局所的な圧迫が低強度な運動中の中枢神経活動に与える影響：機能的ＭＲＩによる研究

課題番号　16500425

平成16年度～平成18年度科学研究費補助金〔基盤研究(C)〕
研究成果報告書

平成19年4月

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1. はじめに

総務省統計局　人口推計月報によれば、平成 18 年 1 月現在、65 歳以上の総人口に占める割合は 20%を超え、2004 年の日本人の平均寿命は 80.5 歳と世界最長を記録している。わが国が本格的な高齢者社会であることを理解するには十分である。また 14 歳までの人口の割合が 13.7%であることを考慮に入れると、今後ともこの傾向の進行を軽減できる可能性は低いと考えられる。

一般に、筋は加齢にともなってその機能を低下させる。この最大の原因は、筋を構成する筋線維の数と断面積の減少にある。すなわち、筋自体の萎縮が起こるのである。この詳細なメカニズムについては不明な点が多いが、全ての（随意）運動が脳の指令の下、有機的なつながりをもって実施されている理解にたてば、筋機能の低下は、結果的に、大脳運動関連領域を中心とした脳機能低下にも大きな影響を与えるに違いない。したがって、高齢者及びその予備軍である壮年者が日常生活を円滑に活動的に過ごすために、加齢にともなう筋—骨格系の機能低下を遅延させ、ある一定水準以上の機能を保持することは重要な課題と考えられる。

一方、局所的な血流制限下で筋運動をおこなうと、その運動強度が筋力の向上や筋肥大を期待できないほどの低強度であっても、顕著な筋力と筋断面積の増加が引き起こされる(Takarada et al. 2000a; 2002)。この大きな効果の要因には、局所的な圧迫に伴う筋内環境の悪化(代謝産物の蓄積や低酸素化)が引き起こす、①運動中の筋の活動レベルや運動後の②成長ホルモン及び③ノルアドレナリンの血中濃度の顕著な増加が挙げられており(Takarada et al. 2000a; 2000b)、この要因には内分泌系や交感神経活動をはじめとした中枢神経系が深く関係していると推察される。しかし、その中枢神経系のメカニズムについては不明な点が多いことも事実である。また近年、コンピュータを用いたイメージング技術の進歩によって、脳活動を非侵襲的に測定することが可能となった。特に、機能的核磁気共鳴断層撮影法(機能的 MRI, fMRI; functional magnetic resonance image)は、脳賦活領域の判定や脳活動の時間的変化の記録が可能である。

そこで本研究の目的は、機能的 MRI を用いて、局所的な血流制限が低強度な運動中の中枢神経活動に与える影響を調べ、血流制限下の筋運動の中枢性のメカニズムを検討することである。

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2. 研究組織

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3. 交付決定額(配分額)

（金額単位：円）

	直接経費	間接経費	合　計
平成 16 年度	3,000,000	0	3,000,000
平成 17 年度	700,000	0	700,000
平成 18 年度	100,000	0	100,000
総　計	3,800,000	0	3,800,000

4. 研究発表

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5. 資料

資 料　　研究論文 1）

Takarada, Y., D. Nozaki and M. Taira.
Force overestimation during tourniquet-induced transient occlusion of the brachial artery and possible underlying neural mechanisms.
Neuroscience Research, 54(1): 38-42, 2006

Available online at www.sciencedirect.com
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Neuroscience Research 54 (2006) 38–42
Neuroscience Research
www.elsevier.com/locate/neures

Force overestimation during tourniquet-induced transient occlusion of the brachial artery and possible underlying neural mechanisms

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Received 13 August 2005; accepted 11 October 2005
Available online 14 November 2005

Abstract

A vascular occlusion by a tourniquet inflated at the proximal end of the upper arm is suggested to affect the estimation of exertion force level. In the first part of this study, subjects were asked to estimate the isometric force exerted by the occluded hand with that of the other hand (matching experiment). We found that the perceived force with arterial occlusion was always overestimated. To examine the underlying neural mechanism for this phenomenon, in the second part, the somatosensory evoked potentials (SEPs) and nerve action potential (NAP) were recorded following electrical median nerve stimulation with or without arterial occlusion. Moreover, the maximum motor response (M response) to median nerve stimuli at the axilla was recorded from the skin surface of the thenar eminence muscle of the hand during with arterial occlusion. The N20 of SEP and NAP at Erb's point were unaffected by the arterial occlusion, and the M response was also unchanged. These results suggest that the tourniquet-induced transient occlusion of the brachial artery does not seriously affect median nerve function. Thus, it is likely that the primary responsible factor for the overestimation of perceived force exertion during arterial occlusion is the centrally generated motor command as previously hypothesized by McCloskey [McCloskey, D.I., Ebeling, P., Goodwin, G.M., 1974. Estimation of weights and tensions and apparent involvement of a "sense of effort". Exp Neurol. 42, 220–232; McCloskey, D.I., 1978. Kinesthetic sensibility. Physiol. Rev. 58, 763–820; McCloskey, D.I., 1981. Corollary discharge and motor commands and perception. In: Brookhart, J.M., Mountcastle, V.B. (Eds.), Handbook of Physiology. American Physiological Society, Bethesda, pp. 1415–1447].

