

### **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<sup>1)</sup>

Distribution of blood flow to and outflow from skeletal muscles

Atsuko Kagaya

## ■本課題の共同研究者

大森 芙美子<sup>1,5)</sup>, 奥山 (清水) 静代<sup>2)</sup>, 村岡 慈歩<sup>3)</sup>, 吉澤 睦子<sup>4)</sup>, 熊谷 真奈<sup>4)</sup>, 森 曜生<sup>6)</sup>, 鈴木 早紀子<sup>6)</sup>, 水村 真由美<sup>7)</sup>, 佐藤 耕平<sup>2)</sup>, 浜岡 隆文<sup>8)</sup>, 小田 俊明<sup>9)</sup>

<sup>1)</sup> 日本女子体育大学基礎体力研究所, <sup>2)</sup> 慶應義塾大学体育研究所, <sup>3)</sup> 明星大学人文学部, <sup>4)</sup> 日本女子体育大学大学院スポーツ科学研究科, <sup>5)</sup> 鹿屋体育大学大学院体育学研究科, <sup>6)</sup> お茶の水女子大学大学院人間文化研究科, <sup>7)</sup> お茶の水女子大学文教育学部, <sup>8)</sup> 鹿屋体育大学体育学部, <sup>9)</sup> 理化学研究所

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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
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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 ( $25.5 \pm 2.2$  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 volun-

tary 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°C 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  $\times$  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  $37.7 (\pm 2.8)$  cm/s at 10%MVC to  $57.9 (\pm 2.9)$  cm/s at 50%MVC, and  $59.5 (\pm 3.9)$  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

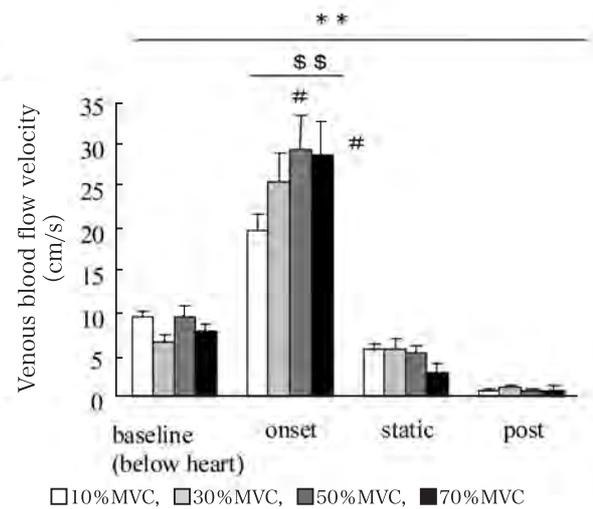


Fig. III.1.2-1 Comparison of venous flow velocity among exercise phases and exercise intensities. \*\*:  $P < 0.01$  among exercise phases, \$\$\$;  $P < 0.01$  among exercise intensities at the onset, #:  $P < 0.05$  vs 10% MVC.

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 relaxation 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

加賀谷淳子, 奥山 (清水) 静代, 大森芙美子, 熊谷 真奈, 吉澤 睦子

### 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  $25.5 \pm 2.4$  yrs) 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  $6.48 \pm 0.71$  at baseline to  $18.98 \pm 3.21$   $\text{cm} \cdot \text{sec}^{-1}$ , 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。

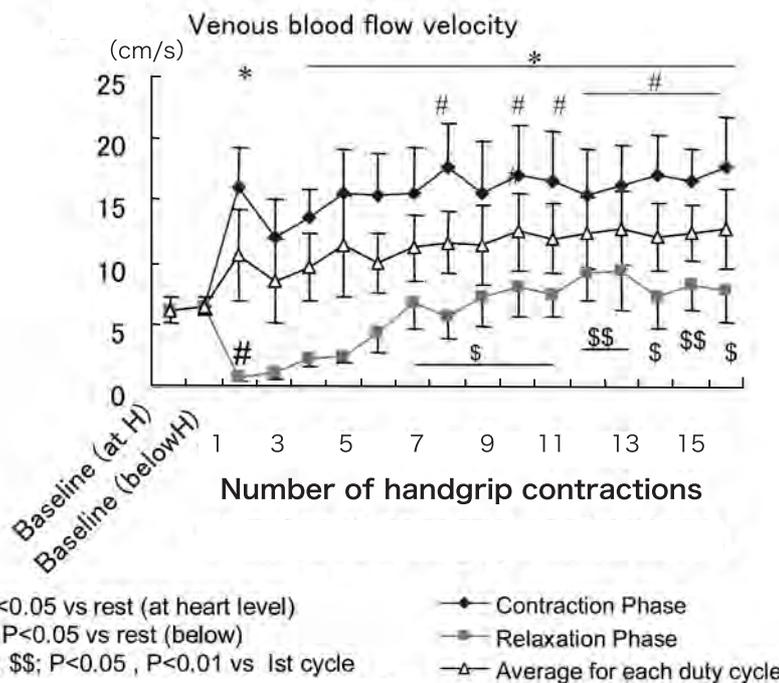


Fig. III.1.3-1 Venous blood flow velocity changes during rhythmic hand grip.

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

加賀谷淳子, 村岡 慈歩, 奥山 (清水) 静代, 大森美美子, 森 曜生,  
鈴木早紀子, 水村真由美, 小田 俊明

### Effects of passive stretching 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 受動的な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) 静代, 大森美美子, 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 stretching

#### 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 decreased 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. 本研究は受動的な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  $21.6 \pm 0.8$  歳) とし、仰臥位で、膝関節角度を  $180^\circ$  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、血压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

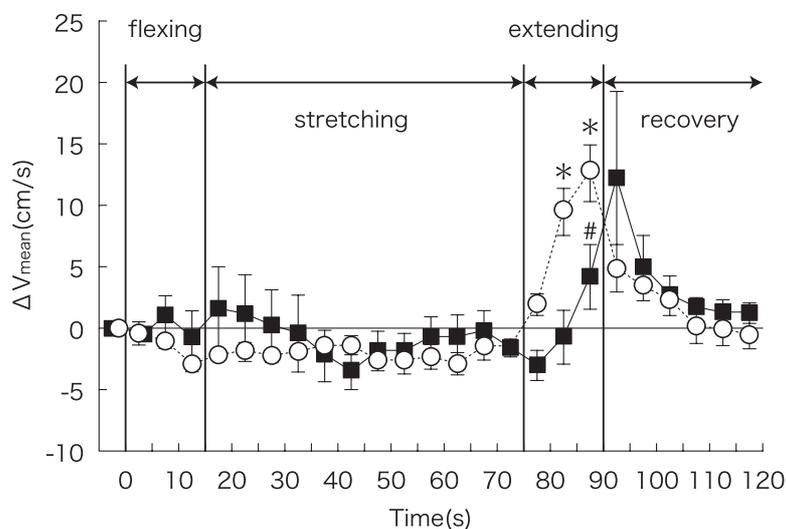


Fig. III.1.4.1-1 Arterial and venous blood flow velocity in popliteal vessels. ○: artery, ■: vein.

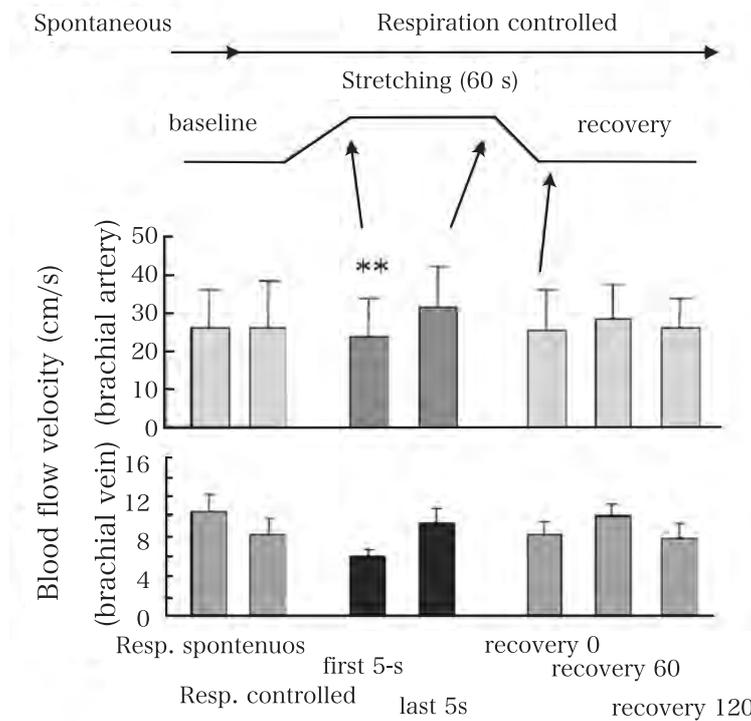


Fig. III.1.4.1-2 Blood flow velocity in brachial artery (upper) and vein (lower). \*\*:P<0.01 vs baseline

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 受動的な下腿ストレッチ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 —

大森美美子, 村岡 慈歩, 奥山 (清水) 静代, 森 曜生, 鈴木早紀子,  
水村真由美, 加賀谷淳子

### Blood flow velocity changes in popliteal artery due to passive stretching 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 comfortably stretched 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, 循環に影響を与えられと考えられる. 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られと考えられる. 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, 仰臥位での受動的な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  $120^\circ$  から解剖学的正位 (AP) まで  $30^\circ$  背屈させる AP と足関節角度  $120^\circ$  から快適最大角度 (痛みを感じる角度から  $3^\circ$  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,

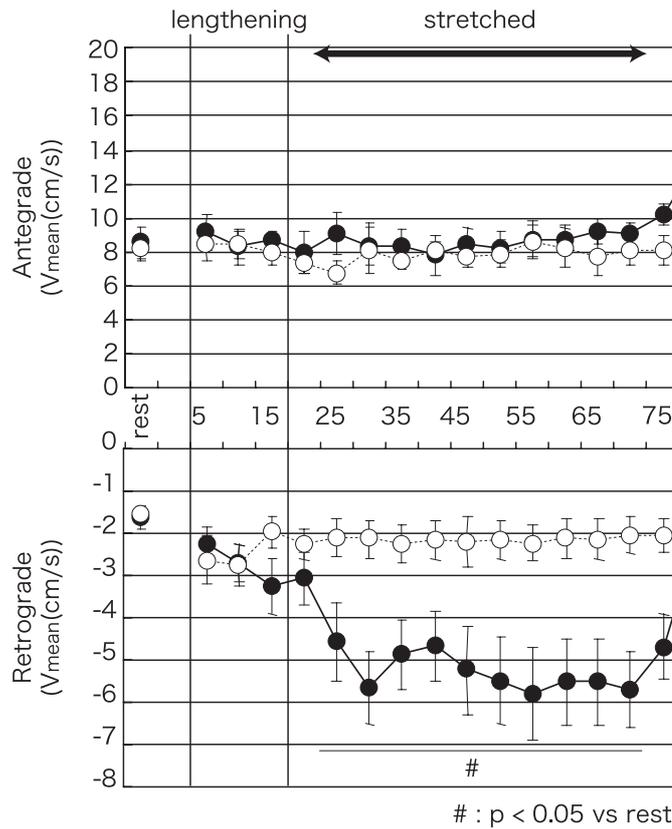


Fig. III.1.4.2-1 Antegrade systolic (upper panel) and retrograde diastolic (lower panel) blood flow during passive stretching. Passive stretching s at two positions were performed. ○; anatomical position, ●; maximal comfortable position.

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

村岡 慈歩, 鈴木早紀子, 森 曜生, 大森美美子, 奥山 (清水) 静代, 水村真由美, 加賀谷淳子

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

##### 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。

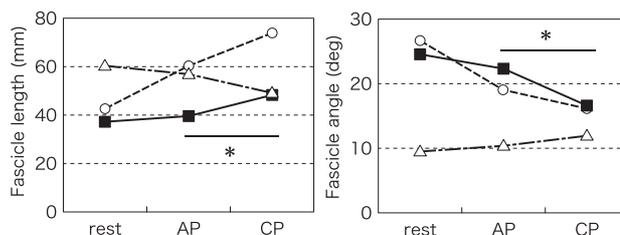


Fig. III.1.4.3-1 Fascicle length (left) and angle (right) of MG (○), SOL (■), and TA (△) during passive stretching. AP; anatomical position, CP; Maximal comfortable stretching without pain. \*P < 0.001 vs rest.

## 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

森 曜生, 村岡 慈歩, 奥山 (清水) 静代, 大森美美子, 鈴木早紀子,  
水村真由美, 加賀谷淳子

### Heterogeneity of blood flow re-distribution during passive stretching 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關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流量の変化も異なると考えられる。本研究は、STによる血流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)、電氣的筋活動 (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が高かった。ST中に筋の電氣的な活動は変化しなかったため、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のように血流量が増加した筋もあったためと考えられる。MGとSOLで血流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流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。

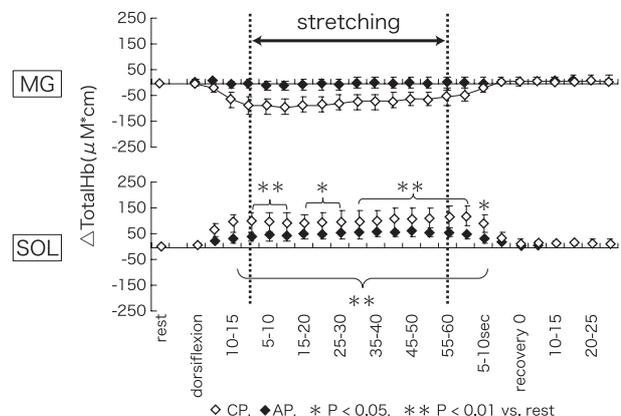


Fig. III.1.4.4-1 Blood volume (total Hb) changes in gastrocnemius medialis (MG) and soleus (SOL) muscles during passive stretching.

## 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

大森美美子, 奥山 (清水) 静代, 村岡 慈歩, 森 曜生, 鈴木早紀子,  
水村真由美, 加賀谷淳子

### Effect of maximal passive stretching 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.

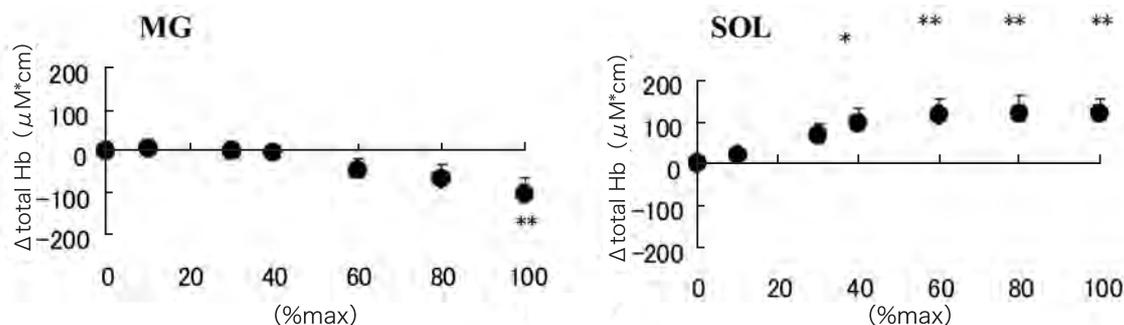


Fig. III.1.4.5-1 Blood volume changes (Total Hb, NIRS) during incremental passive stretching of calf muscles in medial gastrocnemius (MG) and soleus (SOL) muscles. \*, \*\*;  $P < 0.05$ ,  $P < 0.01$  vs. baseline (0).

