both at rest and during exercise, several mechanisms may be involved in attenuating the blood pressure response to exercise. Besides attenuation by the enlarged central blood volume, also enhanced muscle blood flow is likely

to attenuate the muscle pressure reflex and thereby the upward resetting of the arterial baroreceptors. Furthermore, habituation to the exercise mode makes the need for central command smaller, further reducing resetting of the arterial baroreceptors

Also the influence of training on cerebral blood flow and oxygenation is complex. Cerebral blood flow is influenced primarily by the arterial carbon dioxide tension. Thus it is significant for maintained cerebral blood flow that the exponential increase in ventilation with increasing exercise intensity is delayed as the ability to perform more work is enhanced. In other words, only at a higher workload manifests a reduction in cerebral blood flow as the arterial carbon dioxide tension decreases. Yet, at exhaustion the calculated cerebral capillary and mithochondrial oxygen tension decreases and at least indirect evidence point to that exhaustion may be coupled to this reduction in cerebral oxygenation.

Niels H. Secher氏の略歴

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The Danish Cardiovascular Research Academy （2002～
The Academy for Muscle Biology, Exercise and Health Research （2005～
The MuscleCluster, Faculty of Health Sciences, University of Copenhagen （2005～
European Journal of Applied Physiology, editor 2000 -
Editorial Board, Scandinavian Journal of Medicine and Science in Sports and Exercise, section editor 2007～2009.
Journal of Sports Sciences, editorial board 1984
Experimental Physiology, editor （2001～2005）
Journal of Applied Physiology, editorial board 2005～

Sports
Danish championship in rowing × 9 （1964～1974）
Nordic championship in rowing × 3 （1967～1972）
International West German championship in rowing × 2 （1969, 1970）
Holland Becker （1967, 1970）
North American Champion in single scull （1967）
World Champion in double sculls （1970）

本プロジェクトのねらい

加賀谷淳子（日本女子体育大学名誉教授）

本研究プロジェクト「運動時における循環調節機構の統合的解明－スポーツによる健康・体力づくりプログラムの構築に向けて－」は，2004年度の文部科学省学術フロンティア推進事業に選定され，平成16年度～平成20年度の５年間実施された．この事業は，私立大学の大学院，研究所の中から，研究実績をあげ，将来の研究発展が期待される卓越した研究組織を選定し，内外の研究機関との共同研究に必要な研究施設，研究装置・設備の整備に対し，重点的かつ総合的支援を行うものとされている．したがって，本プロジェクトでは課題とする研究を推進して学術的貢献をすると同時に，運動時の循環調節研究の拠点となるようにハード・ソフト両面の研究環境の整備を推進することをねらいとしている．

1．健康・体力づくりプログラム構築にむけた運動時循環調節の研究の推進

運動に対する循環系の適応は極めて巧妙にできていると考えられる．複雑な仕組みになっていることは，ひとつの系が破綻しても他の系が補償し，生命維持に必要な循環システムを破綻させないような安全弁が用意されているということであろう．安静時につくられた循環システムの安定性は，運動という外乱によって一旦はその整合性が破られる．そこで，運動開始と同時に，運動を遂行するに必要な循環調節と生命を維持するための循環調節という二つの方向の再調整がなされる．効果的な運動と同時に運動の安全性を考えなければならない所以である．しかし，運動に対する循環系調整の機序はまだ全貌が明らかにされていない．本プロジェクトでは，運動時の循環調整に関する科学的エビデンスを，運動特性と関連させて蓄積し，それらを統合して得られたエビデンスを基盤とし，健康・体力づくりのための運動プログラムの構築に向けた提案を行うことを目指している．

課題解明に向けた本プロジェクトでの取り組みは図１に示した通りである．５年間のプロジェクト研究期間の最初の３年間（2004～2006年度）は，運動時の循環調節に関する知見を集積し，それを統合して循環調節の解明に貢献することを目指した．そのために，運動時の生体応答研究の基盤となる運動単位の動員特性を明らかにすると共に，人を対象とした循環研究に必要な非侵襲的計測法（近赤外線分光法，超音波法など）の研究への適切な適用等を進めながら，1）運動時の血流再分配と2）循環系に対するセントラルコマンドを中心とした神経性調節に焦点を当てた研究が遂行された．中心的課題である「運動時の血流分配に関する研究」と「運動時のセントラルコマンドが循環に与える影響に関する研究」はプロジェクトメンバー全員が参加する共同研究として行われた．さらに，特化したテーマについては，個別に研究を実施し，プロジェクト全体で討議して統合するという研究体制をつくった．これに関する個々の成果は，2006年11月の中間報告会で公表されている．さらに，それらを統合した運動時の循環調節の機序については，2008年11月の国際シンポジウムで報告した．

プロジェクト最後の２年間（2007～2008年度）では，それまでの成果を様々な身体特性を持つ対象者で検証することと，運動の継続が循環調節に与える影響を横断的，縦断的に明らかにすることを中心課題とした．そして，それまでに得られたすべての知見を基に，スポーツによる健康・体力づくりプログラムの構築に対して，循環調整の観点から提案を行うこととした（2009年２月）．

以上のように，研究面では，本テーマに関して，学術的な貢献をすること，それを基に，運動プログラム構築にむけた提案を行い，社会のニーズに応えることが本プロジェクトのねらいである．

2．運動時循環調整研究の拠点整備

本プロジェクトでは，初年度に脳の酸素動態を非侵襲的・連続的に計測する近赤外線分光法や解像度が高く，画像分析が自動化した超音波測定装置を購入した．２年目以降は既存の計測装置や運動負荷装置をシステム化して，