Keywords: Vascular occlusion; Force perception; SEP; M response; Central motor command; Median nerve

1. Introduction

It is a common experience to feel a weight heavier than normal when we carry it long enough and when the muscles supporting the weight have been fatigued. McCloskey et al. (1974) have actually shown that weight is determined to be heavier than the usual under experimental muscle fatigue condition by a force matching task. In their study, they also showed that weight is overestimated during the inhibition of the motoneurons of the agonist muscle by vibration of its antagonist muscle. Thus, they suggested that the centrally generated motor command (i.e., effort) is involved in the sensation of heaviness rather than factors in the peripheral nerves and/or muscles (see reviews in McCloskey, 1978, 1981).

In preliminary experiments on handgrip contractions with the proximal end of an upper arm occluded by a tourniquet at 250 mmHg, we noticed that subjects reported the need for greater force to keep the same force level during the tourniquet was inflated. However, these were just objective reports. In this study, we first examined how arterial occlusion affects the perception of handgrip force by the force matching experiment. The results showed that the subjects always overestimated their exertion force during arterial occlusion. McCloskey's idea (1974, 1978, 1981) is thought to be the underlying neural mechanisms for this, however the simplest

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0168-0102/$ – see front matter
doi:10.1016/j.neures.2005.10.004

explanation is that ischemia of the forearm and/or the tourniquet itself cause mechanical deformation of the nerves and interfere with conduction of the peripheral nerve. Previous studies showed that the tourniquet-induced ischemia diminishes amplitudes of the early-latency somatosensory evoked potentials (SEPs) (Yamada et al., 1981; Nishihira et al., 1996). Thus, in the second part of the present study, we investigated the early cortical SEPs to median nerve stimuli at the wrist (SEPs experiment), and M waves to median nerve stimuli at the axilla (M response experiment) during arterial occlusion by a tourniquet inflated around the upper arm, in order to elucidate the possible neural mechanisms underlying such a psychological effect of arterial occlusion on the perceived force exertion (matching experiment).

2. Methods

2.1. Matching experiment

2.1.1. Subjects

Eight right-handed volunteers (seven men and one woman) with no history of neurological or other disease participated in the experiments. Their mean age was 19.8 ± 0.46 years old (mean ± S.D., range 19–22). All of the subjects were informed well about the experimental procedures to be performed as well as the purpose of the study, and their written informed consents were obtained. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethical Committee of Faculty of Sport Sciences, Waseda University.

2.1.2. Procedure

The subjects were placed in a sitting position with their upper body upright and their upper arm inclined at about 45° in front of the body with the aid of an armrest. To measure handgrip force, handgrip devices with a strain gage (KFG-5-120-C1-16; Kyowa Electronic Instruments Co. Ltd., Tokyo, Japan) were held in the subject's right and left hands. The measured force was amplified (AD240-A; TEAC Instruments Co., Kawasaki, Japan) and inputted to a visual feedback system (IBM T40) to show the subjects the exerted force and the predetermined target force level on the display. The force was digitized (200 samples/s) and recorded on the hard disk of a data acquisition computer (Macintosh PowerBook G4: M8858J/A).

Before matching measurement (see below), the maximal voluntary contraction (MVC) was measured to calculate 20%, 40%, 60% and 80% MVC, each subject was asked to squeeze the handgrip device with his maximum effort three times with a 120–180 s rest between squeezing. The values of the force exerted were averaged over the middle 1 s during muscle contraction.

During the matching measurements, only the force exerted in the reference (right) hand was displayed on the monitor. The subjects were asked to align the force exerted by the reference hand with a predetermined target force by visual feedback, and simultaneously to contract the indicator (left) hand so as to "make both hands the same", i.e., without visual feedback. In one measurement session, this bilateral isometric contraction (approximately 3–5 s) was performed three times with a 10–15 s rest in between contractions at a given target force (20%, 40%, 60% or 80% MVC) with or without arterial occlusion. There was a rest for 120–180 s between each session and the order of sessions was randomized for each subject. The arterial occlusion was produced by a tourniquet, which was attached at the proximal end of the right upper arm. A pressure of 250 mmHg started to be applied by pneumatic inflation approximately 15 s before each muscle contraction measurement session, which was maintained throughout the each measurement session, and was released immediately after the end of the measurement session. Thus, the arterial occlusion in one measurement session was lasted for 29–45 s.

2.1.3. Analysis

To normalize the differences in exerted handgrip force between the reference hand and the indicator hand, matching value [MV (%)] was calculated.

$$\mathrm{MV}\,(\%) = \frac{\text{Handgrip force of the indicator hand} - \text{handgrip force of the reference hand}}{\text{Handgrip force of the reference hand}} \times 100$$

2.2. SEPs experiment and M response experiment

2.2.1. Subjects

Nine right-handed volunteers (seven men and two women) with no history of neurological or other disease participated in the SEPs experiments. Their mean age was 20.6 ± 0.74 years old (mean ± S.D., range 19–22).

Six (five men and one woman) of the nine subjects participated in the M response experiments. Their mean age was 20.0 ± 0.63 years old (mean ± S.D., range 19–22). All of the subjects were informed well about the experimental procedure to be performed as well as the purpose of the study, and their written informed consents were obtained. The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethical Committee of Faculty of Sport Sciences, Waseda University.