## 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) 静代,  
水村真由美, 加賀谷淳子

### The effect of muscle stretching 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变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、筋線維の形状的变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变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变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。

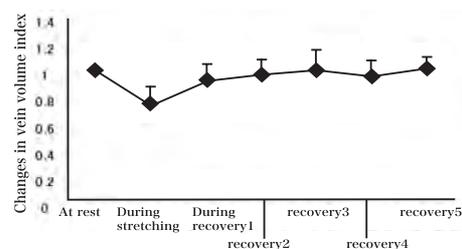
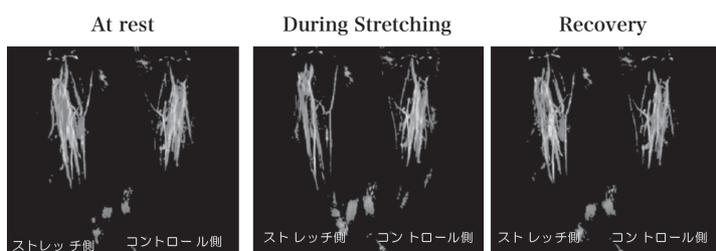


Fig. III.1.4.6-1 The left figures demonstrate the examples of blood vein images over threshold, which were acquired by flesh blood imaging sequence and were conducted by maximal intensity projection. As shown in right graph, the vein area was decreased up to 0.75 by stretching with maximal comfort level 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.

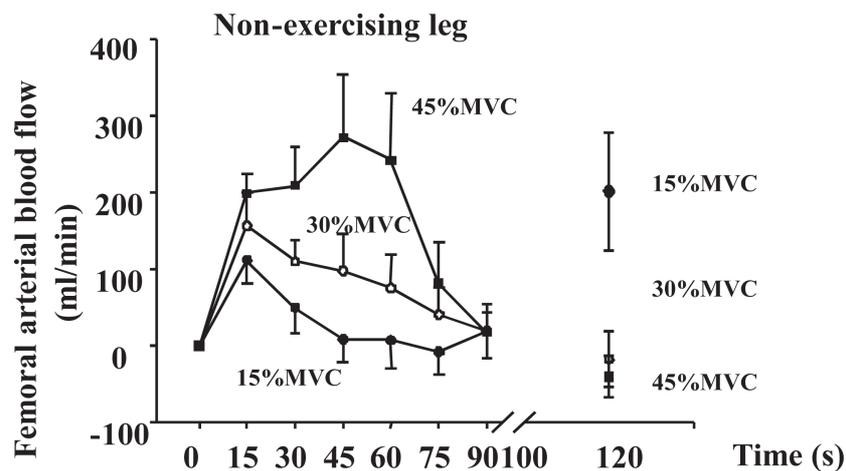


Fig. III.1.5-1 Femoral arterial blood flow to non-exercising leg during contralateral knee extension exercise at 15%, 30% and 45% MVC.

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 been 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 (BF<sub>peak</sub>) during exhaustive dynamic plantar flexion exercise (EDPFEx) and to identify the conditions required for attaining BF<sub>peak</sub> 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 BF<sub>peak</sub> 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  $\times$  heart rate  $\times$  area of the vessel. BF<sub>peak</sub> immediately before and after the end of EDPFEx significantly changed with altering intervals and intensities. The BF<sub>peak</sub> 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 ( $618 \pm 83$  ml/min) and after ( $1246 \pm 108$  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 BF<sub>peak</sub> 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:  $21.9 \pm 0.7$  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  $90^\circ$  and  $180^\circ$ , 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.

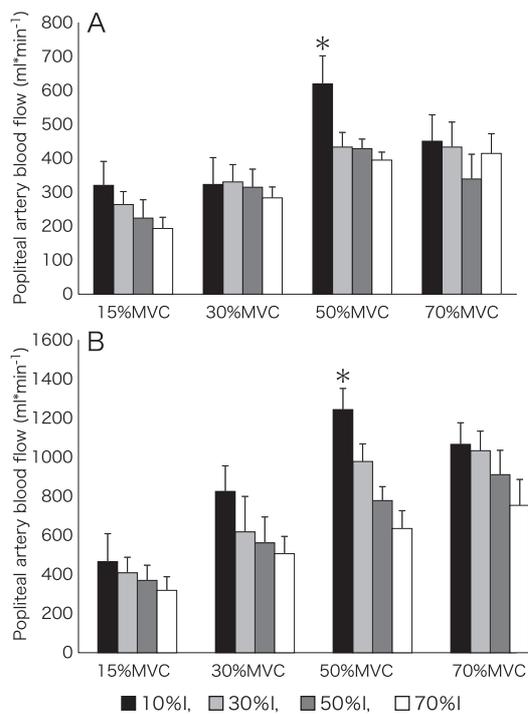


Fig. III.1.6-1 Peak blood flow immediately before (A) and after (B) the end of exhaustive exercise at 4 frequencies and intensities. \*  $P < 0.05$  (significant difference among intervals).

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 ( $618 \pm 83$  ml/min) and after ( $1246 \pm 108$  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

大森美美子, 奥山 (清水) 静代, 村岡 慈歩, 佐藤 耕平, 加賀谷淳子

### 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  $20.1 \pm 1.0$  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 (オメガ: 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の上昇を示した。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:  $14 \pm 1$ kgw, 左:  $13 \pm 1$ kgw) は筋疲労感覚急上昇負荷 (右:  $11 \pm 1$ kgw, 左:  $9 \pm 1$ kgw) 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  $4.0 \pm 0.6$  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

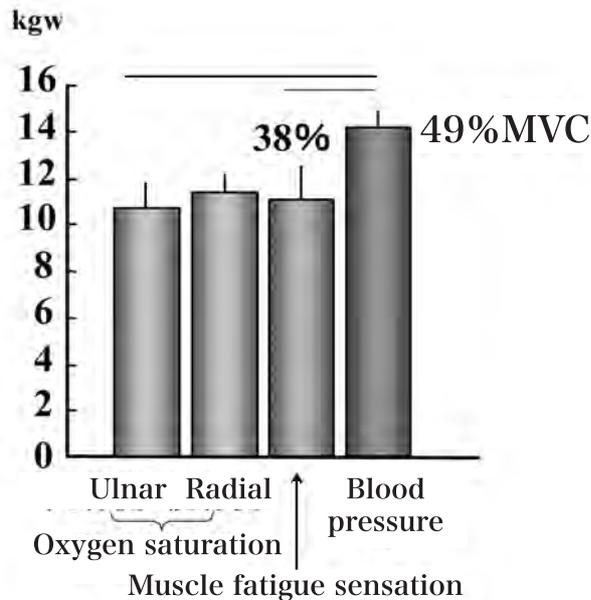


Fig. III.1.7-1 Critical loads for muscle oxygenation, muscle fatigue sensation and blood pressure.

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变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  $20.1 \pm 0.1$  yrs. (mean  $\pm$  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  $20.1 \pm 0.1$  (mean  $\pm$  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  $V \cdot \pi (D/2)^2$  ( $D = 2Dd/3 + Ds/3$ ). 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

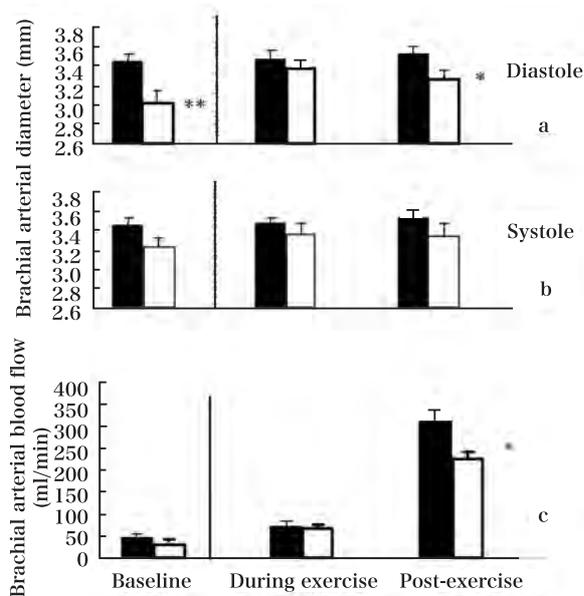


Fig. III.1.8-1 Diastolic (a), systolic (b) vessel diameter and brachial arterial blood flow (c) at baseline, during, and after exercise at the highest loads in dominant (■) and non-dominant (□) limbs. \*, \*\*  $P < 0.05$ ,  $P < 0.001$  between limbs.

( $P < 0.01$ ) 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;  $3.4 \pm 0.1$ , non-dominant;  $3.0 \pm 0.1$  mm) and after exercise at the highest load (dominant;  $3.5 \pm 0.1$ , non-dominant;  $3.2 \pm 0.1$  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 signif-

icantly 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

加賀谷淳子, 奥山 (清水) 静代, 大森美美子, 佐藤 耕平,  
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、上肢を拳上・垂下して、心臓との相対的位置関係を変えたとき、拳上時には、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

加賀谷淳子, 奥山 (清水) 静代, 大森美美子, 吉澤 睦子,  
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

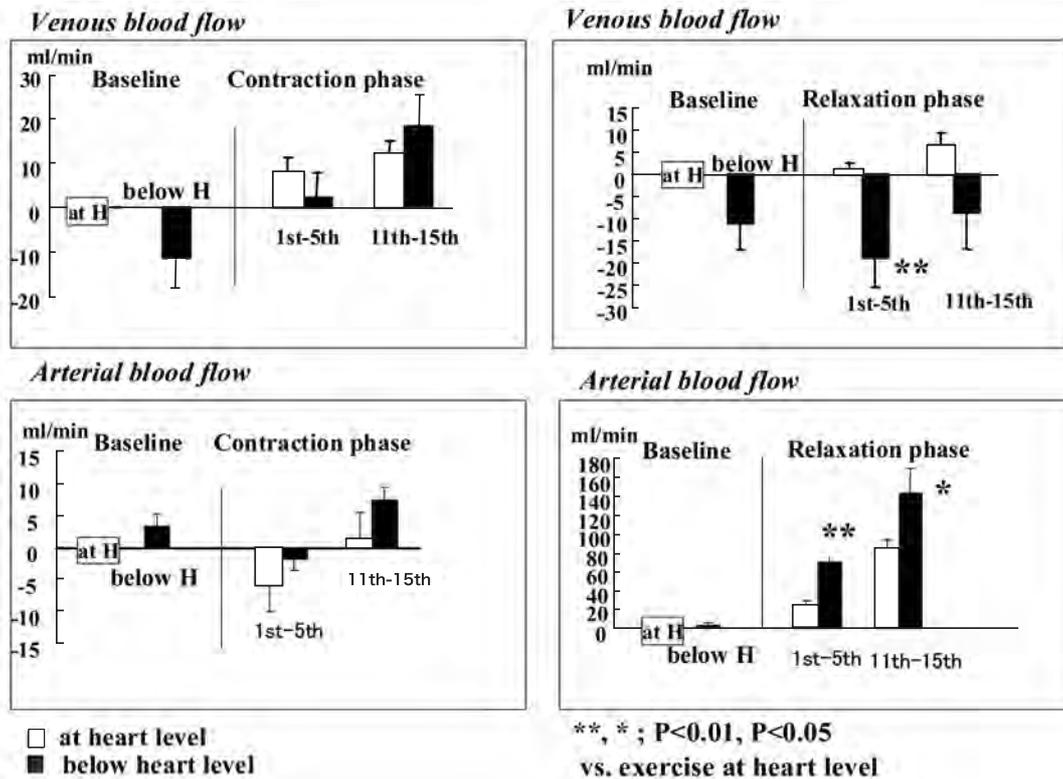


Fig. III.1.9.1-1 Venous (upper) and arterial (lower) blood flow changes during the contraction (left) and relaxation (right) phases of handgrip exercise. Handgrip exercises were performed with the forearm at heart level (at H) or below heart level (below H).

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律動的な握力運動時の循環・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)に体肢において、椅座位で、律動的な握力運動(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<sub>2</sub>Hb)、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

律動的な握力運動を、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<sub>2</sub>Hb, HHb, THbはいずれも開始初期に一旦減少し、その後、O<sub>2</sub>Hb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

加賀谷淳子, 奥山 (清水) 静代, 大森美美子, 佐藤 耕平,  
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

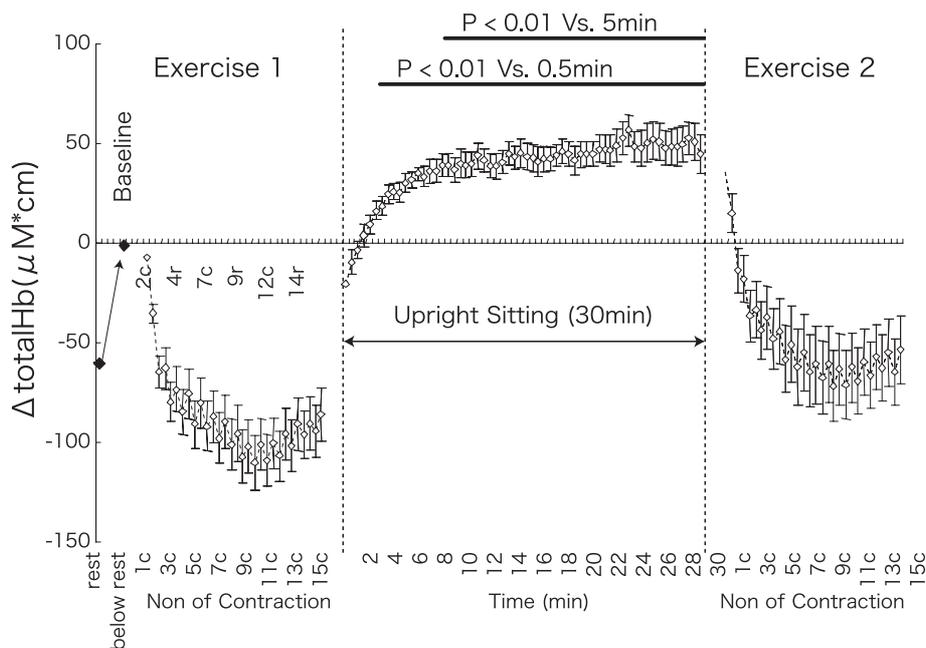


Fig. III.1.9.2-1 The muscle oxygenation changes during upright sitting rest and during dynamic plantar flexion exercise before and after 30-min upright rest. ◇ : O<sub>2</sub>Hb.