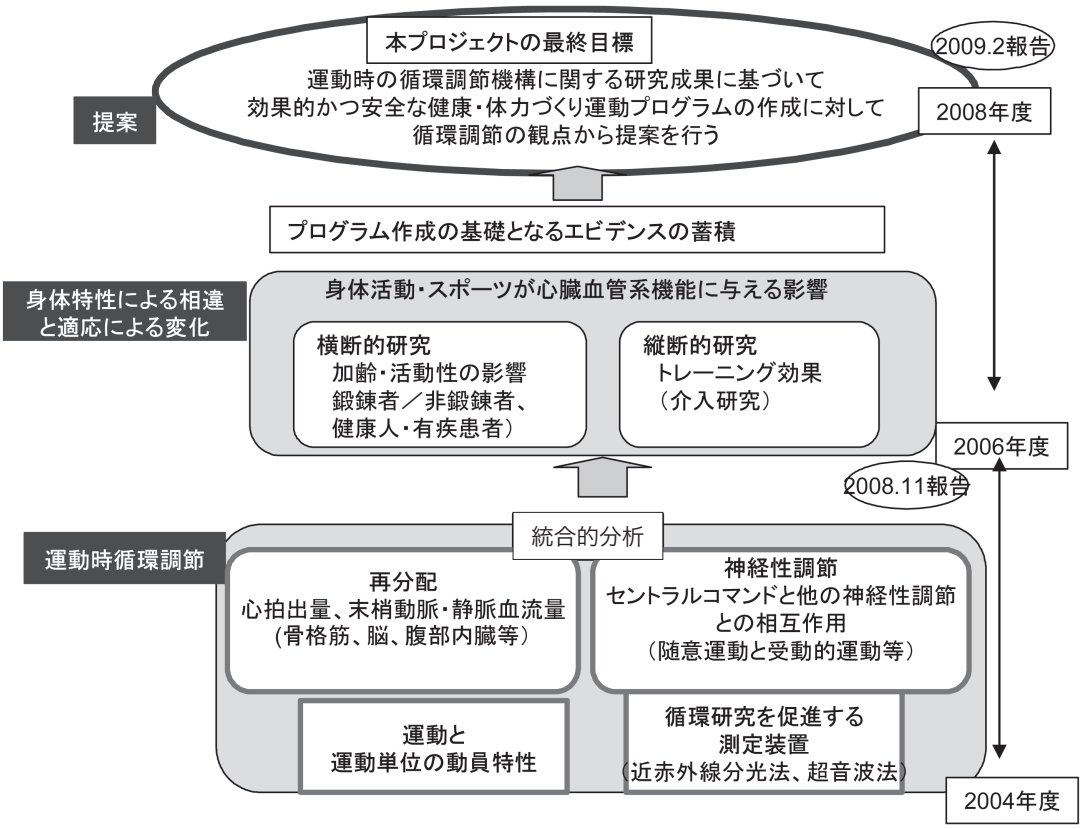

図1　本プロジェクトの研究デザイン

ハード・ソフト面の整備が一段と進んだ．

多様な因子によって調節されている循環調節について，様々な様式・強度・持続時間の運動を用い，異なる姿勢や環境の影響等を考慮しながら，性年齢・身体特性の異なる対象者で検証するには多くの研究者による共同研究が必要である．本プロジェクトでは本研究所と他の研究機関との共同研究や本研究所を拠点として若手研究者が参加する研究プロジェクト実施についてもいくつかの試みを行った．本プロジェクトの実施による拠点整備により，実施母体である日本女子体育大学のさらなる研究活性化と他機関の多くの研究者が参加できる研究拠点となるシステムづくりをすることはプロジェクト実施の大きなねらいであった．

Session 1
プログラム作成の基礎となる科学的エビデンス1
－運動時の循環調節－

運動準備や想起に伴う脳活性

岩館　雅子（日本大学生産工学部助教）

運動時の循環調節は，運動の始まる前からすでに開始されており，運動準備や想起に伴い生じる心拍上昇や筋血流上昇はその代表的な応答である．運動準備期の循環応答は運動時とは異なり筋収縮が生じていないことから，運動性循環反射がない状態で中枢指令（セントラルコマンド）が発現したことによる応答であるといえる．セントラルコマンドの起源は，近年，大脳や視床下部，脳幹部などに存在することが示唆されている．心臓や筋血管で生じる循環応答の神経調節としては，セントラルコマンドが自律神経系を介して標的部位に作用していることが明らかになりつつあるが，一方，セントラルコマンドの中枢と線維連絡のある脳領域は，どう影響を受けるのかは明らかでなかった．特に，運動出力に関連する大脳皮質運動野は視床下部などと密接な連絡がある．そのため，セントラルコマンドにより心臓や筋に予測制御応答が生じているとき，脳においてもすでに変化が生じている可能性があった．従来，運動準備期の運動野周辺領域の脳活動は，非侵襲的手法である脳波を用い，大脳皮質運動野の活動が運動準備期や運動想起時に見られることは多数報告されてきた．一方，運動制御に関する神経科学の研究では，研究視点の違いもあり，循環反応との対応は検討がされてこなかった．その理由の一つは，脳波を用いた研究では，加算平均を必要とするため被験者に同一試行を数十回繰り返し行わせるが，この繰り返しによる慣れや疲労が循環反応を変化させ，両変数の対応関係の検討を困難にするためと考えられた．このような状況の中で，近赤外分光法（NIRS）を用いた大脳皮質酸素動態の計測は，時間分解能にも比較的優れ，脳波のような加算を必ずしも必要としないことから，変動しやすい循環反応との対応関係をみるには，現時点では最も適していた．

そこで本研究では，NIRS を用いた大脳皮質運動野酸素動態の変化を脳活動の指標とし，掌握運動の開始約 1 分前からの大脳皮質運動野酸素動態，心拍数，平均血圧，心拍出量，前腕屈筋酸素動態を同時記録し，これらの対応関係を検討した．

その結果，運動準備や想起に伴い，循環応答としては，心拍上昇および心拍出量増加および筋血流速度上昇という応答がみられた．これに対し，大脳皮質運動野酸素動態においても，oxyHb および totalHb の上昇，deoxyHb の低下傾向という，神経活動賦活に伴う血流増加を反映する脳酸素動態変化がみられた．このことから，運動開始前において運動準備や想起により，心拍数の上昇，心拍出量増加および活動肢の筋血流速度上昇が生じるとき，大脳運動野周辺の脳活動も同時に亢進することが示された．

以上のことから，ヒトは実際に運動を行う前から，心臓，骨格筋における予測制御とほぼ同時期から運動出力を担う大脳皮質運動野の活性化を連動して生じていることが明らかになった．このことは，運動時に適応するためのプログラム化された一連の予測制御が，脳も含め全身性にフィードフォワード的に生じることを示すと考えられる．

運動を持続させる大脳皮質の働き

澁谷　顕一（日本女子体育大学附属基礎体力研究所ポスドク研究員）

1．はじめに

運動中の脳における活動を計測することは，脳が運動をどのようにコントロールしているかを知るだけでなく，運動による身体における変化をどのように捉え，その情報を処理しているのかを理解するために重要である．そして，それにより，運動指令がどのように脳から末梢へ向けて放出されているのかを知ることができる．運動指令に関する知見は運動制御に関する分野だけでなく，循環調節に関わる分野にとっても重要な知見となる．本プロジェクトでは，近赤外線分光法を用い前頭前野および一次運動野の活動を計測し，皮質レベルにおける活動を計測し，運動を持続させるための大脳皮質の働きの一部を明らかにすることを目的とした．

2．運動中の前頭前野における活動

運動の持続に対しては前頭前野における活動が関与している可能性も示唆されている．本研究では，学際的な視点を取り入れ，主に，心臓血管系と代謝は脳と筋の酸素化および代謝に影響を及ぼす心臓血管系および代謝機構について検証してきた．特に，1）運動中の筋疲労のメカニズムや安静から運動への移行期の酸素化動態のメカニズムの理解を進めた．また，2）前腕筋の出力維持と，巧妙な運動の制御と協働を必要とする正確な動作遂行を可能なものとする上で，前頭前野が重要な役割を果たすという仮説を支持する結果が得られた．

3．運動中の一次運動野における活動

しかし，運動に対して実際に指令を出しているのは一次運動野である．その一次運動野における活動動態を知ることで，上記の仮説はより強固なものとなるであろう．そこで，本研究では左右半球における一次運動野の活動を記録した．左右の半球における一次運動野は相互作用を持つことが知られている．これまで，活動肢と同側半球における一次運動野は，活動肢の運動を直接制御することはないと考えられてきた．つまり対側半球一次運動野の制御により行われていると考えられてきた．しかし，近年の研究では，左右半球間の一次運動野の相互作用が存在する可能性が示されている．本研究の近赤外線分光法を用いた脳酸素化動態の時系列的分析により，運動開始後の左半球の一次運動野と右半球一次運動野の酸素化動態に時間的差異が存在することが明らかとなり，運動開始後の左右半球間の一次運動野の相互作用形成の可能性が示された．このような両側半球間の結合は対側半球の一次運動野だけでは力発揮が十分ではない場合に，それを補完するために同側半球一次運動野の活動が動員されると考えられる．また，トップアスリートと一般成人の一次運動野の活動比較から，疲労困憊に至る運動時に一次運動野の酸素化動態に明確な相違があることも示された．