2.2.2. Procedure: SEPs experiment

Electrical stimuli (duration, 0.2 ms; 5 Hz at random; intensity, 110–115% of muscle twitch threshold) were delivered to the right median nerve at the wrist using flat-surfaced disk electrodes by a stimulator (Dia Medical, DPS-1300) and an isolator (DPS-107). The SEP signals and nerve action potentials (NAP) of the median nerve were recorded by silver discs (impedance: <5 Ω) attached to the skin with an EEG paste. The exploring-referential electrodes were placed on C3 (2 cm posterior to Cz and 7 cm lateral to midline in the hemisphere contralateral to the stimulated side)–Ai (earlobe in the hemisphere contralateral to the stimulated side), and Erb's point (contralateral to the stimulated side)–Erb's point (ipsilateral to the stimulated side) (Mauguiere et al., 1999). Signals (analysis time: 40 ms) were amplified (NEC BIOTOP 6R12) using a bandpass filter of 20 Hz–3 kHz, digitized (National Instruments, NI DAQCard-6036E, 2 kHz sampling) and averaged 600 times by a personal computer (Toshiba Dynabook V9/W14DEW).

In one recording session, the SEPs and NAP to the median nerve stimuli were recorded with or without vascular occlusion at a pressure of 250 mmHg applied by a tourniquet at the proximal end of the upper arm. The duration of each recording condition was 120 s (thus 600 sweeps were collected at each condition) followed by a 60 s rest. The session was repeated two times with 3 min rest interval.

2.2.3. Analysis: SEPs experiment

SEP components were labeled according to a polarity–latency convention (negative waves, N; positive waves, P) followed by a number indicating the measured peak latency in milliseconds. In analyzing the amplitude, the peak-to-peak amplitude was measured from the peak of the preceding reversed-polarity component. The amplitude of NAP recorded from the Erb's point (Erb–Erb) was measured from its onset to the major negative peak.

2.2.4. Procedure: M response experiment

Electrical stimuli (duration, 0.2 ms; 3 Hz) were delivered by the stimulator and the isolator to the right median nerve at the axilla using flat-surfaced disk electrodes (12 mm wide and 46 mm long) with the cathode 20 mm proximal to the anode.

The motor response in the EMG was recorded from the skin surface of the thenar eminence muscle in the right hand. Surface electrodes (diameter 8 mm) were placed over the bellies of these muscles, with a constant interelectrode distance of 20 mm. A reference electrode was fixed on the skin overlying the lateral epicondyle near the elbow joint of the right arm. The maximum motor response (M response) was elicited by the supramaximal stimulation of the median nerve at the axilla.

The EMG signals were amplified, filtered through both low (20 Hz) and high (1 kHz) cut filters, digitized (National Instruments, NI DAQCard-6036E, 2 kHz sampling), and stored in the personal computer (Toshiba Dynabook V9/

W14DEW). M response was recorded with and without arterial occlusion. The manner of recording session was the same as that of the SEP experiment.

2.2.5. Analysis: M response experiment

The M waves in response to 10 stimuli of the median nerve were averaged in each subject, and the latencies of these averaged waves were measured from the stimulus to each peak. Also, the time integral (μV ms) under the full-wave rectified M wave recorded by the surface electrodes was adopted as an index of the M response.

3. Results

3.1. Matching experiment

We asked the subjects to determine the magnitude of the handgrip force exerted by the reference (right) hand by producing a brief matching contraction on the indicator (left) hand, to estimate numerically the subjective effort required to exert the handgrip force by the reference hand.

When the handgrip force exerted by the indicator hand was plotted against that by the reference hand, a high correlation was observed ($r = 0.991$; Fig. 1). Thus, the handgrip force exerted by the indicator can be an indicator of that by the reference hand during bilateral isometric handgrip contractions. Such a linear relation was also held during the handgrip force exertion by the reference hand with arterial occlusion ($r = 0.98$). Although there was no difference in the handgrip force of reference hand between with and without arterial occlusion conditions (n.s., Student's paired t-test), statistically significant increases in that of the indicator hand were observed in the occluded condition at all four different levels of the target force ($p < 0.05$, Student's paired t-test). In order to elucidate whether the transient arterial occlusion change precision in perceiving force exertion, we compared the standard deviation of handgrip force of the indicator and reference hand between two conditions (with and without arterial occlusion). In both handgrip forces, there was no statistically significant difference in the standard deviation between two conditions (n.s., Student's paired t-test). Thus, the transient arterial occlusion did not affect on precision in perceiving force exertion.

Fig. 2 shows the MVs in the control and occluded conditions at each level of the target force, which were calculated by the difference of exerted handgrip force between by the reference hand and by the indicator hand (see Section 2). The average MVs in the control condition at the four different target levels were 12.7 ± 7.3%, 9.7 ± 7.8%, 6.5 ± 5.4% and 1.1 ± 5.2% (mean ± S.E.), respectively, and those in the occluded condition were 45.0 ± 10.1%, 30.9 ± 8.9%, 16.8 ± 5.2% and 6.9 ± 4.6% (mean ± S.E.), respectively. These results show that the handgrip forces exerted by the indicator hand increased significantly at all levels of the target force during handgrip contractions of the reference hand when combined with arterial occlusion ($p < 0.05$, Student's paired t-test), suggesting that an arterial occlusion led to the overestimation of the exerted force.