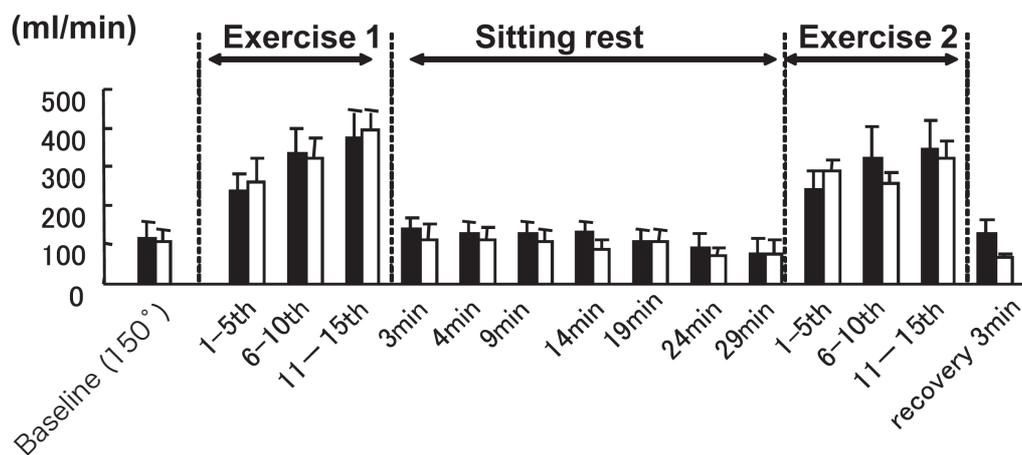


Fig. III.1.9.2-2 Venous (□) and arterial (■) blood flow in popliteal vessels during upright sitting rest and during rhythmic plantar flexion exercise. Significant difference was found between arterial blood flow and venous blood flow, whereas no significant difference was found those parameters between 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。そうすると、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る。

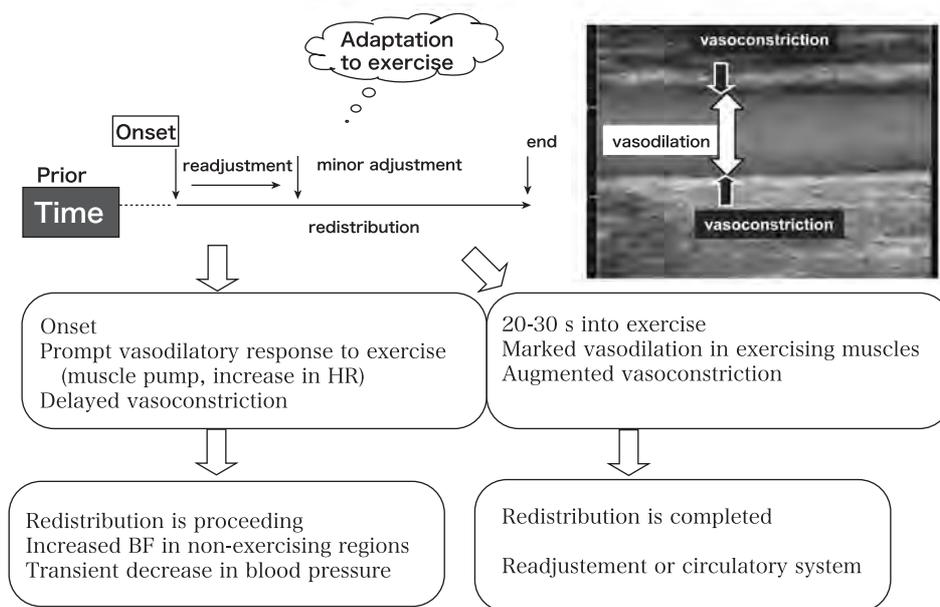


Fig. III.1.10-1 Regional and central circulatory adjustment to exercise.

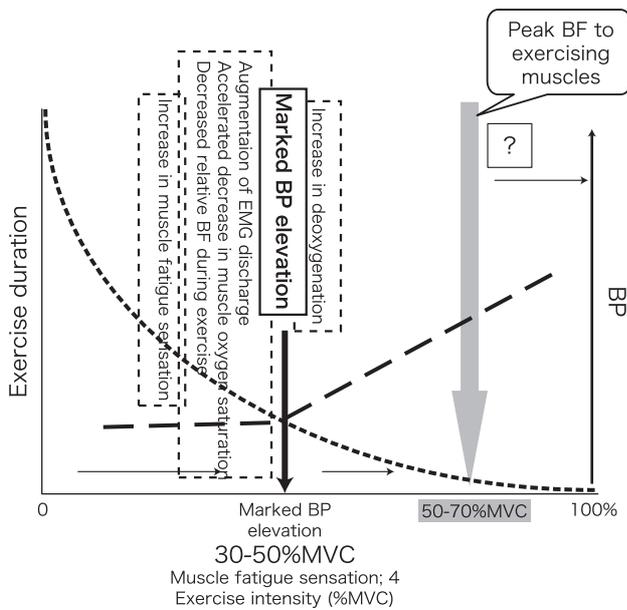


Fig. III.1.10-2 Deflection loads of circulatory and metabolic responses to exercise in relation to exercise intensity, exercise duration and blood pressure. Muscle fatigue sensation is also indicated.

### 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量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、血圧変移点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<sup>1)</sup>

Control of renal and splanchnic circulations during exercise

Tomoko Sadamoto

### ■本課題の共同研究者

佐藤 耕平<sup>1)</sup>, 平澤 愛<sup>1)</sup>, 島田奈央子<sup>1)</sup>, 森山真由美<sup>1)</sup>, 大森芙美子<sup>1)</sup>, 岩館 雅子<sup>1,3)</sup>, 石田 良恵<sup>2)</sup>

<sup>1)</sup> 日本女子体育大学基礎体力研究所, <sup>2)</sup> 女子美術大学, <sup>3)</sup> 日本大学

### 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

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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の血流応答

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定本 朋子, 佐藤 耕平, 森山真由美, 平澤 愛

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### 2.3 発育期の子どもにおける循環機能の発達

定本 朋子, 佐藤 耕平, 大森芙美子, 森山真由美, 岩館 雅子, 石田 良恵



## 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)

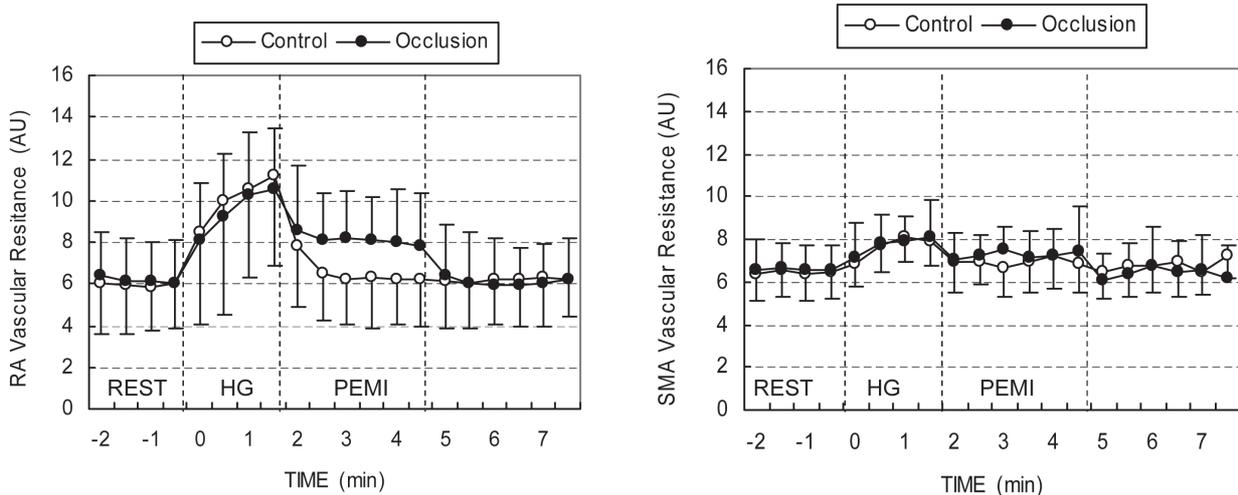


Fig. III.2.1.1-1 Renal artery (RA) vascular resistance and superior mesenteric artery (SMA) vascular resistance during rest, static handgrip (HG) exercise and postexercise muscle ischemia (PEMI) in control and occlusion conditions.

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, Finapres 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 workload

#### 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  $19 \pm 11$  (SD) %,  $29 \pm 13$  %,  $45 \pm 13$  % 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  $5 \pm 15$  %,  $11 \pm 16$  %, and  $19 \pm 16$  % 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

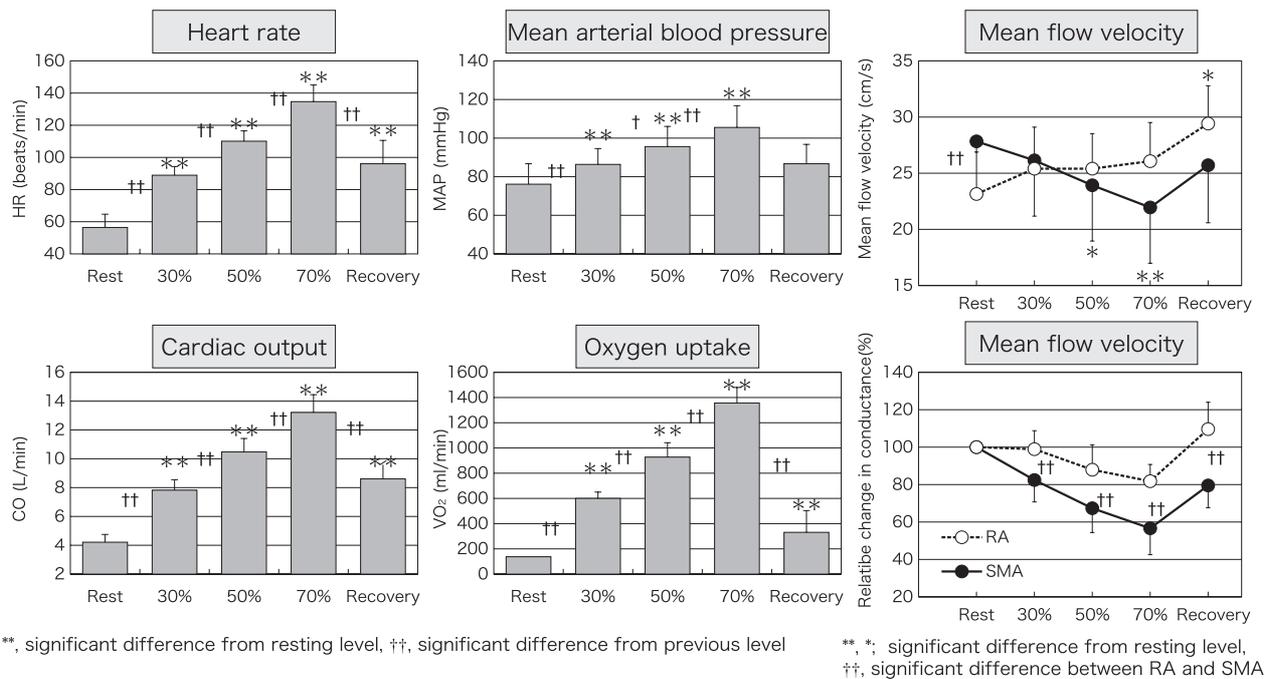


Fig. III.2.1.2-1 Heart rate, cardiac output, mean arterial blood pressure, oxygen uptake, mean flow velocity and peripheral conductance in renal artery (RA) and superior mesenteric artery (SMA) at rest and during exercise with intensity of 30%, 50% and 70% of peak oxygen uptake.

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:  $23 \pm 3$  歳, 身長:  $162 \pm 5$  cm, 体重:  $58 \pm 5$  kg, 最高酸素摂取量  $\dot{V}O_{2peak}$ :  $36 \pm 6$  ml/kg $\cdot$ 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 Puvirajasingham *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, アンジオテンシン 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

定本 朋子, 佐藤 耕平, 森山真由美, 平澤 愛

### 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，島皮質へ灌流）と椎骨動脈経路（主に延髄，小脳，後頭葉へ灌流）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。この両経路が灌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

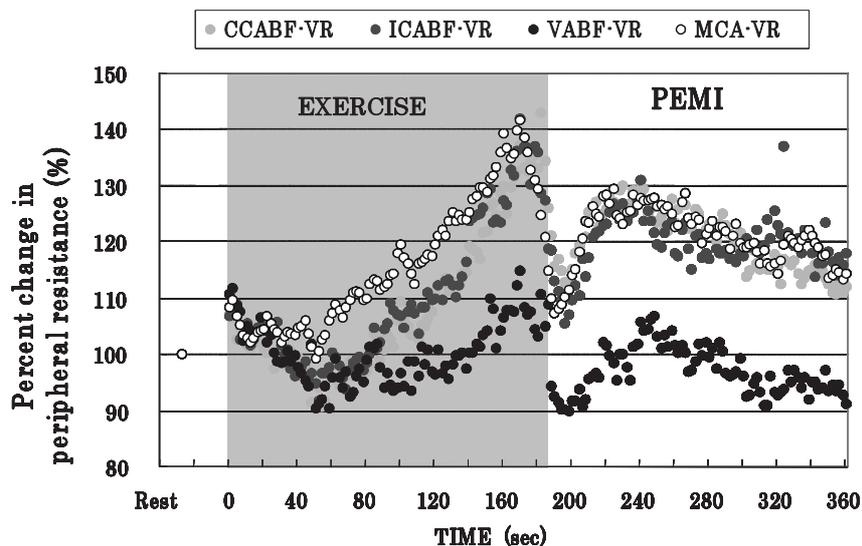


Fig. III.2.2.1-1 Percent changes in vascular resistance in common carotid artery (CCABF-VR), internal carotid artery (ICABF-VR), middle cerebral artery (MCA-VR) and vertebral artery (VABF-VR) during rest, static handgrip exercise, and postexercise muscles ischemia (PEMI). For the calculation of MCA-VR, 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, Finapres 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:  $22.5 \pm 2.5$  years (mean  $\pm$  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  $\dot{V}O_{2\text{peak}}$  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 ( $\dot{Q}_{\text{ICA}}$ ), and vertebral artery blood flow ( $\dot{Q}_{\text{VA}}$ ) at rest and during exercise.  $\dot{Q}_{\text{ICA}}$  and  $\dot{Q}_{\text{VA}}$  was measured by a Doppler ultrasound system and cerebrovascular resistance index (CVR<sub>ICA</sub> and CVR<sub>VA</sub>) were also calculated as MAP divided by CBF. In this study, mean arterial pressure (MAP) and end-tidal partial pressure of CO<sub>2</sub> (P<sub>ET</sub> CO<sub>2</sub>) increased significantly with increase of exercise intensity.  $\dot{Q}_{\text{ICA}}$  increased by  $12 \pm 2\%$  during 30%  $\dot{V}O_{2\text{peak}}$  and reached a maximum  $8 \pm 3\%$  during 50%  $\dot{V}O_{2\text{peak}}$ . However, during 70%  $\dot{V}O_{2\text{peak}}$ , increase in  $\dot{Q}_{\text{ICA}}$  had a level off, in contrast to a continued increase in CVR<sub>ICA</sub> throughout exercise. On the other hand,  $\dot{Q}_{\text{VA}}$  increase in proportion to the increase of exercise intensity ( $17 \pm 3$ ,  $33 \pm 4$ , and  $40 \pm 4\%$  at 30, 50, and 70%  $\dot{V}O_{2\text{peak}}$ , respectively). In addition, CVR<sub>VA</sub> 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 ( $\dot{V}O_{2\text{max}}$ ), heavy exercise (80%  $\dot{V}O_{2\text{max}}$ ) 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:  $22.5 \pm 2.5$  years (mean  $\pm$  SD), height:  $163.0 \pm 5.9$  cm, body mass:  $57.6 \pm 5.1$  kg, and peak oxygen uptake ( $\dot{V}O_{2\text{peak}}$ ):  $37.3 \pm 5.4$  ml/kg  $\cdot$  in<sup>-1</sup>] 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  $\dot{V}O_{2\text{peak}}$  occurred in the upright position, with each stage lasting for 5 min. The mean blood flow in the ICA ( $\dot{Q}_{\text{ICA}}$ ) and the VA ( $\dot{Q}_{\text{VA}}$ ) 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  $SV \times HR$ . 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  $\sim 12\%$  during exercise with  $30\% \dot{V}O_{2peak}$  and with a maximum increase of  $\sim 18\%$  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 specula-