4．まとめ

以上のことから，前頭前野のみならず，一次運動野においても活動肢に対して同側部位の活動が運動の調節に大きく関わっていることが明らかとなった．今後，さらにこれらの検討を行うことで，運動を遂行する命令が脳からどのように発信されているのかを知ることができるであろう．

運動時のモーターユニットの動員特性

加茂　美冬（日本女子体育大学准教授）

運動は，時間的，空間的に様々な組み合わせで起こるモーターユニット（Motor unit; MU）活動を基礎として成り立っている．すなわち，筋力は，筋を構成するMUの発揮張力の総和であり，筋力増大は，活動するMU数の増大と参加したMUの放電頻度の上昇により実現される．MUの収縮は種々の血管拡張シグナルを発すること，また，十分でない酸素供給はMU活動を変化させることなど，MU活動と循環系機能は密接に関わっていることは明らかである．しかしながら，種々の筋力発揮条件における両者の相互関係，さらには各々の動態についても不明な点が多く残されている．本プロジェクトにおいては，以下の３つのアプローチにより両者の関係を探ろうとした．

【動的膝関節伸展運動の強度変化に対する筋・循環系の対応（平成17年度共同研究）】

MU活動〔表面筋電位積分値（IEMG）から評価〕と循環系機能の関係を検討した．各種強度で1分間動的筋力発揮を反復したとき，IEMGは30％MVC以上の強度において時間に伴い直線的に増大した．血圧，筋血流量および筋酸素動態の境界強度も約30％MVCで確認された．IEMG増大は主にMU活動参加を反映することから，新たなMUの動員が，循環系・代謝系機能変化の引き金になることおよびその発現強度は約30％MVCであることがわかった．

【静的（等尺性）一定筋力発揮における運動単位放電特性を規定する因子（個別研究課題）】

等尺性一定筋力を持続的に発揮するとき，MUは放電間隔を時間と伴に延長させる．この延長は全ての筋力レベルにおいて観察される特徴的な現象であることから，筋力調節および筋疲労発現に重要な役割を担っていることが示唆されている．したがって，この現象を理解することは，筋力発揮時の循環応答の統合的解明において意義をもつ．本実験では，その合目的性および発現メカニズムを“反復電気刺激に対する誘発張力応答”および“振動刺激による末梢感覚情報操作”から検討した．その結果，放電間隔延長現象は筋反復収縮初期の不完全強縮張力増強に対して抑制効果をもつことが確かめられた．さらに，低筋力発揮レベルではその効果は充分でないことを新たに見出した．また，人為的な末梢感覚刺激の増減により放電間隔延長は必ずしも消失しなかったことから，MU放電間隔延長の発現に対するcentral driveによる制御の重要性が示唆された．

【静的（等尺性）筋力発揮における運動単位活動と循環系機能の関係（個別研究課題）】

Ascending ramp 収縮（～10％MVC，30 s）を緊張性振動反射（RC）と随意収縮（VC）で行い，両条件におけるMU活動と循環系・代謝系機能を比較した．IEMGはVCよりRCにおいて有意に大きいあるいは大きい傾向にあった．VCにおいて心拍数と血圧はこれまでに報告されている随意筋力発揮におけるcentral cardiovascular commandの制御による変化と同様な傾向を示したが，RCでは観られなかった．筋酸素化ヘモグロビンの筋力発揮開始時低下の大きさはVCに比較しRCで大きかった．これらのことは，随意収縮では，central motor commandによる効率のよいMU活動とcentral cardiovascular commandによる循環系機能制御が効率のよい酸素利用もたらすことを示唆している．

活動筋代謝の有酸素性依存から無酸素性依存への変移

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1．はじめに

筋収縮の強度は活動筋への血流を規定する重要な要素であり，筋内圧の機械的変化と筋の代謝性変化を伴い，活動筋における動脈血流入量と静脈血流出量を決定する．運動強度が異なると，動員される筋線維タイプが異なり，活動筋への酸素需要の増加による応答として，循環システムは心拍出量の増加や他の組織への血流減少という形で調節を行うが，その詳細については十分には検討されていない．本研究では，運動強度の変化に対する筋代謝と循環器系の調節との関係を解明することを目的とした．

2．動的運動時の筋酸素動態と運動強度

動的運動時の筋代謝の時間経過に伴う変化が運動強度により異なるか否か，さらに筋代謝に部位特異性があるか否かを明らかにするため，筋の浅部と深部や内側と外側で筋酸素動態の変化を測定し，さらに筋疲労感覚や血圧との関係を検討した．低，中，高強度の動的膝伸展運動を行った結果，①低強度運動では筋脱酸素化は時間経過に伴い小さくなったが，中・高強度運動においては筋脱酸素化は運動継続中維持された．②筋の部位特異性は見られなかった．③さらに筋脱酸素化と筋疲労感覚は血圧の上昇しない低強度運動でのみ相関関係がみられた．低強度での筋酸素動態は筋疲労感覚に関与しているが，中・高強度では血圧上昇と関連した他の要因が筋疲労感覚に関与しているものと考えられた．

3．静的運動後の筋再酸素化時間と運動強度

運動中の筋酸素動態は，筋内圧の上昇による活動筋への血流制限の影響が大きい．一方，運動後の筋再酸素化時間（運動後の回復期に酸素動態が元に戻るまでの時間で，この時間が延長すると筋の有酸素性代謝貢献が低いという関係性が示されている）はより筋代謝の影響を反映すると考えられる．運動中の筋内の酸素化動態が遠位と近位では異なることは既に知られているが，筋の浅部と深部間の不均一性については検討がなされていない．浅部では速筋線維が多く，深部では遅筋線維が多いといわれ，その酸素化動態が筋の深さにより異なることは十分に仮定される。筋再酸素化時間の延長し始める運動強度があるか否か，あるとすればその強度に筋内で部位特異性があるか否かついて検討した．その結果①筋再酸素化時間が顕著に延長する運動強度が存在することが明らかになった．②どの強度においても筋再酸素化時間は浅部と深部で差がみられなかった．静的膝伸展運動時に活動筋における代謝が有酸素性依存から無酸素性依存へと移行するのは，比較的高強度（最大随意筋力の70％）であり，筋の有酸素性代謝貢献度が深さによって相違があるとは言えないことが示唆された．