3.2. SEPs experiment

We analyzed the amplitudes and latencies of NAP recorded from the Erb's point (Erb–Erb), and SEPs (N20 and P23 component) recorded from the parietal area (C3–Ai). Fig. 3 shows the SEPs and NAP waveforms, which were averaged for all the subjects ($n = 9$) to the median nerve stimuli in the control and occluded condition. The peak latencies of NAP, N20 and P23 in the control condition were 8.6 ± 0.3 ms, 19.1 ± 0.2 ms and 22.8 ± 0.5 ms, respectively. The peak latencies of NAP, N20 and P23 in the occluded condition were 8.7 ± 0.3 ms, 19.1 ± 0.2 ms and 22.7 ± 0.6 ms, respectively. These results showed that the peak latencies of NAP, N20 and P23 of SEP components were unchanged in the occluded condition. The amplitude of the N20 component recorded from the parietal area was unchanged; that of the P23 components recorded from

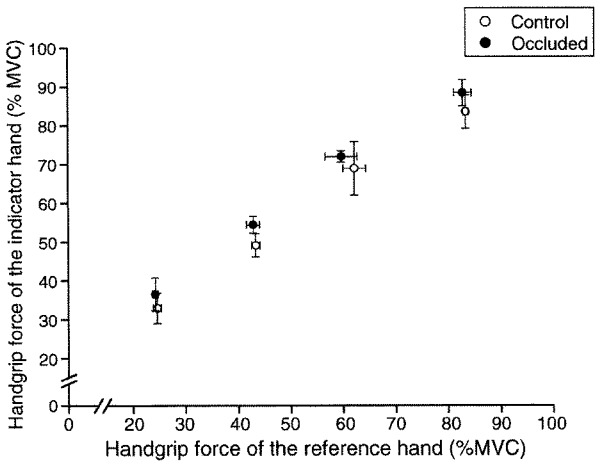

Fig. 1. Relationship between reference and indicator handgrip forces with (filled circle) or without arterial occlusion (unfilled circle). The values of the reference and indicator handgrip forces were normalized to those of the maximal voluntary contractions (MVCs) on the reference and the indicator hands, respectively, and means with S.E. ($n = 8$) were plotted.

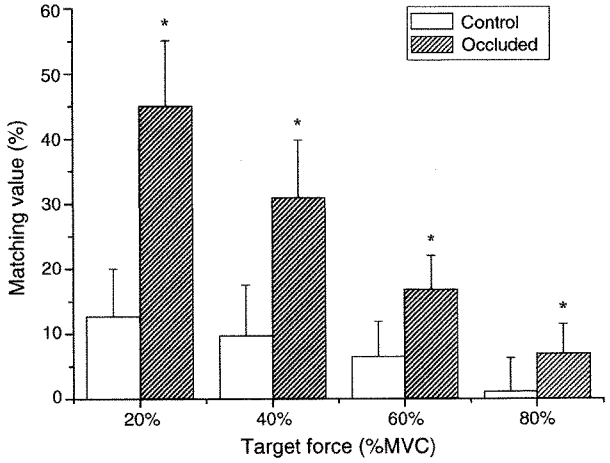

Fig. 2. Matching values with (hatched square) or without (square) arterial occlusion at four different target forces (20%, 40%, 60% and 80% MVC). Values are expressed as means with S.E. ($n = 8$). The asterisk represents statistically significant differences between the control and occluded conditions ($p < 0.05$, Student's paired t-test).

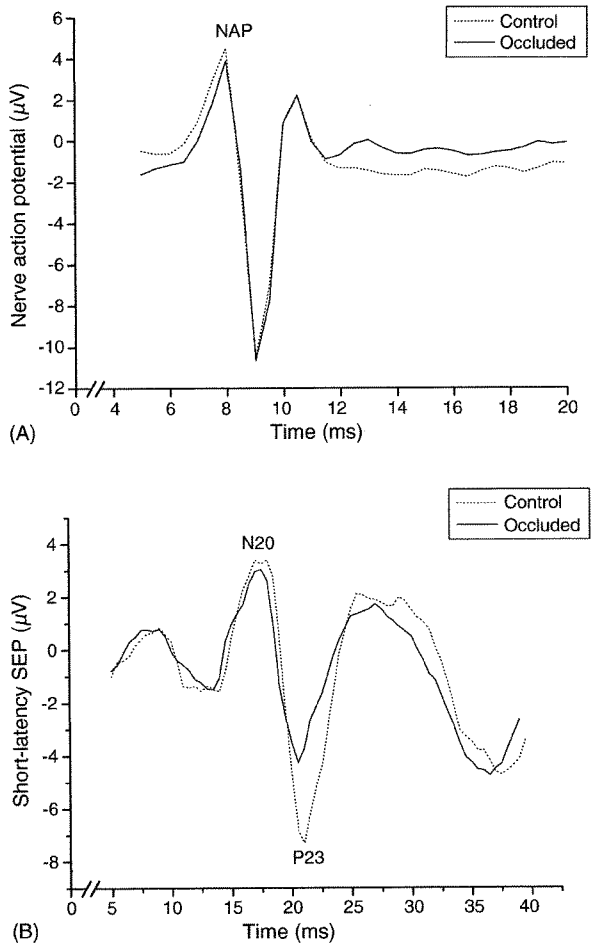

Fig. 3. Nerve action potential at the Erb's point (NAP; A) and short-latency SEPs (N20 and P23; B) at C3 during median nerve stimuli with (filled circle) or without arterial occlusion (unfilled circle) in one subject.

the parietal area was significantly decreased in the occluded condition ($p < 0.01$, Student's paired t-test). The amplitude of the P23 component decreased from 6.49 ± 0.59 μV in the control condition to 4.01 ± 0.65 μV in the occluded condition.