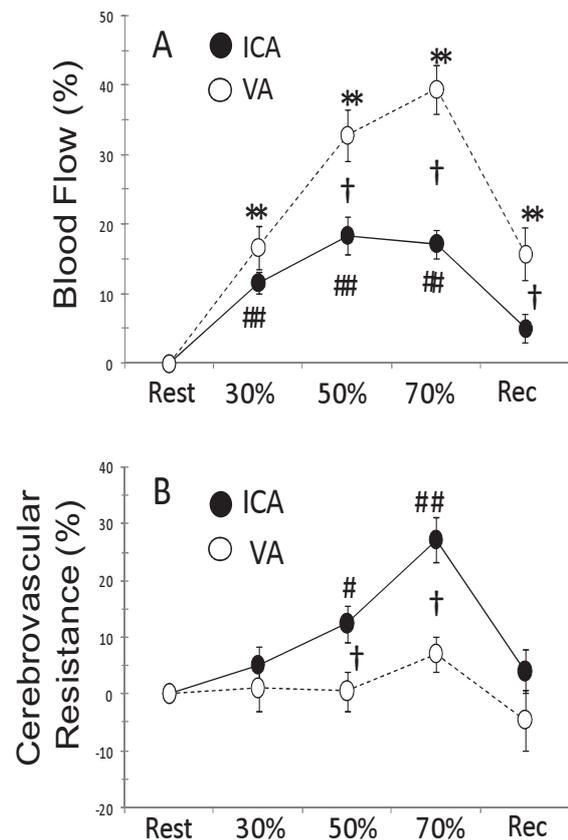


Fig. III.2.2.2-1 (A) Change (%) in blood flow in the ICA and VA during dynamic exercise and recovery. (B) Change (%) in the cerebrovascular resistance in ICA and VA during dynamic exercise and recovery. Values are means  $\pm$  SE. 30%,  $30\% \dot{V}O_{2peak}$ ; 50%,  $50\% \dot{V}O_{2peak}$ ; and 70%,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

tion, 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-

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

定本 朋子, 佐藤 耕平, 大森芙美子, 森山真由美,  
岩館 雅子, 石田 良恵

### 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 (BF<sub>CCA</sub>) 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<sub>CCA</sub> 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<sub>CCA</sub> 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<sub>CCA</sub>）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<sub>CCA</sub>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、脳血流配分指標（%）は $BF_{CCA}/CO \times 100$ 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）

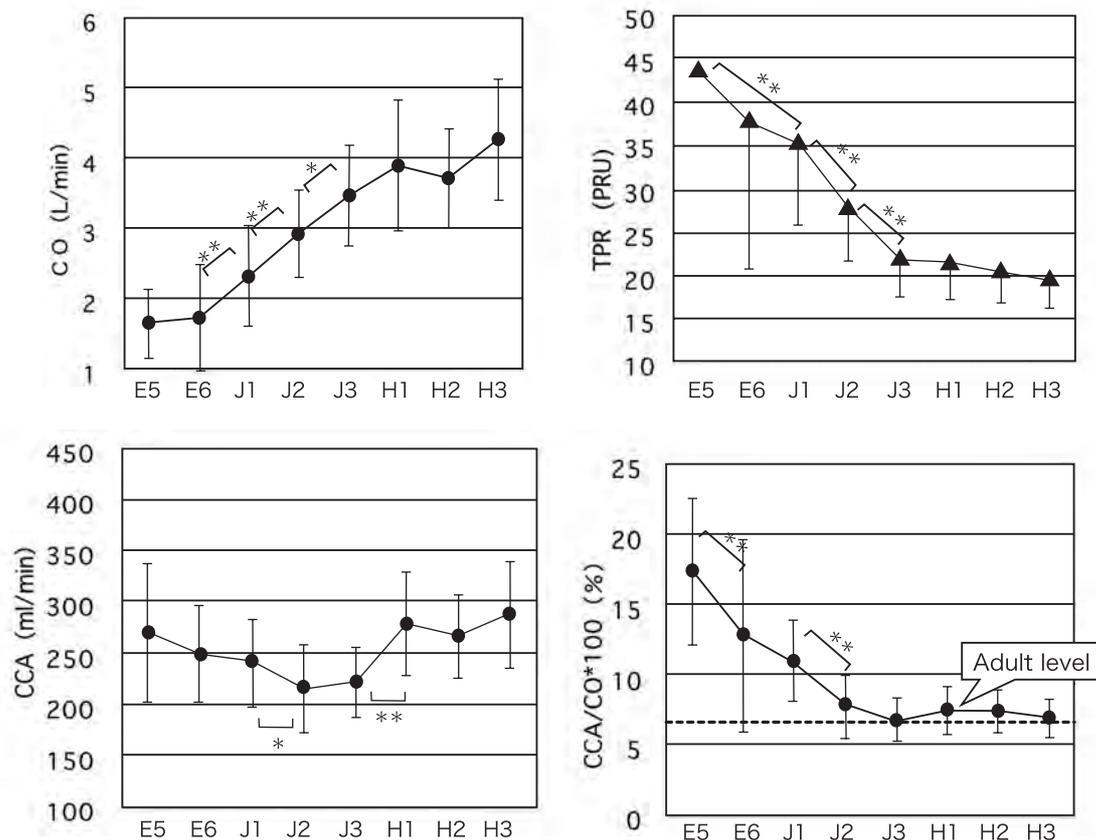


Fig. III.2.3-1 Developmental changes in cardiac output (CO), total peripheral resistance (TPR) and cerebral blood flow (CCA) and index of cerebral flow distribution (CCA/CO\*100) from 10 to 18 years of age in female. The horizontal axis indicates the grade of elementary school (E), junior high school (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<sub>CCA</sub>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<sub>CCA</sub>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 (Schöning and Hartig, 1996; 1998)。上述したように、BF<sub>CCA</sub>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、最も発達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

齊藤 満<sup>1)</sup>

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

相澤 清香<sup>1)</sup>, 神谷 厚範<sup>2)</sup>, 蜂矢 鉄心<sup>1)</sup>, 岩瀬 敏<sup>3)</sup>

<sup>1)</sup> 豊田工業大学, <sup>2)</sup> 国立循環器病センター, <sup>3)</sup> 愛知医科大学

3.1 利き腕, 非利き腕運動時の交感神経反応

齊藤 満, 相澤 清香, 神谷 厚範

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

齊藤 満, 蜂矢 鉄心, 岩瀬 敏



### 3.1 利き腕, 非利き腕運動時の交感神経反応

齊藤 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事ができる。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  $48 \pm 2$  kg,  $44 \pm 2$  kg (SD  $\pm$  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

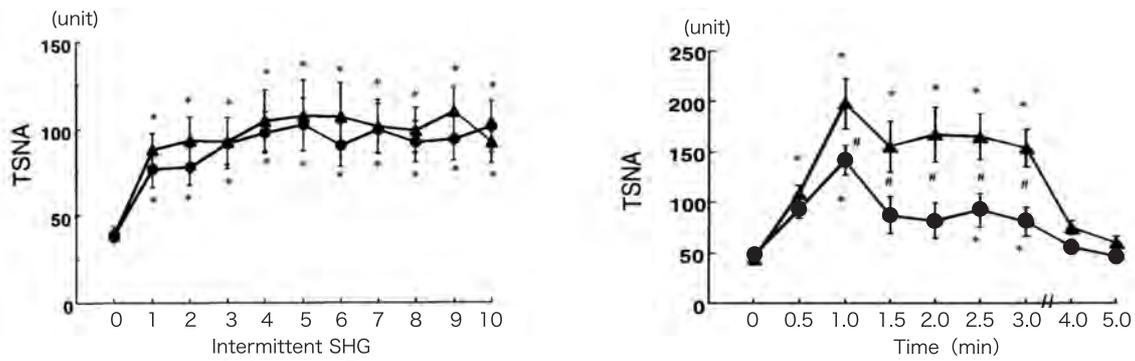


Fig. III.3.1-1 Comparison of muscle sympathetic nerve activity between dominant and nondominant arm during intermittent static handgrip exercise (left panel) and ischemic rhythmic handgrip exercise and post exercise arterial occlusion (right panel). ▲: dominant arm, ●: nondominant arm, \* p < 0.05 compare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

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<sup>3)</sup>、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。

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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

齊藤 満, 蜂矢 鉄心, 岩瀬 敏

### 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 ( $52 \pm 5$  vs.  $40 \pm 4$  bursts/min (mean  $\pm$  SEM) respectively). However, at detraining, MSNA activity returned to PRE level ( $44 \pm 5$  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 (齊藤 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

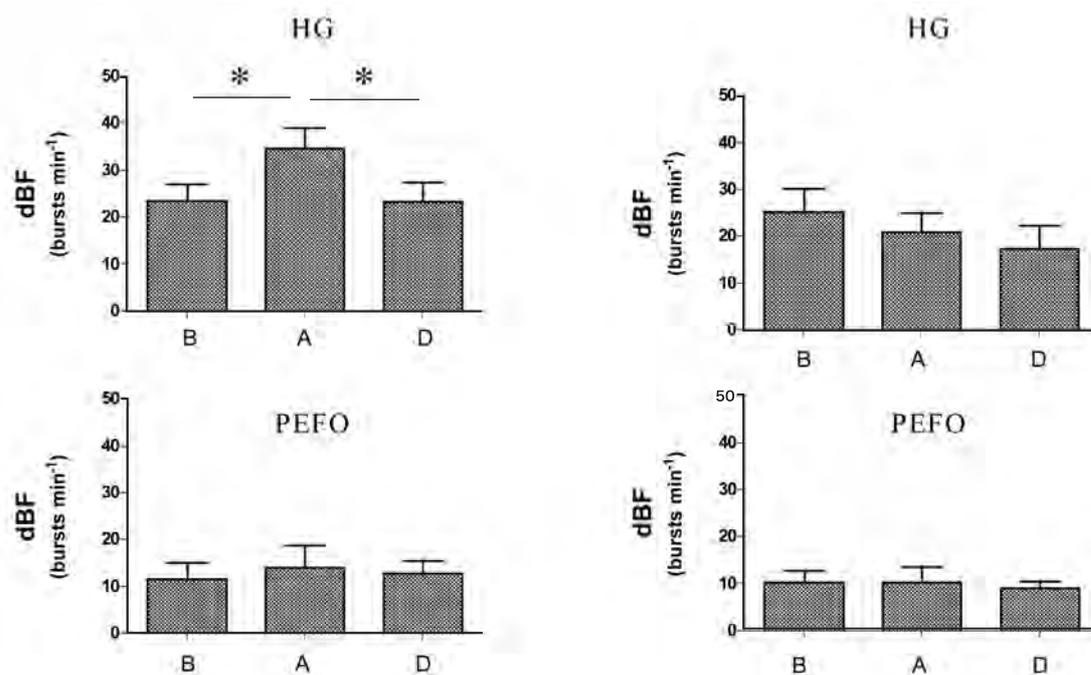


Fig. III.3.2-1 Comparison of the changes in burst frequency (dBF) during fatiguing handgrip exercise (HG) and post exercise forearm occlusion (PEFO) at pre-training (B), 1 week post-training (A) and 4 weeks post-training (D) in the trained (left panel) and control group (right panel). \*  $p < 0.05$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

Valentina Quaresima<sup>1)</sup>

■ Co-worker (本課題の共同研究者)

Marco Ferrari<sup>1)</sup>

<sup>1)</sup> Department of Health Sciences, University of L'Aquila

- 4.1 Metabolic pattern of the leg skeletal muscle groups during very short and intense isometric exercise
- 4.2 Acute effects of whole body vibration exercise (an alternative exercise intervention) on gastrocnemius medialis and vastus lateralis oxygenation
- 4.3 Biceps brachii myoelectric and oxygenation changes during static and sinusoidal isometric exercises
- 4.4 Auxiliary muscles oxygenation during a rowing exercise
- 4.5 Effects of handgrip exercise on frontal cortex oxygenation



# 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 an 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

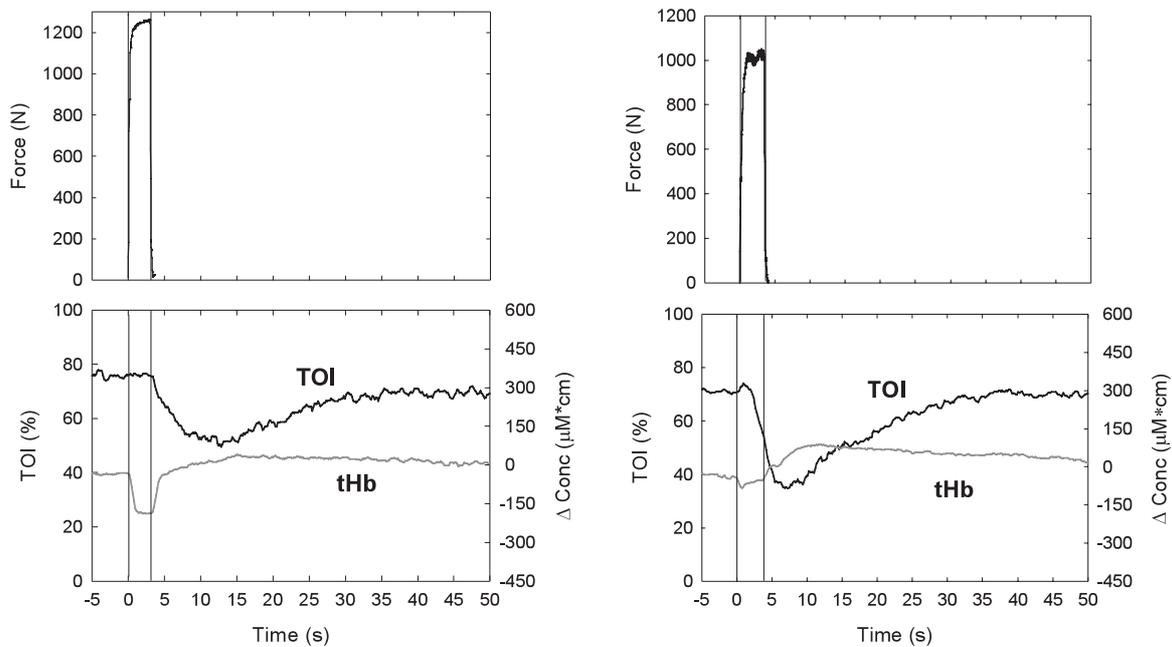


Fig. III.4.1-1 Left: Time course of leg force output (upper panel), and vastus lateralis TOI and tHb (lower panel) before, during, and after static leg press exercise. Right: Time course of leg force output (upper panel), and vastus lateralis TOI and tHb (lower panel) before, during, and after static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

ment by time interactions in both TOI and  $\Delta$  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  $40 \pm 20$  and  $60 \pm 20\%$  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 ( $343.9 \pm 232.2 \text{ ml} \cdot \text{min}^{-1}$ ) than for arms ( $795.6 \pm 405.6 \text{ ml} \cdot \text{min}^{-1}$ ) and legs ( $695.8 \pm 292.8 \text{ ml} \cdot \text{min}^{-1}$ ) exercise modes. The same result was found when the slow component amplitude was calculated as percentage of  $VO_{2 \text{ peak}}$  ( $7.1 \pm 5.0 \%$  for Rowing;  $17.2 \pm 6.6 \%$  for Arms;  $17.3 \pm 6.4 \%$  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 ( $\pm$  SD) age, height, and body mass of the 12 right-handed subjects were  $27 \pm 4$  y,  $177 \pm 5$  cm and  $76 \pm 12$  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 col-

lecting 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 ( $10 \times 8$  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) ( $5.13 + 0.07 \times \text{age}^{0.81}$ ). 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  $\pm$  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