筋代謝や循環指標等の複数のパラメータの代謝変移点を知ることで，健康・体力づくりにおいて安全且つ効果的な運動強度の設定に役立つと考えられる．

筋活動による心拍出量の変化と血流分配

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1．はじめに

運動時の循環系の対応は手際よくシステム全体の再調整が行われるため，筋活動による血流再分配を明らかにすることにより，安全で効果的な健康のための運動に貢献できる．

2．筋の活動による心拍出量の変化と骨格筋，脳，腹部内臓への血流分配

骨格筋への血流量が心臓の拍出量とどう対応するかについて，局所運動時に低負荷では心拍出量の増加を伴わずに活動筋への血流再分配が起こり，強度が高くなると心拍出量を増加させて骨格筋へ血流分配を行うことが示された．一方，骨格筋への動脈血流量は，筋収縮期は一旦安静時より低下するが，筋収縮中止直後は顕著に増加する．逆に静脈血流速度は筋収縮期に加速され，筋弛緩期には顕著に低下し，両者は筋内圧の局所的変化により関連していることが示された．また筋活動が繰り返される動的運動時の動静脈血流量は相互に関連していることが明らかになった． 骨格筋の血流がどこまで増加するか，最高血流量に達する運動条件を調べた結果，動的運動時筋弛緩期の膝窩動脈血流量は，運動強度とテンポが密接な関係を保って変化し，両者の組み合わせによって運動時血流量が最高値に達することが示された．一方，運動時の非活動肢血流量は，運動開始初期は一過性に強度依存の増加が起こるが，時間経過に伴い減少が起こった．このことは，運動開始後活動筋へ特化して血流量増加が起こるように調節されるまでには時間を要することを示唆している．さらに，運動時の脳への血流再分配は，内頸動脈血流量の変化はみられないのに対して，椎骨動脈経路では血流量が増加することが明らかになった．また運動に直接関与しない腹部内臓への血流量は，運動時の腎動脈血流の減少がみられたが，上腸間膜動脈では顕著な変化はみられず，運動時の腹部内臓器官への血流再分配は一律の変化ではなかった．加えて，重力の影響に対する血流量の応答をみると，掌握運動時の前腕を心臓より垂下した場合や下肢の血液プーリングの影響をみた結果，静脈血流量が減少し筋血液量が増加を示した．

3．運動強度と循環系応答：血圧変移点

筋収縮がある強度を超えると血圧の上昇が顕著になる（Kagaya *et al*. 2001）．そこで血圧上昇が高くなる負荷を基準として強度をとらえ血流再分配をみると，運動後血流量に対する運動中血流量の比は，血圧変移点負荷とほぼ類似の負荷強度で急激に低下し，運動中の血流需要を満たす割合が低くなることが確認された．さらに，筋の酸素代謝は運動時の活動肢筋酸素動態が負荷強度に対して低負荷と異なる対応を示すのは，血圧変移点よりやや低い負荷からであった．また運動時の活動筋での変化を中心に身体の様々な変化を統合して感知する主観的筋疲労感覚は，血圧変移点より低い負荷（38％MVC）から急上昇した．

4．血流再分配からみた運動プログラム作成への提案

運動時の循環系応答や主観的筋疲労感覚の変化がみられる時点が血圧変移点の出現付近の負荷強度に類似したことから，運動プログラム作成では適切な運動強度を選択する基準として血圧変移点の負荷を手がかりにすることが有用であると考えられる．

筋形状の変化が筋循環に与える影響

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1．はじめに

運動の実践現場では，筋腱を伸張させるストレッチングが良く用いられている．その効果は，筋腱だけでなく，循環系の活性化にも影響を及ぼすと考えられるが，ヒトについてのそのエビデンスは十分ではない．もし，ストレッチングにより，循環系機能が促進あるいは抑制することが明らかになれば，循環機能を促進する効果的なストレッチングの方法を明らかにすることにより，健康・体力づくりのための運動プログラム作成に貢献できる．

2．ストレッチングが筋循環に与える影響

ストレッチングが筋循環に与える影響を明らかにするために，仰臥位での下腿筋受動的ストレッチングを２種の角度[解剖学的正位（AP）と快適最大角度（痛みを感じる角度－３° ：CP）]を用いて行った．そして， 1）筋束長の変化，2）筋酸素動態の変化，3）ストレッチング部位より上位に位置する当該筋へ血液を供給する膝窩動脈および静脈血流速度の変化，について検討した．

その結果，1）足関節の背屈に従って，腓腹筋内側頭（MG）とヒラメ筋（SOL）は筋束が伸長し，それらの拮抗筋である前脛骨筋（TA）は短縮し，協働筋であるMGとSOLの筋束長伸張率が異なることを示した（伸長率：MG73％，SOL30％，短縮率：TA19％）．2）ストレッチング中，SOLでは両角度において筋血液量は増加したが，MGにおいては，APではほとんど変化せず，CPでは減少したことから，筋血液量の応答には下腿協働筋間で相違があり，ストレッチングによって減少する（MG）だけではなく増加する（SOL）筋もあることがわかった．3）ストレッチング中の動脈血流速度および静脈血流速度は有意な変化を示さなかったが，ストレッチング終了に伴う足底屈と共に，動脈血流速度は有意に上昇し，静脈血流速度はそれより数秒遅れて有意に増加した．動脈血流量の増加に遅れて起こる静脈血流量の増加は動脈血流依存であると考えられた．また，ストレッチング中の血流速度を順行成分速度と逆行成分速度に分けて計測すると，CPでは安静時より有意に速度が速くなることが示された．筋束長の伸長度が高いCPでは，ストレッチによって当該筋内の血管が大きく伸長され，血管径が短縮し，血管抵抗が増加したことにより，逆行成分速度が速くなったと考えられる．

次に，MRI（Flesh Blood Image法）を用いて，ストレッチング中の末梢血管の撮像を行った．その結果，静脈血indexがストレッチング中に減少することが示された．ストレッチングによる筋線維の形状的変化が各筋の血管形状をどのように変化させるはまだ明らかにされていないので，今後は，この方法を用い，各筋別に検討していく必要がある．

3．循環機能促進に効果的なストレッチングプログラムについて

以上のことから，筋形状を変化させるストレッチングは，その角度や時間等を適切に選定すれば，筋循環へ効果を及ぼすことが確かめられた．本結果からは，快適最大角度で１分間のストレッチングを行うことにより，筋循環への効果が認められた．より効果的なプログラム作成には，まだ更なる検討が必要である．

随意運動時の呼吸・循環応答にみられるセントラルコマンドの働き

佐藤　耕平（日本女子体育大学助教）

1．セントラルコマンドとは？

運動時に起こる呼吸・循環活動の制御機構の一つとしてセントラルコマンド説がある．このセントラルコマンドは，大脳皮質から生じる運動指令と同期して高位中枢から起こり，呼吸・循環機能を修飾する，フィードフォワード型の調節であると定義されてきた．一方，運動時に筋弛緩薬を投与し，運動努力（effort）を増加させた侵襲的な実験モデルでは，運動努力に比例した循環応答の増加がみられることが報告されている．また，運動をイメージしただけでも，呼吸・循環応答が引き起こされることが知られている．これらは，セントラルコマンドによる循環調節が，必ずしも運動指令を伴わないものであること，さらには努力感や疲労度を反映したセントラルコマンドが循環応答に作用するという，フィードバック型の調節機構であることも示唆する．