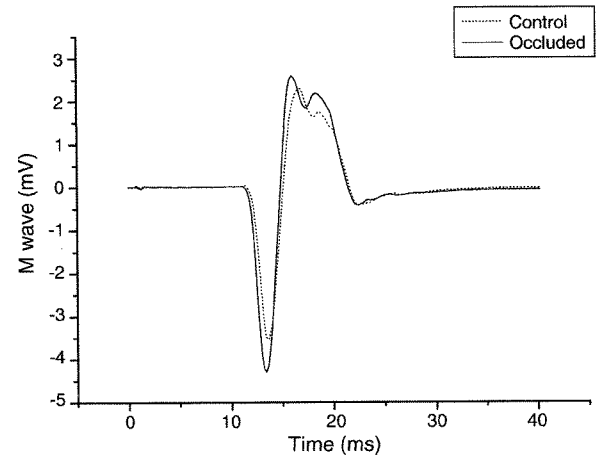

Fig. 4. M waves following median nerve simulation during rest (dashed line) and arterial occlusion (solid line) in one subject.

These results showed that the transient arterial occlusion does not significantly affect the cortical SEP component, N20 and median nerve function.

3.3. M response experiment

The amplitudes of M waves recorded from the thenar eminence muscle in the control and occluded condition were 7.01 ± 3.01 μV and 6.67 ± 2.70 μV, respectively (Fig. 4). The time integral under the full-wave rectified M wave in the control and occluded conditions were 6.34 ± 2.51 μV ms and 5.68 ± 1.87 μV ms, respectively. No statistically significant differences between the control and occluded conditions were observed in the amplitudes and the time integral of M waves (n.s., Student's paired t-test), showing that such an arterial occlusion around the upper arm did not produce any substantial change in the M response.

4. Discussion

It is a common experience to feel a weight heavier than normal when we carry it long enough and when the muscles supporting the weight have been fatigued. In preliminary experiments, arterial occlusion at the proximal end of the upper arm caused the same effect on handgrip contractions; we noticed that subjects reported the need for greater force to keep the same force level during the arterial occlusion. The force matching experiment in this study revealed that arterial occlusion applied around the upper arm by a tourniquet elevates the perceived magnitude of the force exerted during handgrip contractions (Figs. 1 and 2). Although there was no difference in the exerted force by reference hand between with and without arterial occlusion conditions, the exerted force by indicator hand revealed that subjects felt exerting more force during arterial occlusion. McCloskey et al. (1974) hypothesized that the centrally generated motor command (i.e., effort) is involved in the sensation of heaviness. Thus, this mechanism may similarly operate in the overestimation of exerted force during muscular contractions with arterial occlusion in this study. At the same time, however, we cannot deny the possibility that ischemia of the forearm and/or the tourniquet itself cause the mechanical deformation of the nerves and interferes with conduction of the peripheral nerve.

Indeed, several previous studies demonstrated that a tourniquet-induced vascular occlusion of the upper arm markedly attenuated the amplitudes of early-latency SEPs and Erb's potential to median nerve stimuli at the wrist (Yamada et al., 1981; Nishihira et al., 1996). In this study, however, there were no significant changes in the peak latencies and amplitudes of NAP (Fig. 3A), and of the early-latency SEP, N20 (Fig. 3B) to the median nerve stimuli during arterial occlusion. This inconsistency of the effect of vascular occlusion on median nerve function may be mainly caused by the difference in the duration of occlusion, rather than the degree of occlusion. In previous studies, the duration of vascular occlusion was relatively long [from 24 min (Yamada et al., 1981) to 30 min (Nishihira et al., 1996)], however, duration was

not exceeded more than 150 s in our experiments. In other words, vascular occlusion with a short duration of not more than 150 s does not induce any deterioration of median nerve function, whatever inflation pressure magnitude is applied by a tourniquet. This conclusion is also reinforced by the results on M response experiment in which no significant changes were observed in the peak-to-peak amplitudes and the time integral of M waves recorded from the thenar eminence muscle to median nerve stimuli at the axilla during arterial occlusion (Fig. 4).

When the tourniquet was inflated to 250 mmHg, subjects felt pressure on the skin and a light tingling sensation in deep tissue, however, these sensations were immediately disappeared with deflation. It is well known that cutaneous afferent nerves innervate to spinal motoneurons through excitatory or inhibitory interneurons. Previous studies (Goodwin et al., 1972; McCloskey et al., 1974; also see reviews in McCloskey, 1978, 1981) shown that, if the spinal motoneurons of the agonist muscle were inhibited by the spindle afferents of the vibrated antagonist muscle, subjects overestimated the perceived force exertion in the matching test. Thus, it is suggested that the same neural mechanisms are involved in the present study; inhibition of the spinal motoneurons by the somatic sensations through the cutaneous afferent nerves might be one of the underlying neural mechanisms for the overestimation of force. It is, also, fact that the amplitude of the P23 component significantly decreased during arterial occlusion ($p < 0.01$, Student's paired t-test). In general, subsequent components to N20 at 20–30 ms, including P23, are thought to reflect activities of higher cortical areas, however, the generator locations of those components have not been confirmed yet (Allison et al., 1991; Kakigi, 1994; Waberski et al., 1999; Hoshiyama and Kakigi, 2001). Thus, the attenuation of P23 might be related to the neural aspects of the overestimation of perceived force exertion, however, we need further experiments to clarify the underlying neural mechanisms.

The results presented above show that a tourniquet-induced transient occlusion of the brachial artery does not inhibit the normal efferent and afferent functions of the median nerve. Thus, it is likely that the primary responsible factor for the overestimation of perceived force exertion during arterial occlusion is the centrally generated motor command as previously hypothesized by McCloskey (1978, 1981).