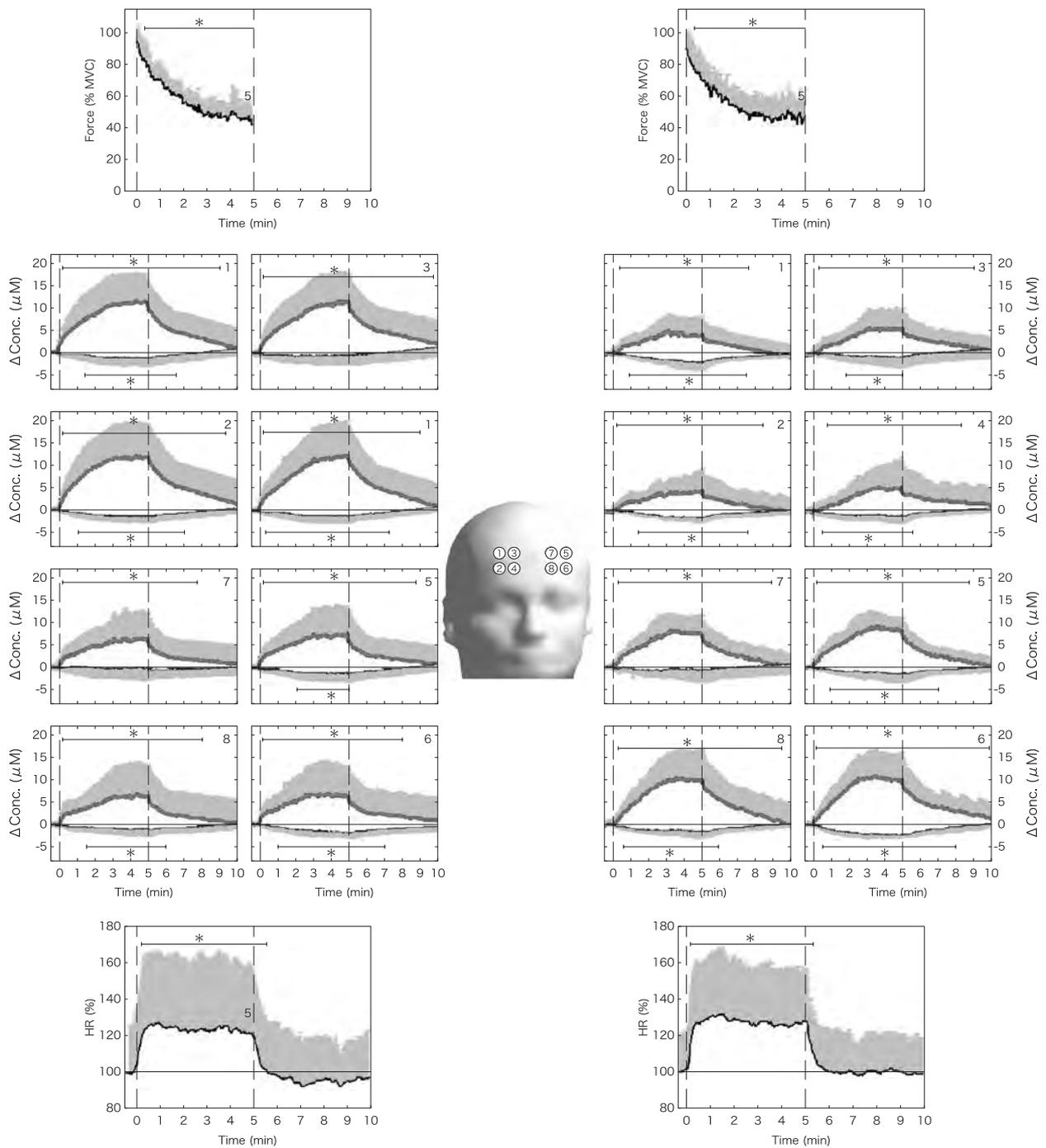


Fig. III.4.5-1 Force tracings; heart rate tracing and FC oxygenation changes during right and left handgrip exercise (left and right panels, respectively). Although the force was decreasing and the HR was constantly high during the exercise period, FC was found activated (increase in  $O_2Hb$  and a 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  $\pm$  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

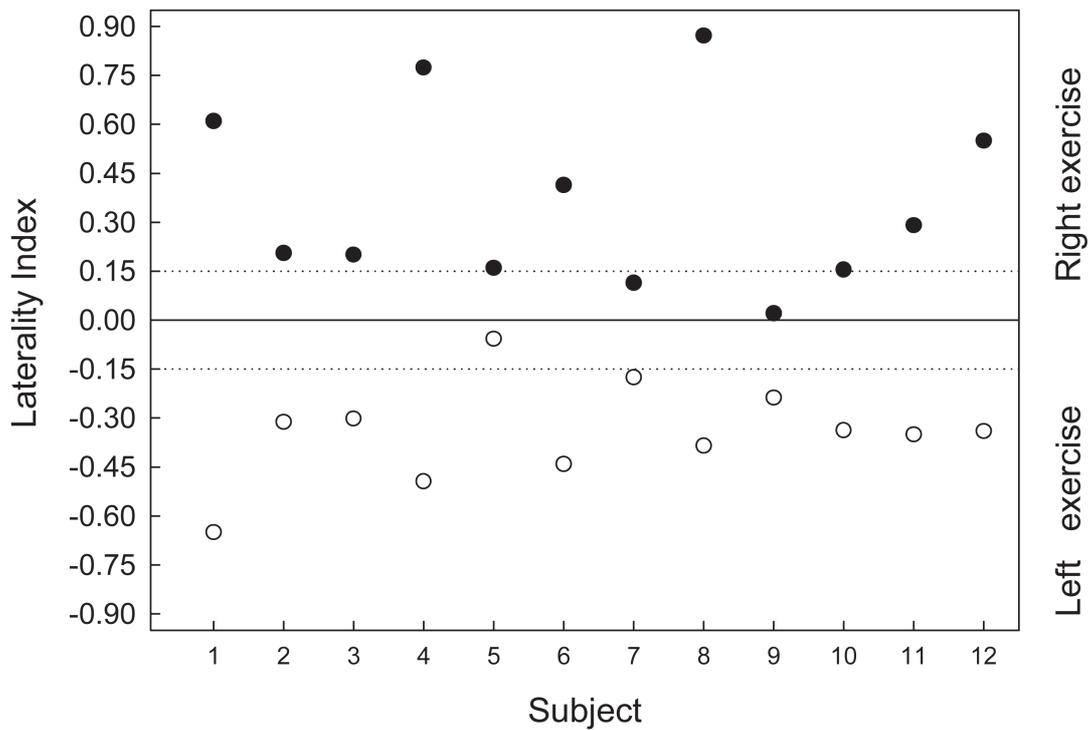


Fig. III.4.5-2 Laterality index for the [O<sub>2</sub>Hb] and [HHb] changes of the 12 subjects for the right (filled circle) and left (empty circle) hand exercises. The two dashed lines indicate the significant thresholds for the two exercises.

(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<sub>2</sub>Hb] 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<sub>2</sub>Hb changes suggest that the observed FC oxygenation changes were task related. The laterality index for [O<sub>2</sub>Hb] changes (the most sensitive parameter to cortical blood flow changes) is reported in Fig. III.4.5-2. The amplitude of [O<sub>2</sub>Hb] 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

Marco Ferrari<sup>1)</sup>

■ Co-worker (本課題の共同研究者)

Valentina Quaresima<sup>1)</sup>

<sup>1)</sup> Department of Health Sciences, University of L'Aquila

- 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<sub>2</sub>Hb)) was observed over the 31 measurement points in the right and left frontal cortex (source-detector distance: 3 cm). The highest increase in O<sub>2</sub>Hb 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](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 ( $10 \times 8$  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 Bioengineering 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.

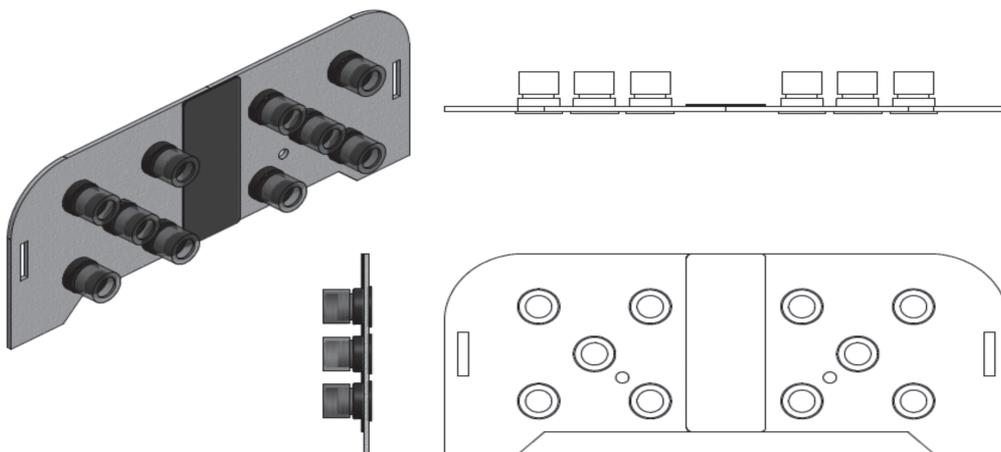


Fig. III.5.2-1 Schematic drawing of the flexible probe holder.

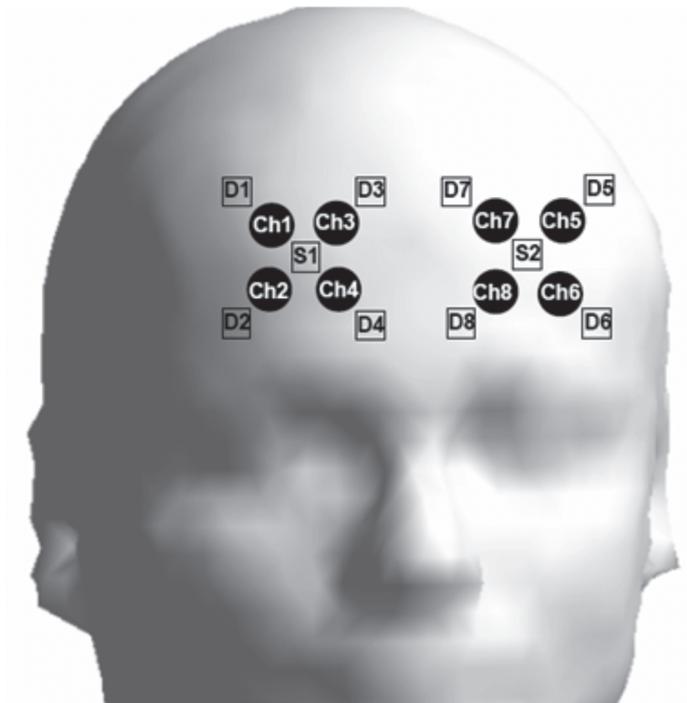


Fig. III.5.2-2 Eight measurement points (channels, Ch) over the frontal lobe. S: source; D: detector.

### 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 ultra-short 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 tHb 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

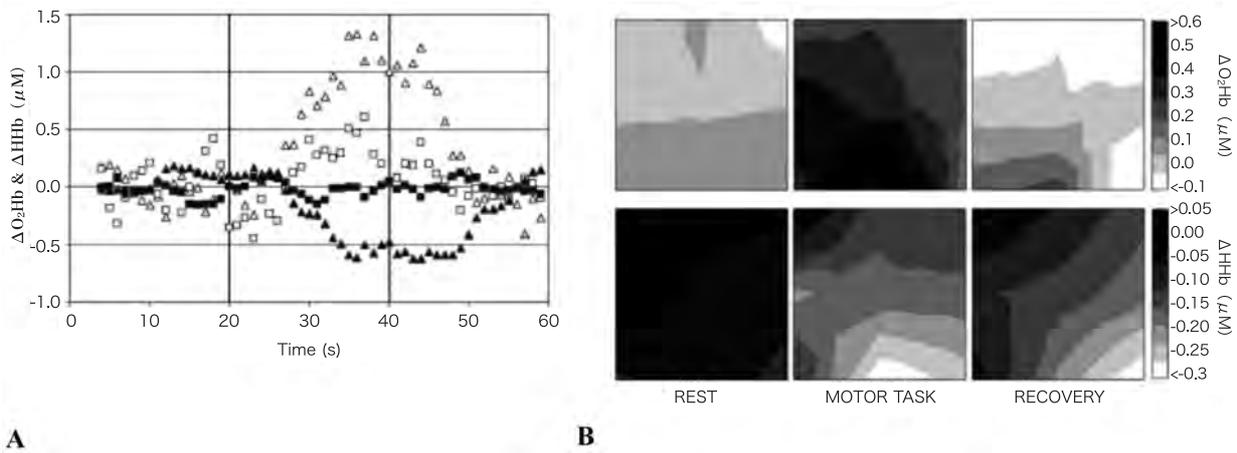


Fig. III.5.3-1 Panel A) Time course of changes in O<sub>2</sub>Hb (open symbols) and HHb (filled symbols) of the left motor area during the exercise performed with the right hand (triangle) and with the left hand (square). The vertical lines represent the task interval.