2．セントラルコマンドと運動時の循環調節

本プロジェクトでは，運動時の循環調節に対するセントラルコマンドの役割を検討した．検討した課題は主に，1）運動時の脳・内臓血流に対するセントラルコマンドの役割と，2）身体トレーニングに伴う筋交感神経活動の変化に対する，セントラルコマンドの影響である．課題1）では，セントラルコマンドが運動時における脳血流調節に関与するか否かを，2つの実験モデルを用いて検討した．一つ目は「随意-受動運動モデル」，二つ目は「バイブレーションモデル」である．「無負荷随意-受動運動モデル」を用いた実験では，動的運動開始初期に起こる脳血流の増加は，セントラルコマンドが関与する可能性が示唆された．また，セントラルコマンドの脳血流に対する影響は，部位差（地域差）がある可能性が示された．さらに，「バイブレーションモデル」を用いて静的運動時の努力感・疲労感を低下させた場合，努力感に応じた脳血流の応答が見られることが明らかになった．しかしながら，このモデルでは，腎血流応答に対するセントラルコマンドの影響は認められなかった．これらの知見は，セントラルコマンドは，交感神経系を介して応答を調節しているとされているが，交感神経全体に均一して作用するのではなく，地域差があることを示唆するものである．課題2）では，最大努力での局所的なレジスタンストレーニングを介入することにより，上位中枢機能（セントラルコマンド）に刺激を与え，運動時の筋交感神経活動がトレーニング前後において変化するか否かを検討した．その結果，トレーニング後に静的運動時の筋交感神経活動は増加することが明らかとなり，その亢進は筋からの末梢神経反射よりも，セントラルコマンドの増加が関与する可能性が示唆された．

3．高強度運動時の循環調節

セントラルコマンドの活動が極めて亢進するような，高強度運動時の循環調節の解明は，安全で有効な運動プログラムを構築するうえで重要な課題である．稀にではあるが，ウエイトリフティングやレジスタンス運動時には，脳出血や失神・眩暈を起こすことが報告されている．これは，過度の血圧および脳血流の増減が影響しており，これらの応答には運動中の呼吸法が密接に関連すると考えられている．本研究では運動時の息こらえと，運動前の過換気が脳血流調節に及ぼす影響を検討した．その結果，高強度運動時に息こらえをした場合，運動中の脳血流の低下と，運動後の急激な増加を誘発することが明らかになった．また，運動前の自発的な過換気による脳血流の低下は，運動後まで持続することが明らかになった．これらの結果は，息こらえによるバルサルバ呼吸と，過換気による低炭酸ガス血症が，運動時の脳血流応答に作用したと考えられる．また，運動前の過換気および運動中の息こられを防いだ場合，脳血流の増減は抑制された．本研究は，アスリートや一般人がウエイトトレーニングを行う際の，安全な呼吸法を提言するものでると考えられた．

Session 2
プログラム作成の基礎となる科学的エビデンス２
－発育，老化，疾患およびトレーニングによる循環系の変化－

子どもの循環機能の発達

佐藤　耕平（日本女子体育大学助教）

身体を構成する各部位の形態や諸機能の発達は一様ではなく，部位および機能により相互に異なる発達過程を持つと言われている．他の組織に比べ，脳神経系の発達は早期に完了すると言われているが，脳の神経細胞がその機能を十分に発揮するには，エネルギー供給を担う脳循環の発達が不可欠と言える．先行研究における，脳血流の発育に関する研究は極めて少ない．また，これら研究においては脳血流量の絶対値を算出し，その経年的な変化にのみ注目し，脳循環機能の発達を捉えている．しかしながら，発育期においては，脳循環の発達と同時に，心拍出量などの心臓を中心とした中心循環機能も発達する．故に，脳循環と中心循環の相対的・相互的な発達過程を把握することも重要であると考えられる．このような観点から本研究プロジェクトでは，発育期の子どもの，心拍出量（Cardiac Output: CO）に対する総頸動脈血流量（Common Carotid Artery Blood Flow: Q_{CCA}）の比（%）を脳血流配分比率として算出し，脳循環と心循環の相対的・相互的な発達過程を検討した．

本研究の被験者は，小学校高学年男女66名（男35：女31），中学生男女96名（男38：女58），高校生女子83名であった．測定項目は，椅子座位での安静時の循環機能の指標として，動脈血圧，心拍数（Heart Rate: HR），一回拍出量（Stroke Volume: SV），COをフィノメータ連続指血圧測定装置（Finapres Medical Systems）により測定した．またQ_{CCA}を超音波画像診断装置（Logiq5, GE）により算出した．脳血流配分比率は，Q_{CCA}／COの計算式から算出した．

脳血流配分比（%）の経年的変化を男女毎に下図に示した．男女ともに小５が最も高く，中２から中３にかけて漸減することが示された．女子では小５-小６間および中１-中２間で有意な減少が見られ，中３以降でほぼ成人の値になることが示された．小学および中学期には男女差は認められなかった．本研究における女子における小学５年生から中学３年生にかけての脳血流配分比率の低下は1）小６以降のCO（SV依存）の増加と，2）Q_{CCA}の低下によりもたらされた．この小学期に見られる高い脳血流配分比率は，おそらく発育期における脳神経機能の発達を反映したものである可能性が高い．また，中学後期において脳血流配分比率が，ほぼ成人の値に達する現象は，発育に伴って効率的な脳機能が形成され，余剰な血流が不要になったことを示唆する可能性がある．しかしながら，この発達過程の生理学的な意味については今後の検討が必要である．本研究は，発育期における運動指導や体力作りを行う上での基礎的な資料となるものであり，循環系に対するトレーニングの至適年齢を考慮する上でも興味深いものである．

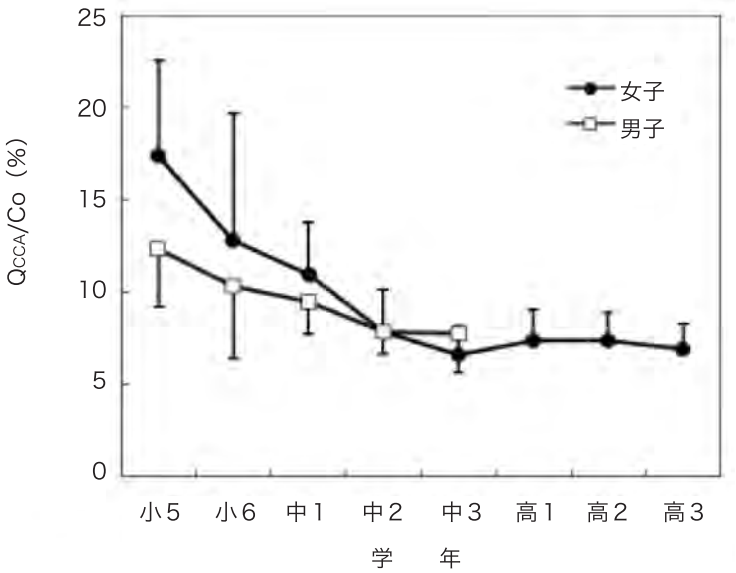


図１　発育期における脳血流配分比の経年的変化

有疾患者における運動および筋虚血に対する血流調節プロファイル

長田　卓也（東京医科大学講師）

背景：閉塞性動脈硬化症保有者は，下肢動脈血管の動脈硬化に伴う血流障害のために歩行距離の低下が認められ，運動による疾病下肢筋血行動態への影響が示唆される．

目的：一過性運動時における血流動態を検討する事を目的とし，末梢循環障害（Fontaine分類第II度）をきたす下肢閉塞性動脈硬化症保有者を対象に，運動時における血行動態について検討を行うこととした．