The present study does not indicate directly the source of the centrally generated motor command, however, it is reasonable to assume that the activity of MI is closely involved in such an increase in the perceived magnitude of handgrip force during arterial occlusion. To investigate this possibility, further studies are being carried out with functional magnetic resonance imaging (fMRI) and trans cranial magnetic stimulation (TMS).

Acknowledgments

This study was supported by Academic Frontier Project for Private Universities: "Brain Mechanisms for Cognition, Memory and Behavior" at Nihon University matching fund subsidy from MEXT and a Grant-in-Aid for Scientific Research on Priority Areas-Advanced Brain Science project-from MEXT (No. 16500425).

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資 料　　学会発表等 1）

宝田雄大，泰羅雅登．張力の知覚に一致した一次運動野の活動性．
日本大学医学部 学術フロンティア研究会「皮質運動野を考える：機能とその関連領域」．
2005（2/19）

学術フロンティア研究会

「皮質運動野を考える: 機能とその関連領域」

平成17年2月19日午後1時～19時

日本大学・医学部・リサーチセンター4F ホール

挨拶 13:00～13:05 泰羅雅登 日本大学 総合科学研究所

○座長:稲瀬正彦 近畿大学医学部 生理学第一講座

13:05～13:45

精密把握／到達運動課題遂行中におけるサル錐体路細胞の活動様式:一次運動野と補足運動野との比較

中隋 克己 近畿大学医学部 生理学第一講座

13:45～14:25

随意運動における皮膚感覚の制御機構

関 和彦 生理学研究所 認知行動発達機構部門

14:25～15:05

○皮質脊髄路の損傷後の手指の巧緻運動の機能回復過程における脳の再組織化

伊佐 正 生理学研究所 認知行動発達機構部門

コーヒーブレイク 15:05～15:15

○座長:高田昌彦 東京都神経科学総合研究所 統合生理研究部門

15:15～15:55

第一次運動野損傷後の把握機能の回復とその分子的基盤

肥後範行 産業技術総合研究所 脳神経情報研究部門

15:55～16:35

前頭前野から一次運動野への多シナプス性入力

宮地 重弘 東京都神経科学総合研究所 統合生理研究部門

コーヒーブレイク 16:35～16:45

○座長:南部 篤 生理学研究所 生体システム研究部門

16:45～17:25

経脳硬膜超音波ドプラー法を用いた脳機能解析

畑中 伸彦 生理学研究所 生体システム研究部門

17:25～18:05

張力の知覚に一致した一次運動野の活動性

宝田 雄大 早稲田大学 スポーツ科学部

泰羅 雅登 日本大学 総合科学研究所

18:05～18:45

運動学習の結果起こるヒトで見られる神経回路効率変化

大木 紫 杏林大学 医学部 統合生理学教室

日本大学医学部　学術フロンティア研究会「皮質運動野を考える：機能とその関連領域」.
2005（2/19）

力の知覚に一致した一次運動野の活動性　－機能的 MRI による研究－

宝田雄大[1]、土師知己[2]、泰羅雅登[2, 3]
[1]早稲田大学スポーツ科学学術院、[2]日本大学大学院医学研究科、[3]日本大学総合科学研究所

重さあるいは力の知覚に、運動指令が重要であることは以前から指摘されている（McCloskey, 1978）。実際、あるレベルの力を出しているときに、脊髄の運動ニューロンレベルの興奮性を変化させて、必要とする運動指令の大きさを変化させると知覚される重さが変化することが知られている（Aniss, 1987）。脊髄の運動ニューロンへの運動指令の起源は皮質運動野であり、重さあるいは力の知覚にこの領域の活動が深く関与することが考えられる。しかし、これまでの研究は末梢レベルでの研究がほとんどであり、重さあるいは力の知覚と大脳皮質との関連についての研究は行われていない。一方、虚血による麻痺は重さあるいは力の知覚の過大評価を引き起こすことが知られている(Goodwin, 1972)。そこで、本研究では、重さあるいは力の知覚に関する中枢神経機構を明らかにする目的で、虚血による重さあるいは力の知覚の変化と皮質の一次運動野(MI)の活動との関連について機能的 MRI を用いて調べた。

被検者は右利きの健常者 10 名（男子 7 名と女子 3 名、19-22 歳）で、書面によるインフォームドコンセントを得ている。各被験者が、自然血流下と虚血下（250mmHg の上腕基部への圧迫による）で、最大随意等尺性筋力の 20%, 40%, 60%, 80%の筋力で等尺性ハンドグリップ運動（握力）を行っている際の脳活動を機能的 MRI によって測定し、さらに、左右の flexor carpi radialis と flexor carpi ulnaris muscles の筋電図、及び被験者の発揮筋力を同時に測定した。また、被験者の力の知覚の指標として、各運動直後に CR-10 scale によって発揮した筋力の評価をおこなった。皮質の活動性については個人レベルにおいて解析をおこない、1x1x1mm で撮像した個人の T1 画像に activation 画像を重ね合わせ、活動領域が MI にあることを確認したのち、z-score ならびに% signal change でその活動性を評価した。さらに、虚血の末梢神経の伝導に対する影響を調べるため、自然血流下と虚血下での正中神経刺激に対する体性感覚誘発電位（SEP）の比較をおこなった。