Panel B) Grey level maps representing changes in O<sub>2</sub>Hb (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<sub>2</sub>Hb and HHb for a single detection channel. The grey level maps of O<sub>2</sub>Hb 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<sub>2</sub>Hb (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 mus-

cle 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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Wolf M, Quaresima V, Ferrari M : Progress of near infrared spectroscopy and topography for brain and muscle clinical applications. *J Biomed Opt*, 12: 062104, 2007.



## 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<sup>1)</sup>

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

Mifuyu Kamo

■本課題の共同研究者

森本 茂<sup>2)</sup>, 板倉 尚子<sup>3)</sup>

<sup>1)</sup> 日本女子体育大学, <sup>2)</sup> 横浜国立大学, <sup>3)</sup> 日本女子体育大学健康管理センターリハビリテーション室

### 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

### 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

### 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

### 6.4 膝関節前十字靭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



## 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。

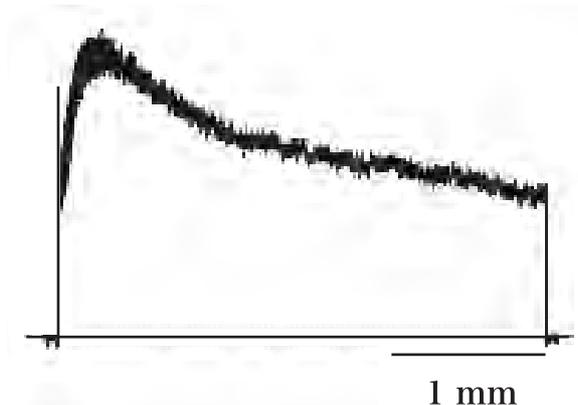


Fig. III.6.1-1 Representative changes pattern of evoked force during constant inter-stimulus interval stimulation at 100ms. Vertical line shows magnitude of peak force of twitch.

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。

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## 6.2 最大下一一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（DeLuca *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5mm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

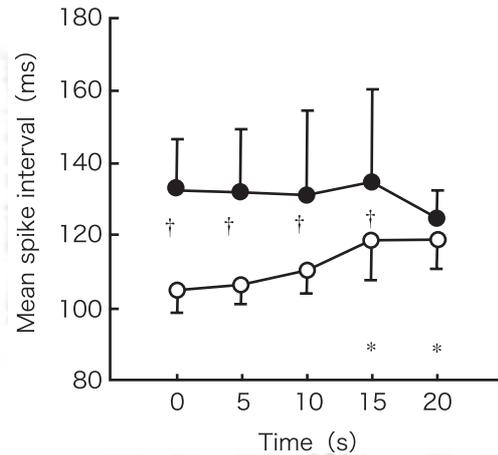


Fig. III.6.2-1 A typical change in the mean spike interval of a single motor unit during contractions. Filled and open points respectively represent the means ( $\pm$  SD) of results in vibration-induced response (Vib) and voluntary reproduction (Vo). Asterisks and daggers indicate statistically significant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

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。

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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

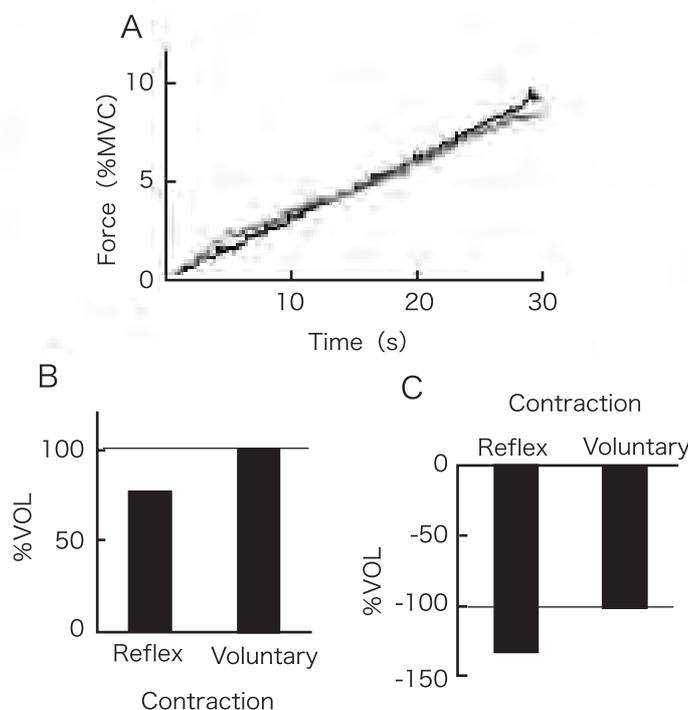


Fig. III.6.3-1 Motor unit activities and oxygenated hemoglobin during a representative experiment.

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 膝関節前十字靭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 program on the recovery of muscle 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

膝前十字靭帯（以下、ACL）再建術後3ヵ月間は再建靭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。

● 膝関節前十字靭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

膝関節前十字靭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

- ・膝前十字靭帯再建術を施行（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/

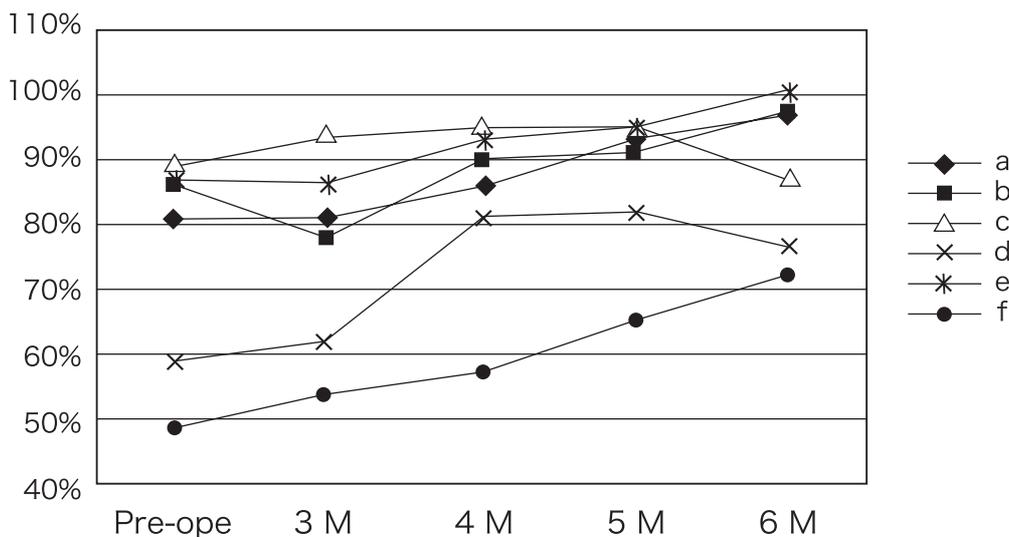


Fig. III.6.4-2 Peak force during dynamic knee extension at the speed of 60 deg/sec before operation and 3 month to 6 month after operation.

Pre-op; before operation, 3M; 3 month after operation, 4M; 4 month after operation, 5M; 5 month after operation, 6M; 6 month after operation.

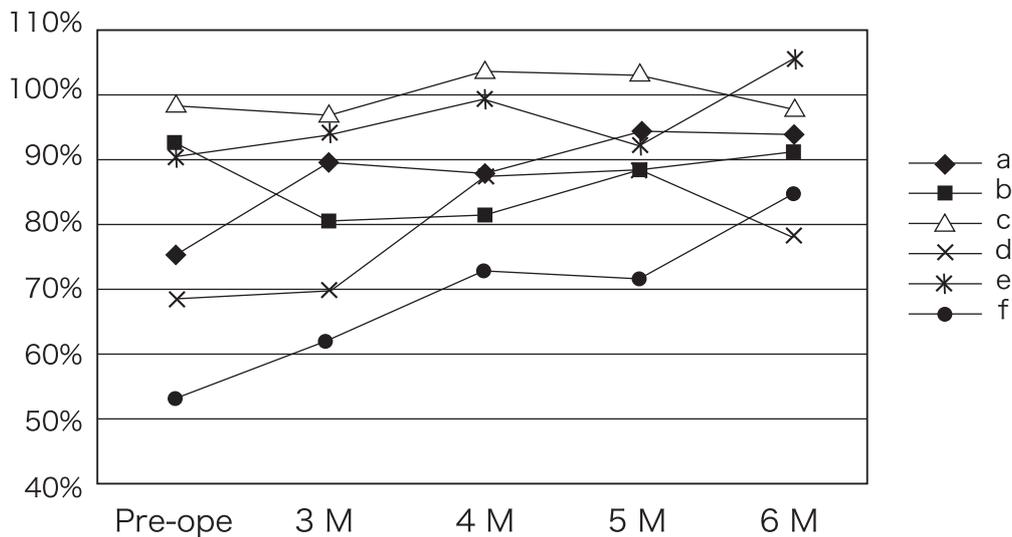


Fig. III.6.4-3 Peak force during dynamic knee extension at the speed of 180 deg/sec before operation and 3 month to 6 month after operation.

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、前十字靭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、再建靭帯の治癒、再構築が期待されるものに進化されてきている。これに

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、再建靭帯が治癒、再構築するまでの期間であり、再建靭帯への伸張ストレスを回避したり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、膝前十字靭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）静代<sup>1)</sup>

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<sup>2,3)</sup>, 佐藤 耕平<sup>3)</sup>, 村岡 慈歩<sup>4)</sup>, 岩館 雅子<sup>3,5)</sup>, 加賀谷淳子<sup>3)</sup>

<sup>1)</sup> 慶應義塾大学, <sup>2)</sup> 鹿屋体育大学大学院, <sup>3)</sup> 日本女子体育大学, <sup>4)</sup> 明星大学, <sup>5)</sup> 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

### 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

### 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）静代, 村岡 慈歩, 大森芙美子, 加賀谷淳子



## 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 ( $3.8 \pm 0.1$  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 plantar 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-dependent.

#### ● 目的

循環の中核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 $22 \pm 1$ 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 ( $3.8 \pm 0.1$  l/min)まで変化しなかったが、55% MVC ( $4.5 \pm 0.3$  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 ( $0.6 \sim 0.8$  l/min)以上では、安静時 ( $0.1 \pm 0.01$  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( $p <$

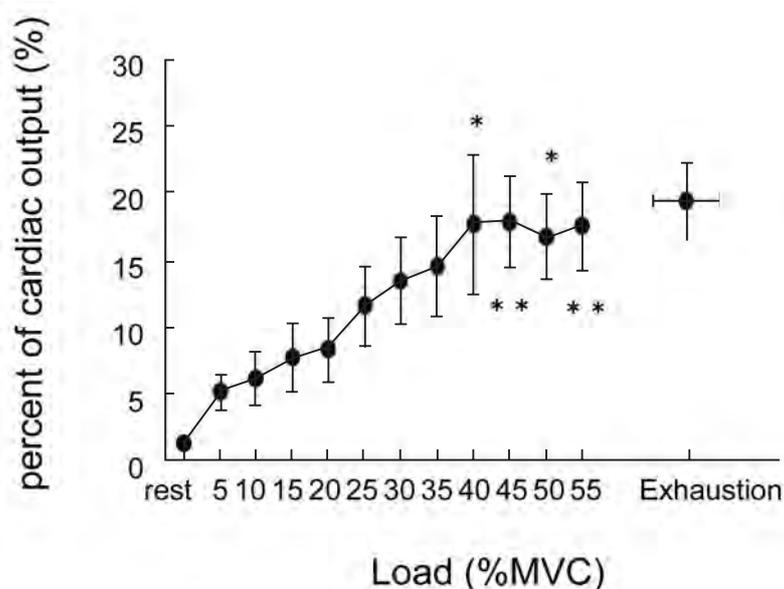


Fig. III.7.1-1 Popliteal arterial blood flow of cardiac output during incremental plantar flexion exercise to exhaustion.

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，大森美美子，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  $22.4 \pm 1.9$  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 ratios were  $-67.4 \pm 9.2\%$  (10%MVC), and  $-80.6 \pm 4.9\%$  (50%MVC) during the contraction phase. However, during the relaxation phase, they were  $30.0 \pm 11.6\%$  (10%MVC),  $50.7 \pm 22.3\%$  (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 $22.4 \pm 1.9$ 歳）を被験者とし，股関節角度 $110^\circ$ とした椅座位姿勢で右脚による動的膝伸展運動（ $30^\circ$ 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

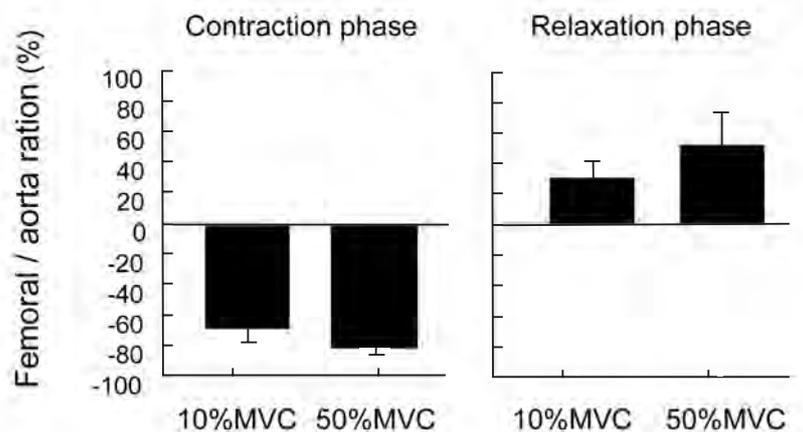


Fig. III.7.2-1 The femoral/aorta ratios during the contraction and relaxation phases at 10, 50%MVC. The femoral/aorta ratios were  $-67.4 \pm 9.2\%$  (10% MVC), and  $-80.6 \pm 4.9\%$  (50% MVC) during the contraction phase. However, during the relaxation phase, they were  $30.0 \pm 11.6\%$  (10% MVC),  $50.7 \pm 22.3\%$  (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）静代，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間を明らかにし、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:  $75.6 \pm 5.2$  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 (SYS-TEM 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。

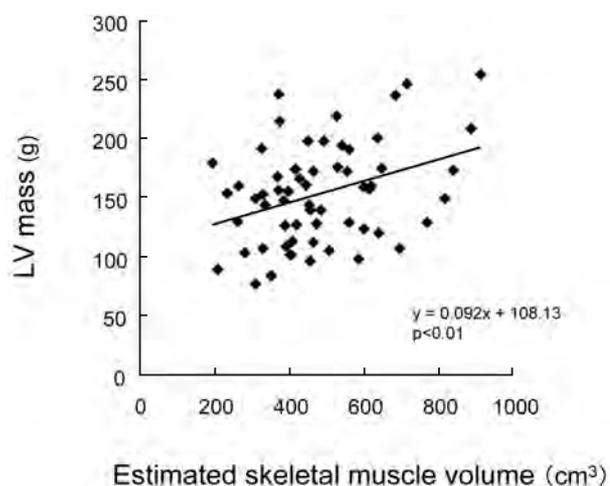


Fig. III.7.3-1 Relationship between estimated skeletal muscle volume and left ventricular muscle mass [LVmass] in elderly women.