方法：末梢循環障害（血管造影にて確認されている）をきたす５名の男性閉塞性動脈硬化症保有者（平均年齢71±２歳）を対象に，座位姿勢での多段階負荷等尺性片側膝伸展運動を行った．運動開始前の安静時に足関節上腕血圧比（ABI）を測定し，運動は一足ごとに両側について行った．両下肢でABIが低い下肢を患測とし，反対側の下肢を健側とした．運動強度は，最大随意収縮力の５％，10％，30％そして50％とそれぞれの強度で３分間とし，多段階的漸増負荷とした．下肢運動の頻度は，５秒間の等尺性膝伸展運動（筋収縮）にひき続き，５秒間の休止期（筋弛緩）を１サイクルとした．下肢血流の評価は，超音波ドプラー法にて大腿動脈部位において行い，血管径と血流速度により算出した．血流速度は，５秒間の等尺性膝伸展運動及び５秒間の休止期のそれぞれに得られた３～４拍動の波形を計測し，血流量評価に使用した．運動中の血流反応は，筋弛緩期である休止期血流量から筋収縮期のそれを差し引いた血流増加量を指標とした．

結果：安静時において患測下肢のABI値は，健側に比べ低い値を示した．安静時下肢血流量は，患測が健測より低い傾向を示したが，運動中の下肢血流増加量は，患測において大きい傾向を示した．

考察：動脈硬化が強い下肢動脈血管（ABI値が低い下肢側）における筋収縮血流増加反応が高い事が示唆された．この事はより運動強度の上昇に伴う骨格筋酸素消費量を代償するための血流増加調節，筋虚血に伴う血管拡張代謝産物なの影響が強い事が示唆される．本研究では，運動に伴う患側下肢血流反応は，健側と比べて異なることが明かとなり，今後は末梢循環障害が安静時のみならず運動中の骨格筋循環に与える影響を検討する必要があると思われる．

高齢者の左室重量と骨格筋量の関係

奥山　靜代（慶應義塾大学講師）

1．はじめに

心臓は活動筋の酸素需要に応えるために，心拍出量を増加あるいは血流配分を増減させ運動に必要な酸素の需要を満たそうとする．一方，骨格筋では筋収縮時に筋ポンプ作用が働き，静脈還流量を高め，心臓の前負荷を増加させるので，加齢による骨格筋量の低下は，心筋や血管動態に対する刺激を低下させると考えられる．したがって，骨格筋量の低下がみられる高齢者において，心筋と骨格筋のバランスを取りながら，両機能を高めることが重要であると考えられる．

2．左室重量と骨格筋量の関係

心筋と骨格筋の関係をみるために，高齢者（15名，76±5.4歳）安静時の心形態（心室中隔厚，左室後壁厚，左室拡張・収縮末期内径），および大腿部筋厚（大腿直筋，中間広筋）を超音波Bモード法で測定した．その結果，心筋の厚さ（左室後壁厚＋心室中隔厚）と大腿部筋厚（大腿直筋＋中間広筋）との関係をみると，両者には有意な相関関係（$r = 0.647$，$p < 0.01$）がみられた．さらに大腿部筋厚から推定した大腿部筋体積と，心形態より算出した左室重量との間において，正の相関関係（$r = 0.561$，$p < 0.05$）がみられ（図1），左室重量は大腿部筋体積との間に密接な関係があることが示唆された．

3．提　案

以上のことから，高齢者の心臓の形態（左室重量）は大腿部筋体積と密接に相関することが示された．このことから，高齢者においても骨格筋量の保持が心臓の容量保持に有効であるといえ，高齢者も身体運動による筋量の維持が必要といえる．

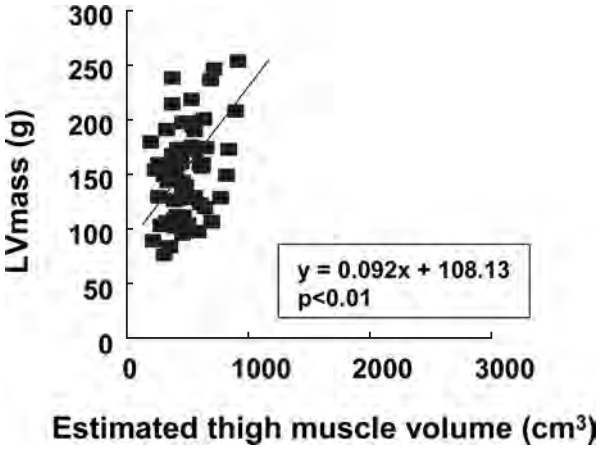


図1　左室重量と大腿部筋体積との関係

身体トレーニングによる循環機能の向上

斉藤　　満（豊田工業大学教授）

1．はじめに

生活習慣や加齢変化に伴う健康・体力の低下は最終的に高血圧，心疾患などの循環機能の低下や障害としてみられる．この予防には身体活動が有効なことは広く認められているが，その方法論についてはまだ開発の余地が残されている．

2．循環機能向上を目指す身体トレーニングとしてのハンドグリップ運動

健康の維持・増進をQOLからみると，循環機能に定量的な変化が認められなくても主観的効果として評価されることが少なくない．この背景には定量的には表現できない循環調節システムの機能の向上の存在が考えられる．

心拍出量などの定量的な循環機能向上にハンドグリップ運動はほとんど期待できないことから，トレーニング運動としての有用性についてはあまり注目されない．しかし，身体運動の一つとして循環調節システムに影響を及ぼす可能性は十分考えられ，何と言っても手軽に行えることから，「トレーニング運動」としての応用可能性は高い．本研究では，ハンドグリップ運動の循環機能向上への効果について，律動的，静的運動，運動時間や強度などを目的合わせて選定し，心拍・血圧反応，循環調節システムの代表としての交感神経活動及び主観的運動感覚の面から検討した．

検討内容は，1）ハンドグリップ運動時の運動意欲・頑張り，疲労感覚や循環反応と交感神経活動の関係，2）高強度ハンドグリップ運動が循環調節に及ぼす影響，3）長期トレーニングモデルとしての利き腕と非利き腕運動時の交感神経活動と循環反応の比較，4）神経性循環調節機能に与えるレジスタンストレーニングの効果とその後の脱トレーニングの影響，である．

結果の概要は，1）小筋群の運動でも全身の循環調節に携わる交感神経活動に十分刺激が与えられる，2）使用頻度の高い利き腕運動の循環調節は非利き腕運動とは異なる，3）短期間の強いハンドグリップレジスタンストレーニングは運動時の交感神経活動反応をより高めるが，この効果はトレーニング停止により速やかに消失する(図1)，にまとめられる．

以上の結果から，ハンドグリップを用いた運動トレーニングは，その運動強度や時間等を適切に選定すれば，心拍や血圧などの定量的な改善が認められなくても，循環調節システムとしての交感神経系に十分効果を及ぼすことが確かめられた．