筋電図のレベルにおいては、上腕基部への局所的な圧迫による虚血は運動中の筋活動に変化は見られなかった。被験者の力の知覚は被験者の発揮筋力と比例関係にあり、虚血下では自然血流下に比べ、いずれの発揮筋力レベルでも有意に増加していた($p < 0.01$)。MI の活動も、虚血の有無にかかわらず、筋力に比例して増加し、被験者の力の知覚にも比例していた。しかし、虚血下の MI の活動は、被験者の力の知覚と同様に、自然血流下に比べ全ての発揮筋力レベルで有意に増加した ($p < 0.01$)。一方、正中神経刺激による SEP の EP, N9-13, N20 の潜時及び最大振幅を自然血流下と虚血下で比較したが変化はみられなかった。

重さあるいは力の知覚と MI の活動が密接に関与していることを示す以上の結果は、重さと力の知覚の形成に大脳皮質からの出力自体が強く寄与している可能性を示唆している。

資 料　　学会発表等 2)

Masato Taira and Yudai Takarada.
Somatosensory evoked potentials during tourniquet-induced
transient occlusion of the brachial artery.
The 82nd Annual Meeting of the Physiological Society of Japan. 2005 (5/18-20)

379 (2P169)

Somatosensory evoked potentials during tourniquet-induced transient occlusion of the brachial artery

Taira, Masato[1]; Takarada, Yudai[2] (*[1]Univ. Research Center, Nihon Univ., Tokyo, Japan; [2]Faculty of Sport Sciences, Waseda Univ., Saitama, Japan*)

It has been well known that one of most rapid and efficient method for complete paralysis in whole arm is to inflate a tourniquet, which is positioned on the arm proximal to the axilla (Goodwin et al., 1972). This method may have direct effects on the distal motor organs, but also on the central neuronal system. Somatosensory evoked potentials (SEP) is one of useful techniques to detect the influence on the somatosensory system. However, there are very few previous studies which focused on the influence of arterial occlusion on SEP to median nerve stimuli. In the present study, we investigated the SEP to median nerve stimuli during the arterial occlusion.Ten right-handed volunteers (seven men and three women, 19-22 years old) with no history of neurological or other disease participated in the study. The SEP to right median nerve stimuli delivered at a rate of five per second was recorded during rest (control condition) and during vascular occlusion at a pressure of 250 mmHg applied by at a tourniquet to the proximal end of the upper arm (experimental condition). Each length of control and experimental conditions was 120 s. Although no significant change was observed in the amplitudes of Erb's potential and N13, that of N20 significantly decreased during arterial occlusion ($p < 0.01$) with the enhanced sensitivity of the thenar eminence muscle to median nerve stimuli. These results suggest that the transient, arterial occlusion around the upper arm will induce attenuation of the function in the median nerve.

380 (2P170)

Polymorphisms of ENaC subunits have no relation with mouse strain differences in amiloride-sensitive salt responses

Shigemura, Noriatsu[1]; Bachmanov, A.A.[2]; Sadamitsu, Chiharu[3]; Yasumatsu, Keiko[1]; Yoshida, Ryusuke[1]; Beauchamp, G.K.[2]; Ninomiya, Yuzo[1] (*[1]Oral Neurosci., Kyushu Univ., Fukuoka, Japan; [2]Monell Chemical Senses Center, Philadelphia, PA; [3]Pharmaceutical Sciences, University of Tokyo, Tokyo, Japan*)

Amiloride-sensitive epithelial Na^+ channels (ENaCs) are proposed to be involved in salt taste transduction. Electrophysiological studies in C57BL/6 (B6) mice demonstrated that responses to NaCl are inhibited by amilolide in the choda tympani (CT) but not in the glossopharyngeal nerve, suggesting a lack of amiloride sensitivity (AS) in the posterior tongue. The AS also differs among inbred mouse strains. Unlike B6 mice, 129P3/J (129) mice showed almost no amiloride inhibition of NaCl responses even in the CT. In this study, using B6, 129 mice and their F_2 hybrids, we examined possible relationships of the AS with mRNA expression levels in fungiform papillae (FP) and single nucleotide polymorphisms (SNPs) of three subunits of ENaC (α,β,γ). The mRNA expression levels of each ENaC subunit examined using RT-PCR analysis were similar in the B6 and 129 strains. Sequencing detected three SNPs in the α-subunit. One of these SNPs resulted in an amino acid substitution, R616W, near the predicted 2nd transmembrane domain in the 129 strain. No SNPs were found in sequences of β- and γ-subunits. Electrophysiological and sequencing analyses in F2 hybrids indicated that there was no relation between the AS and the α-subunit SNP (R616W). These results suggest that neither expression levels of the three ENaC subunits, nor the SNP in the α-subunit participate in the mouse strain differences in the AS.

381 (2P171)

Transcranial autofluorescence imaging of cortical activities elicited by amplitude-modulated sounds of various envelops in the mouse auditory cortex

Kubota, Yamato; Takahashi, Kuniyuki; Kudoh, Masaharu; Shibuki, Katsuei (*Department of Neurophysiology, Brain Research Institute, Niigata University, Niigata ,Japan*)

Flavoprotein autofluorescence is intimately coupled with neural activities and applicable for functional brain imaging. Autofluorescence imaging is especially useful for observing mouse cortical activities, because the skull of mice is transparent enough to visualize cortical autofluorescence via the intact skull. In the present study, we investigated neural activities in the auditory cortex of anesthetized mice with this technique. C57BL/6 mice were anesthetized with urethane (1.6 g/kg, i.p.). The skin covering the skull was incised, and the temporal muscle over the right auditory cortex was removed. The exposed surface of the skull was covered with liquid paraffin to prevent drying and to keep the skull transparent. Autofluorescence responses in the auditory cortex were elicited by various sound stimuli at 5–20 kHz for 500 ms. Sound stimuli were applied as pure tones or amplitude-modulated (AM) tones with a sawtooth wave at 20 Hz. Cortical responses were recorded with a cooled CCD camera attached to an epifluorescence binocular microscope. Neural activities elicited by sound stimuli at 5–20 kHz exhibited a tonotopic map in the auditory cortex. Although AM sounds modulated by a fast-rise sawtooth wave and a slow-rise sawtooth wave have the same spectral patterns, the neural activities elicited by the former were larger than those elicited by the latter, indicating neural activities in the auditory cortex are strongly influenced by the temporal profile of sound stimuli.