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<sup>1)</sup>

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

Takuya Osada

### ■本課題の共同研究者

勝村 俊仁<sup>1)</sup>, 村瀬 訓生<sup>1)</sup>, 木目良太郎<sup>1)</sup>, 下村 浩祐<sup>1)</sup> および東京医科大学病院血管外科学スタッフ

<sup>1)</sup> 東京医科大学健康増進スポーツ医学

### 8.1 有疾患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



## 8.1 有疾患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  $71 \pm 2$  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

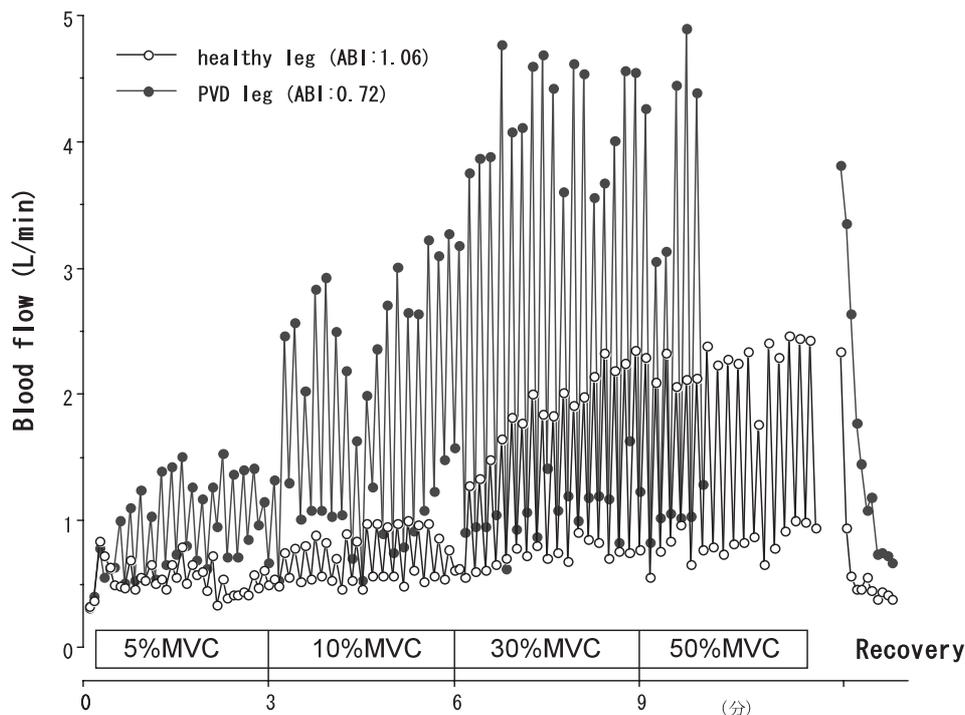


Fig. III.8.1-1 Limb blood flow response during incremental intermittent isometric knee extensor exercise. Changes in blood flow during exercise tend to be higher in the more-affected leg (PVD side) than the control healthy leg.

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らかとなった。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ど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<sup>1)</sup>

Central and peripheral neural control of respiration and circulation  
during exercise

Kohei Sato

### ■本課題の共同研究者

森山真由美<sup>2)</sup>, 平澤 愛<sup>2)</sup>, 定本 朋子<sup>1)</sup>

<sup>1)</sup> 日本女子体育大学, <sup>2)</sup> 日本女子体育大学基礎体力研究所

#### 9.1 Cerebral blood flow response at the beginning of voluntary exercise and passive movement

Kohei Sato, Mayumi Moriyama, Tomoko Sadamoto

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

Kohei Sato, Ai Hirasawa, Tomoko Sadamoto



## 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,  $23.5 \pm 0.7$  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  $50^\circ$  and  $90^\circ$  ( $0^\circ$  equaling full extension) at an angular velocity of  $90 \text{ deg} \cdot \text{sec}^{-1}$  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

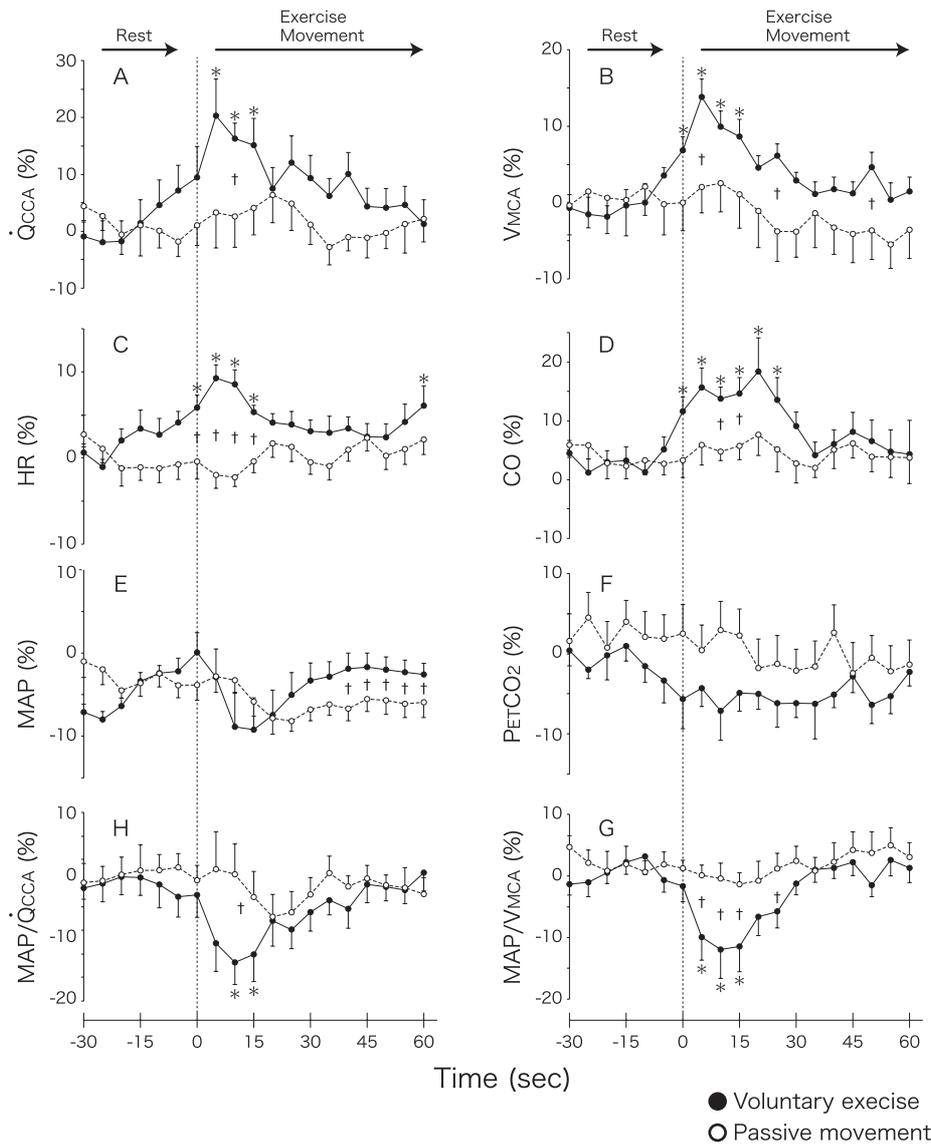


Fig. III.9.1-1 Changes in the cardiorespiratory and cerebral blood flow responses at the onset of voluntary exercise and passive movement. Relative changes were obtained by normalizing to the resting values. The time courses of the variables are shown from 30 s before to 60 s after the onset of exercise 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 com-

mand-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  $V_{\text{mean}}$ ) 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  $V_{\text{mean}}$  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 ventila-

tion 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  $\pm$  SD: 21.2  $\pm$  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

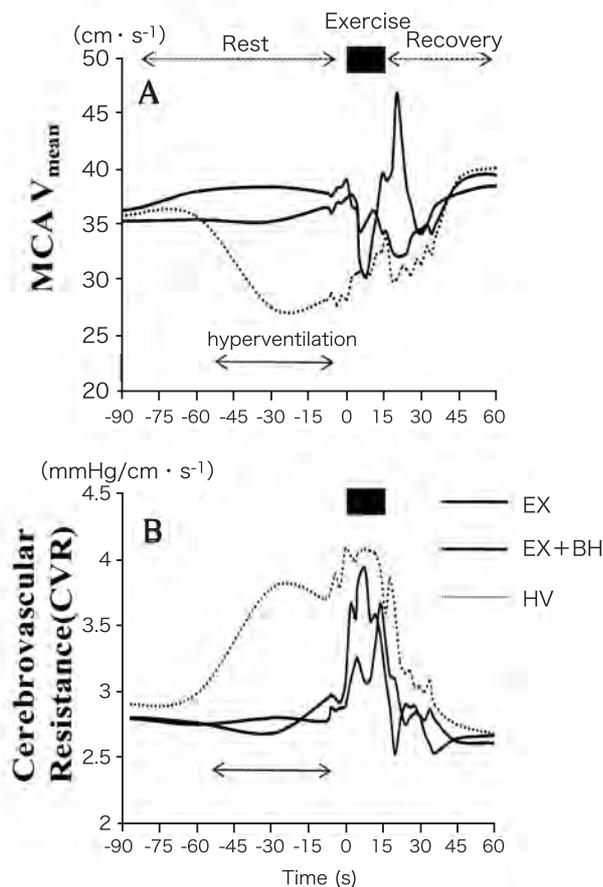


Fig. III.9.2-1 Cerebrovascular responses at rest, during, and after heavy exercise. (A) MCA  $V_{\text{mean}}$ , Mean middle cerebral artery mean blood velocity and (B) CVR, Cerebrovascular resistance index.

ventilation (EX), 2) exercise with concomitant breath holding (EX+BH), and 3) pre-exercise hyperventilation till an end tidal partial pressure of  $\text{CO}_2$  ( $P_{\text{ET}} \text{CO}_2$ ) 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  $P_{\text{ET}} \text{CO}_2$  of  $\sim 3.5\%$ . After the 1-min hyperventilation, the subjects performed 15-s static exercises with continued normal ventilation. MCA  $V_{\text{mean}}$  measurement was performed with an ultrasound system (Vivid 7pro; GE Yokogawa Medical Systems) equipped with a 2.0 MHz sector transducer. The MCA  $V_{\text{mean}}$  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  $\text{MAP}/\text{MCA } V_{\text{mean}}$  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  $V_{\text{mean}}$  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  $V_{\text{mean}}$  and the increase in the CVR may be induced by sympathoexcitation due to heavy exercise and/or the reduction in CO and  $P_a\text{CO}_2$ . 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  $V_{\text{mean}}$  immediately after the end of exercise may be induced by rapid decrease in CVR, with rapid recovery of CO and  $P_a\text{CO}_2$ .

In the HV trials, reduced MCA  $V_{\text{mean}}$  occurred in conjunction with increased CVR. This reduction in MCA  $V_{\text{mean}}$  before, during, and after exercise was attributable to the reduction in  $P_a\text{CO}_2$ . 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 combina-

tion 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<sup>1, 2)</sup>

Central command during the preparatory period before voluntary exercise

Masako Iwadate

■本課題の共同研究者

定本 朋子<sup>2)</sup>, 澁谷 顕一<sup>2)</sup>

<sup>1)</sup> 日本大学, <sup>2)</sup> 日本女子体育大学基礎体力研究所

### 10.1 運動準備期の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

### 10.2 運動準備期と運動時の脳皮質運動野酸素動態

岩館 雅子, 澁谷 顕一, 定本 朋子



## 10.1 運動準備期の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、脳皮質運動野周辺領域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。

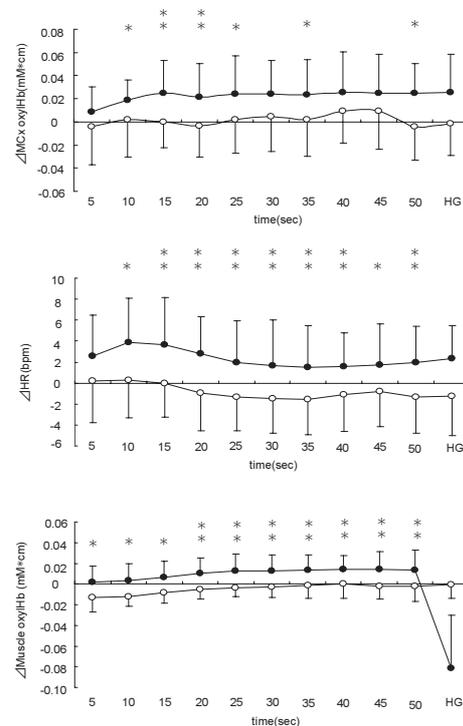


Fig. III.10.1-1 Changes in oxygenated hemoglobin obtained left motor cortex (MCx oxyHb), Heart Rate (HR), oxygenated hemoglobin obtained right forearm flexors muscles (muscle oxyHb) during preparatory period before handgrip exercise (HG). Values are means  $\pm$  SD in 13 subjects.  $\circ$ , control condition;  $\bullet$ , 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。

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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

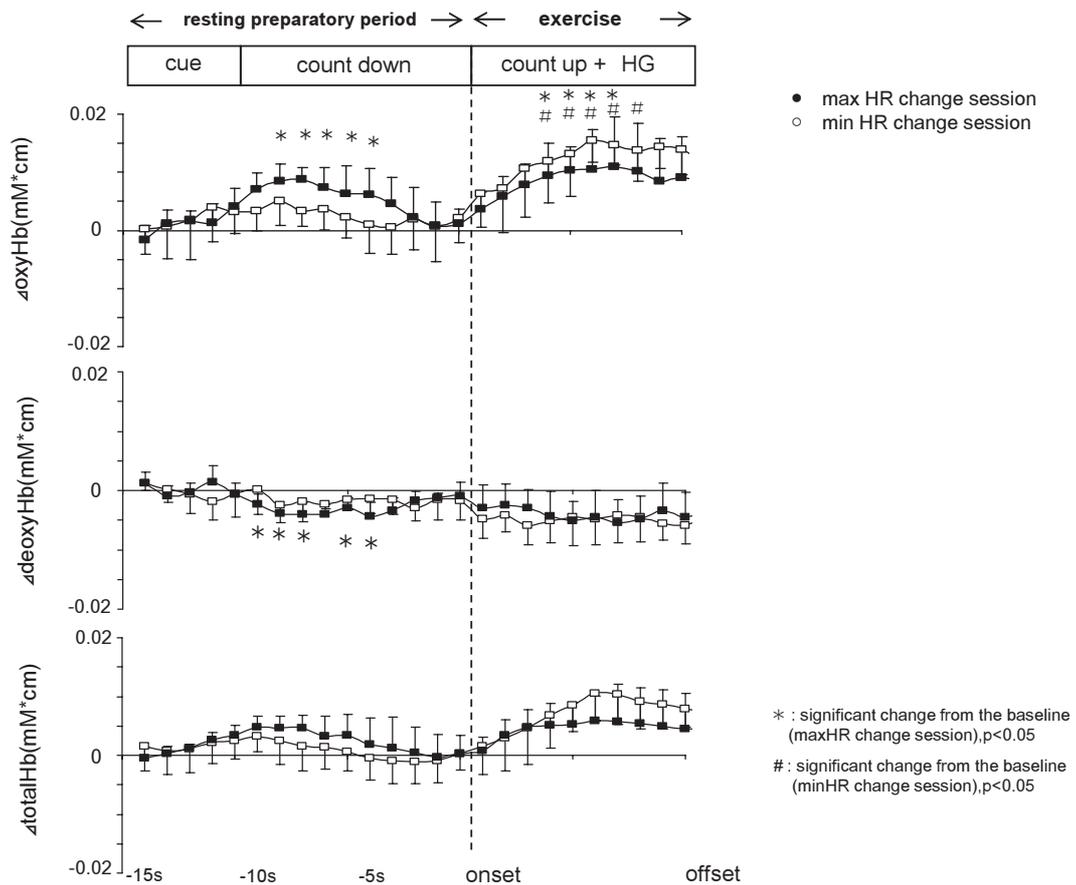


Fig. III.10.2-1 The oxygenation in the contralateral motor cortex during the resting preparatory period and the sustaining right hand grip exercise. Filled circles show that of maximal HR change session during the resting preparatory period and open circles show that of minimum HR change session during 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<sup>1,2)</sup>