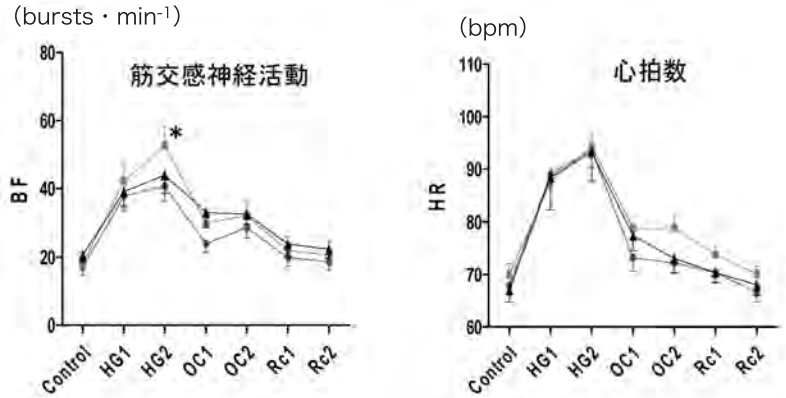


図1　4週間のハンドグリップトレーニング及び脱トレーニングに伴う運動及び運動後阻血時の交感神経活動，心拍反応の比較．運動時の交感神経活動反応はトレーニング後高まるが，心拍反応の変化はみられない．

Session 3
提　案
－安全で効果的な運動プログラム構築に向けて－

運動に対する循環応答からみた提案

定本　朋子（日本女子体育大学教授）

本プロジェクトで得た運動時の循環応答に関する知見をもとに，安全で効果的な運動プログラムの構築に向けて次のような提案をする．

1．運動様式について

1）動的運動・静的運動

動的運動は心拍数や心拍出量を増加させ，血液循環を促進する運動様式といえる．また筋の収縮と弛緩がリズミカルに繰り返され（収縮期には静脈血が筋から流出し，筋弛緩期には動脈血の流入量が増加する反応をもたらす），活動筋の十分な血管拡張により，運動時の血圧上昇が低く，生体への負担度が少ないという特徴をもつ．また軽強度による脚の動的運動時には，筋交感神経活動が安静時よりも低下することから，安静にするよりもゆっくり歩く方がリラクゼーション効果をもつと示唆される．一方，筋収縮が持続する静的運動は，心拍数や心拍出量の著しい上昇はみられないが，活動筋での血液の流入・流出が制限されるため，動脈血圧を上昇させやすい運動様式となる．特に強度が高くなると，心臓や血管系への負担も大きくなりやすい．このような動的運動と静的運動の特徴を理解した運動プログラムの作成が必要である．

2）大筋群運動（全身的運動）・小筋群運動（局所的運動）

大筋群を用いた全身運動による持久性運動は呼吸循環機能の維持向上のために有効であり，既に運動処方で広く活用されている．本プロジェクトでは，掌握運動のような小筋群の局所的運動であっても，活動筋のみならず非活動筋への血流量を増加させ，循環機能を活性化させることが示されている．運動強度が高くなると，脳血流増加の頭打ち，腎血流の減少，筋交感神経活動の亢進をもたらすことになる．また高強度負荷の掌握運動レジスタンストレーニングが運動時の頑張り・努力感に関わる中枢指令（セントラルコマンド）を増強させる効果をもつことも示されている．したがって，対象者の特性を考慮した適切な運動様式や運動強度を選択することにより，小筋群の局所的運動も循環機能の活性に有効な手段となる．

3）上肢の運動・下肢の運動

上肢の運動と下肢の運動では，一定の酸素摂取量に対する動脈血圧，心拍数，毎分換気量などが異なり，いずれも上肢で高くなることが既に知られている．循環機能からみると，上肢の運動は，心臓との位置関係（重力作用）によって循環応答が変動することを考慮する必要がある．一方，心臓よりも低い位置で運動することが一般的である下肢の運動は，重力作用による血液貯留を避けるよう留意する必要がある．

4）一側性の運動

循環促進に有効なサイクリングやウォーキングのような両側性運動が運動プログラムの主体となっている．しかし，腕や脚の運動を片側だけで行った場合でも，運動を行なわない対側や他の体肢（脚運動をしている時の腕

など）の骨格筋血流量を一時的に変化させることから，一側性の運動も運動プログラムとして活用できると考えられる．

5）その他の運動や運動想起

ストレッチングのように筋の長さを変える運動も，筋内循環を促進させることから，ウォーミングアップやクーリングダウンに用いるだけでなく，要介護者や病床にある患者の筋循環の促進を目的とした運動プログラムとしても活用できる．

運動の準備・想起（イメージ）は，運動野皮質関連領域の脳活性，心拍数，活動筋の酸素化動態，脳血流量（椎骨動脈経路）を上昇させたことから，随意的に運動を準備し運動遂行のイメージを持つことは，運動開始後の循環調節および動作をスムーズにさせる手段となる．

2．運動強度の選定について

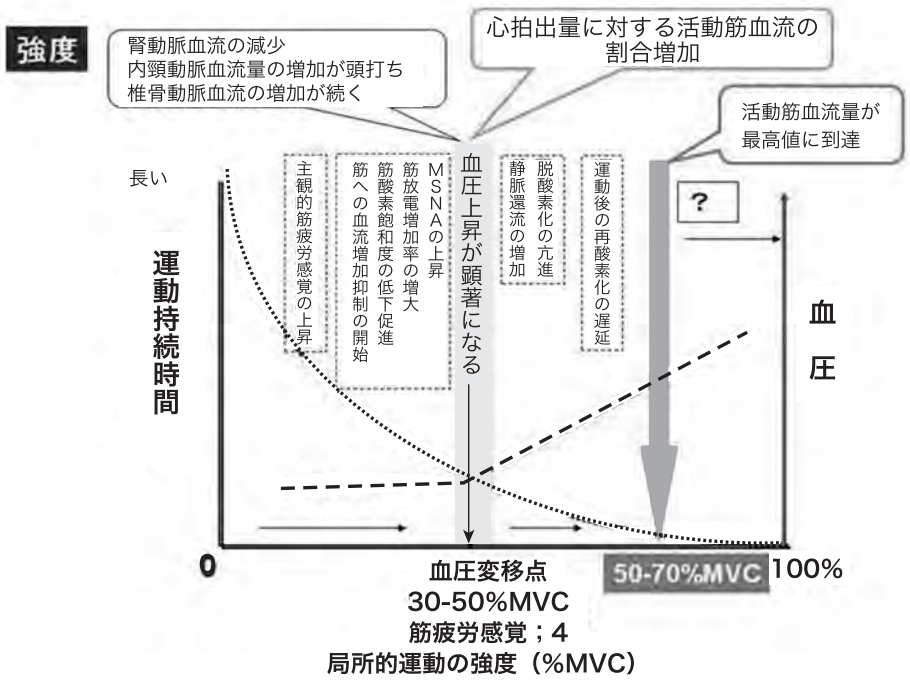
運動プログラムの作成において，適切な運動強度を選択することは重要課題である．全身的運動における強度設定指標は確立されているが，局所的運動については未だ確立されてはいない．本プロジェクトの結果から，次の二つの強度選定指標を提案する．

1）負荷増加に対して血圧上昇が顕著になる「血圧変移点」を指標とする．

「血圧変移点」を調べると（下図），随意最大筋力（MVC）の30～50％の運動強度に分布する．この血圧変移点の出現付近の負荷強度から，血液供給が不足し，筋交感神経活動の亢進も起こる．そして，腎動脈および内頸動脈血流量の減少や頭打ちがみられる．なお，血圧変移点を超えて50～70％MVCまで上がると，活動筋代謝は有酸素系から無酸素系へとシフトし，活動筋中には代謝産物・局所性ホルモンが蓄積されることになる．

2）主観的筋疲労感覚を指標として活用する．

筋疲労感覚は筋交感神経活動を反映する指標であり，血圧変移点負荷に相当する筋疲労感覚は「4」であり，これは「疲れた」と「かなり疲れた」の中間の感覚である．この指標は誰もが容易に活用できることから，単独で，あるいは他の強度指標と併用して用いることを提案する．また，運動実施時には常にモニターすることを推奨する．



3. 運動実施にあたっての留意点

本プロジェクトの成果に関連する運動実施上の留意点をまとめた．

1）運動時間の観点から

①運動開始前：運動への準備やイメージを持つことは運動開始後の循環調節および動作をスムーズにさせる有効な手段となる．

②運動開始時：運動に適した循環システムを再調整するには，運動開始後約30秒間は必要である．この調整がうまく運ばないと，血圧が低下することもある．したがって，運動開始時の急激な負荷上昇を避け，ゆっくりと徐々に運動強度を上げるようにする．

③運動終了前（疲労時）：運動持続時間とともに活動筋の疲労が始まる．筋疲労に抗して「頑張り・努力感」を働かせると，交感神経活動を介した力の維持が可能となる．しかし，運動経験の少ない人や低体力者の人は，無理のない時点で運動を終了させるようにする．その判断基準には主観的運動強度や筋疲労感覚を用いる（図参照）．

④運動終了直後：運動終了とともに，身体の各部位の調節機能は運動前のレベルに戻ろうとする．しかし，活動筋では運動時に生じた血管拡張物質が洗い出されるまで，血流増加が続くことになる．この運動後の著しい血流増加が静脈還流量を低下させ，ひいては運動終了後低血圧を招く場合もある．そのため，軽い運動（クーリングダウン）を運動終了後にも行い，筋ポンプ作用により静脈還流の急激な低下を予防する必要がある．

2）対象者の身体特性の観点から

①発育期の子どもにおける循環機能の発達：心機能および脳循環が著しく発達する時期は，心機能（推定心拍出量）が10～12歳頃であり，脳循環（頸動脈血管内径）が12～15歳である（男女差がある）．したがってこのような心臓および血管機能が発達する時期を考慮した運動のプログラムが発育期には必要である．

②高齢者における筋量の保持：高齢者の心臓の形態（左室重量）は大腿部筋体積と密接に相関することが示された．このことから，高齢者においても骨格筋量の保持が心機能の保持に有効であるといえ，高齢者も筋量の維持に結びつく運動プログラムが必要である．

③末梢循環系有疾患者の運動：閉塞性動脈硬化症保有者は筋虚血を代償するために著しい血流量増加が生じる．しかし，運動時の心拍出量の増大には限界があることを考えると，健常人よりも運動時の血流および血圧調節が難しい．このことを踏まえたプログラム作成が必要である．

3）呼吸法との関連について

短時間の高強度レジスタンス運動時の脳血流応答から，息こらえは脳血流減少を，過呼吸は運動終了後の著しい血流増加（オーバーシュート）をもたらせることから，運動時の呼吸をコントロールすることに留意する必要がある．

4）運動時の姿勢（重力作用）について

活動筋と心臓との位置関係によって生じる重力作用が循環応答を大きく変動させることに留意する必要がある．活動筋が心臓よりも高い位置にある場合は，筋への動脈血流量が低下し筋から流出する静脈血流量が増加し，運動遂行には不利なことが多い（上肢の運動・下肢の運動参照）．

学術フロンティアセミナー

(1) 学術フロンティア国際セミナー

実施日：2004年10月26日（火）

テーマ：Brain and muscle oxygenation/hemodynamics during exercise monitored by different approaches of near infrared spectroscopy.

Valentina Quaresima（University of L'Aquila, Italy）

(2) 第1回 学術フロンティアセミナー

実施日：2004年12月18日（土）

テーマ：筋疲労とタスクーアメリカ研究生活で学んだこと，学んでいることー

篠原　稔 先生（Department of Integrative Physiology, University of Colorado, Boulder, Colorado, USA）

(3) 第2回 学術フロンティアセミナー

実施日：2005年5月11日（水）

テーマ：Exercise induced hypoxemia and excessive respiratory muscle work

Craig A. Harms（Department of Kinesiology, Kansas State University, USA）

(4) 第3回 学術フロンティアセミナー

実施日：2005年5月30日（月）

テーマ：動脈硬化に対する運動の効果

田中弘文 先生（Department of Kinesiology, University of Wisconsin, Madison, USA）

(5) 第4回 学術フロンティアセミナー

実施日：2005年10月18日（火）

テーマ：Human Calf Metabolism by ^{31}P-NMR and NIRS

Valentina Cettolo（University of L'Aquila, Italy）

(6) 第5回 学術フロンティアセミナー

実施日：2006年2月15日（水）

テーマ：Why is maximal cardiac output reduced in chronic hypoxia ?

Jose Antonio Lopez Calbet（Professor of Exercise Physiology in the Department of Physical Education, University of Las Palmas de Gran Canaria, Canary Islands, Spain）

(7) 第6回 学術フロンティアセミナー「若手研究者・大学院生のためのセミナー I」

実施日：2006年3月4日（土）

第一部

テーマ：日本女子体育大学学術フロンティア若手研究者の課題への取り組み

佐藤耕平（日本女子体育大学・助手）

岩館雅子（学術フロンティア研究支援スタッフ・ポスドク研究員）

大森芙美子（日本女子体育大学・技術職員）

第二部

テーマ：よりよい科学論文を書く

「神経生理学の立場から」

Charles L. Rice（The University of Western Ontario, Canada）

「循環研究の立場から」

西保　岳 先生（筑波大学体育科学系）

「環境生理学の立場から」

近藤徳彦 先生（神戸大学発達科学部）

（8）第7回 学術フロンティアセミナー「若手研究者・大学院生のためのセミナー II」

実施日：2006年6月10日（土）

第一部

テーマ：初心者のための運動と循環研究

斉藤　満 先生（豊田工業大学教授）

第二部　レクチャー・デモンストレーション

『超音波ドップラー法による循環調節の研究法』

「骨格筋への血流分配」

長田卓也 先生（東京医科大学助手）

「脳への血流分配」

定本朋子 先生（日本女子体育大学教授）

（9）第8回 学術フロンティアセミナー

実施日：2006年6月22日（木）

テーマ：乳酸シャトルへのアプローチ

橋本健志 先生（University of California, Berkeley, USA）

（10）第9回 学術フロンティアセミナー

実施日：2007年7月23日（月）

テーマ：力調節の神経筋メカニズムと交感神経活動

篠原　稔 先生（School of Applied Physiology Georgia Institute of Technology, Atlanta, USA）

（11）第10回 学術フロンティアセミナー

実施日：2007年12月13日（木）

テーマ：筋機械受容器反射と循環調節

松川寛二 先生（広島大学大学院保健学研究科）

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運動時における循環調節機構の統合的解明

－スポーツによる健康・体力づくりプログラムの構築にむけて－

研究代表者　定本　朋子