Associated changes in muscle oxygenation with circulatory responses during exercise

Chihoko Ueda-Sasahara

■本課題の共同研究者

加賀谷淳子<sup>2)</sup>

<sup>1)</sup> 東海学園大学, <sup>2)</sup> 日本女子体育大学基礎体力研究所

### 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連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か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  $T_{1/2}$  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

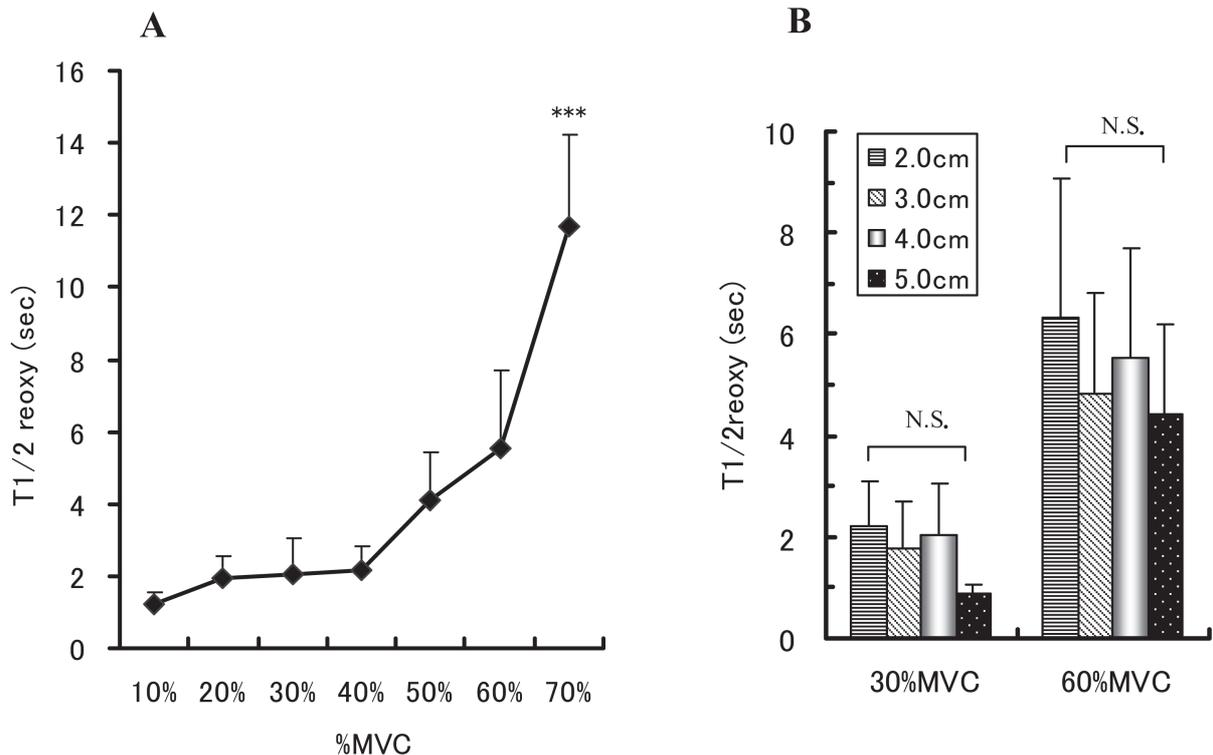


Fig. III.11.1-1 Half time reoxygenation (T1/2 reoxy time) after knee extension exercise. (A) The effects of exercise intensities. Light source and detector distance of NIRS probe was 4 cm. (B) The effects of light source and detector distance at the intensities of 30% and 60% MVC. Values are expressed as mean  $\pm$  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<sup>1)</sup>

Oxygenation kinetics in the primary motor cortex area during exercise

Kenichi Shibuya

■本課題の共同研究者

定本 朋子<sup>1)</sup>, 佐藤 耕平<sup>1)</sup>, 森山真由美<sup>1)</sup>, 岩館 雅子<sup>1,2)</sup>

<sup>1)</sup> 日本女子体育大学基礎体力研究所, <sup>2)</sup> 日本大学

**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

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

Kenichi Shibuya, Masako Iwadate, Tomoko Sadamoto

**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



## 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<sup>-1</sup>]. 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<sub>2</sub>]) 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:  $21.4 \pm 0.2$  y, height:  $159.1 \pm 1.3$  cm, weight:  $56.3 \pm 1.9$  kg, MVC:  $315.6 \pm 11.8$  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 appara-

tus (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 Electroencephalographic 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. Asterisks shows significant differences between the response on hemispheres ( $p < 0.05$ ).

	Contralateral	Ipsilateral
HbO <sub>2</sub>	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<sup>-1</sup>). 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<sub>2</sub>):  $p = 0.8050$ ; deoxyhemoglobin (Hb):  $p = 0.8036$ ), while those of the ipsilateral M1 significantly decreased across the trials (HbO<sub>2</sub>:  $p = 0.0371$ ; 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

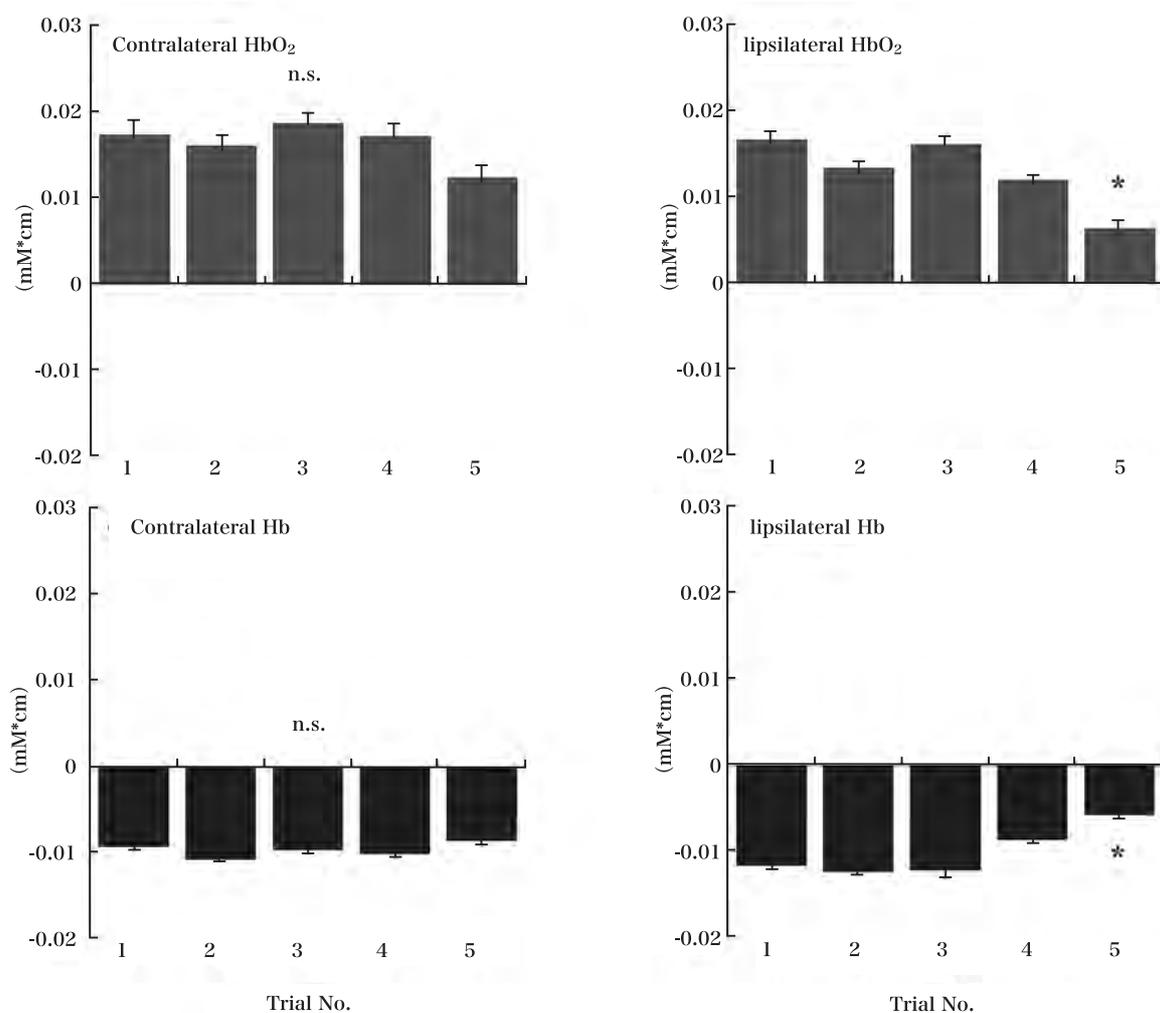


Fig. III.12.2-1 The peak value changes in oxygenation from resting levels. Upper panels represent the results of oxyhemoglobin (HbO<sub>2</sub>) changes. Lower panels represent the results of deoxyhemoglobin (Hb) changes. Right panels represent the results of ipsilateral primary motor cortex oxygenation 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<sub>2</sub> and Hb after the start of exercises. The previous studies found the gradual changes in HbO<sub>2</sub> 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<sub>2</sub> 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<sub>2</sub> 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<sub>2</sub> 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 trial 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 *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<sub>contralateral</sub>). The signals from the M1<sub>contralateral</sub> 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<sub>contralateral</sub> decreased significantly at voluntary exhaustion compared with the resting values ( $p < 0.05$ ). On the other hand, in sedentary subjects, oxygenation in the M1<sub>contralateral</sub> 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.

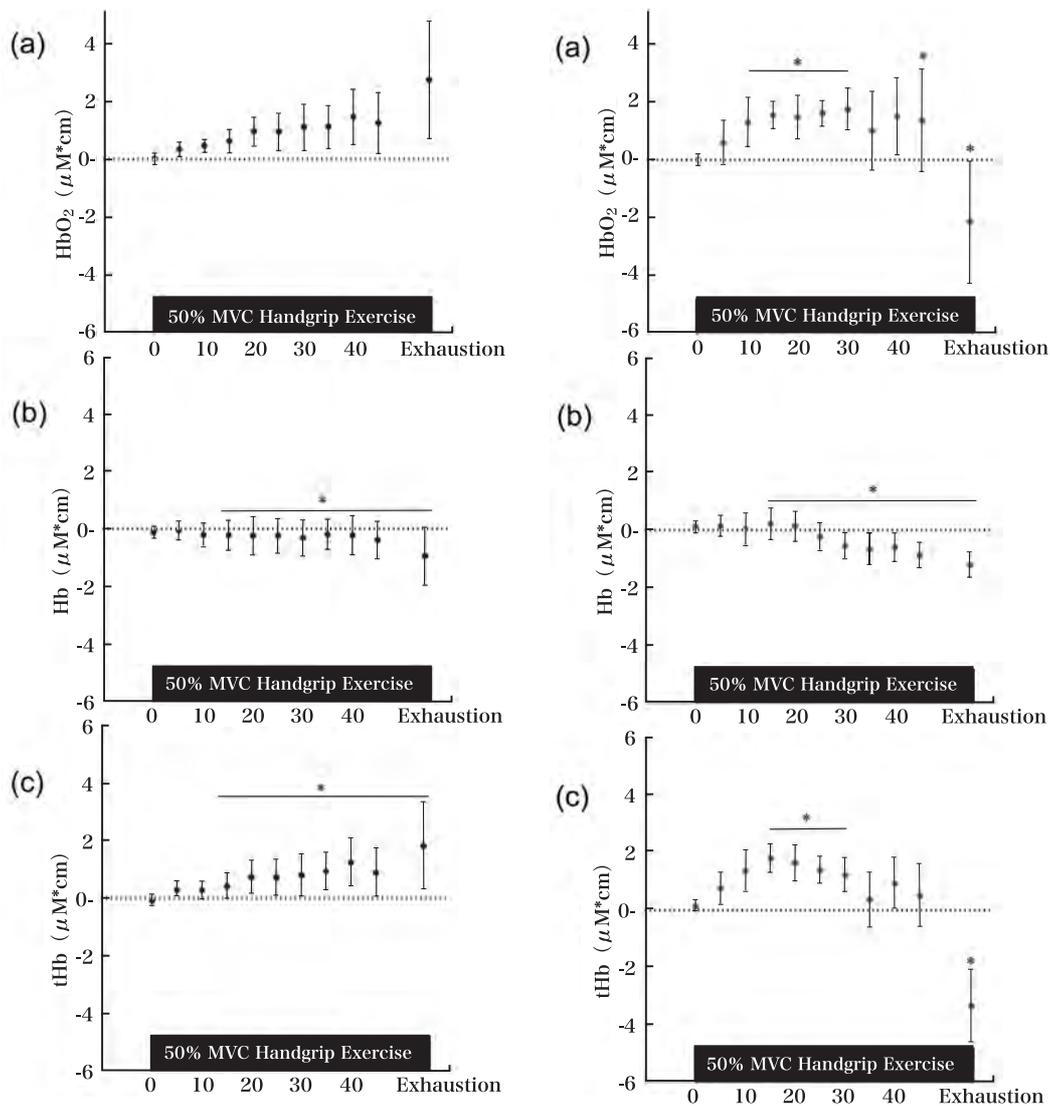


Fig. III.12.3-1 The values of changes in the sedentary subjects in the contralateral motor cortex from resting values in (a) oxyhemoglobin concentration (HbO<sub>2</sub>), (b) deoxyhemoglobin concentration (Hb), and (c) total-hemoglobin concentration (tHb) during the handgrip exercise in left panels, and in the athletes in the right panels. Values are represented as means  $\pm$  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<sub>contralateral</sub> 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<sub>contralateral</sub> 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  $MI_{\text{contralateral}}$  continued to increase even at voluntary exhaustion. By contrast, in the athletes, the oxygenation in the  $MI_{\text{contralateral}}$  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  $MI_{\text{contralateral}}$  were different between elite athletes and sedentary subjects during the handgrip exercise leading to voluntary exhaustion.