382 (2P172)

Retinal ganglion cell activities during fish optic nerve regeneration

Tsunoda, Shingo[1]; Watanabe, Yuta[13]; Muramoto, Kenichiro[3]; Nakashima, Hiroshi[2]; Kato, Satoru[1] (*[1]Dept. Mol. Neurobiol., Grad. Sch. Med.,; [2]Dept. Lab. Sci., Grad. Sch. Med.,; [3]Dept. Electric. Computer Eng., Grad. Sch. Nat. Sci. Tech., Kanazawa Univ., Kanazawa, Japan*)

Fish retinal ganglion cells can survive and regrow their axons after optic nerve transection. The regenerating optic axons reach to the optic tectum 1 month and thereafter the visual function recovers 3–4 months after axotomy. Therefore, we followed up spike activities of ganglion cells in the carp retina during optic nerve regeneration. The spike activity of ganglion cells (both types of ON and OFF cells) suddenly declined by less than 20% of the control value in frequency 5 days after nerve injury. The spike frequency at 50 days after axotomy was 50% of the control and it was recovered to control level at 100 days after axotomy. In contrast, the area-dependency of ganglion cells to various spots of central light stimuli (0.3–4 mm in diameter) recovered a little bit more later. The area-dependency of ganglion cell response could never be seen 5–50 days after optic nerve transection. The normal area-dependency of ganglion cell response could be only seen just 100 days after optic nerve injury. On the other hand, horizontal cell response (S-potentials) in the carp retina did not change both in amplitude and in area dependency during this long period (0–100 days) after optic nerve transection. These results strongly indicate that the recovery of area-dependency of ganglion cells in the carp retina is just well correlated with that of visual function from the optic nerve injury and horizontal cell activities in the outer retina are not affected during this period.

The 82nd Annual Meeting of the Physiological Society of Japan. 2005 (5/18)

Somatosensory evoked potentials during tourniquet-induced transient occlusion of the brachial artery

Masato Taira and Yudai Takarada

University Research Center, Nihon University, Tokyo, Japan
Faculty of Sport Sciences, Waseda University, Saitama, Japan

It has been well known that one of most rapid and efficient method for complete paralysis in whole arm is to inflate a tourniquet, which is positioned on the arm proximal to the axilla (Goodwin et al., 1972). This method may have direct effects on the distal motor organs, but also on the central neuronal system. Somatosensory evoked potentials (SEP) is one of useful techniques to detect the influence on the somatosensory system. However, there are very few previous studies which focused on the influence of arterial occlusion on SEP to median nerve stimuli. In the present study, we investigated the SEP to median nerve stimuli during the arterial occlusion.

Nine right-handed volunteers (seven men and three women, 19-22 years old) with no history of neurological or other disease participated in the study. The SEP to right median nerve stimuli delivered at a rate of five per second was recorded during rest (control condition) and during vascular occlusion at a pressure of 250 mmHg applied by at a tourniquet to the proximal end of the upper arm (experimental condition). Each length of control and experimental conditions was 120 s.

Although no significant change was observed in the amplitudes of Erb and N13, that of cortical complex (N20/P25) significantly decreased during arterial occlusion ($p<0.01$). No delays were found in the latencies of Erb, N13 and N20. These results suggest that the transient, arterial occlusion around the upper arm will have specific effects on the function in the somatosensory cortex, we will discuss underlying neural mechanisms for these results from central and peripheral viewpoints.

Key words: arterial occlusion, median nerve, somatosensory system

資 料　　学会発表 3)

Yudai Takarada, Tomoki Haji, and Masato Taira.
Activity of primary motor cortex closely correlated with sensation of force.
The 28th Annual Meeting of the Japan Neuroscience Society. 2005 (7/26-28)

P3-261 Nitric oxide-cGMP pathway is critical for cAMP-dependent long-term memory formation in the cricket

Yukihisa Matsumoto[1], Sae Unoki[1], Hitoshi Aonuma[2], Makoto Mizunami[1]
[1]Graduate School of Life Sciences, Tohoku University, Sendai, Japan; [2]Research Institute for Electronic Science, Hokkaido University, Sapporo, Japan

In some species, nitric oxide (NO)-cyclic GMP pathway is shown to act in parallel and complementary to cAMP pathway for long-term memory (LTM) formation. Here we show a new role of NO-cGMP pathway, namely to stimulate cAMP pathway to induce LTM. Multiple-trial olfactory conditioning in crickets led to LTM that lasted several days, while memory induced by single-trial decayed away within several hours. Injection of inhibitors of enzyme forming NO, cGMP or cAMP before multiple-trial blocked LTM, whereas injection of NO donor, cGMP or cAMP analogue before single-trial conditioning induced LTM. LTM induced by injection of NO donor or cGMP analogue paired with single-trial was blocked by inhibitors of cAMP pathway, but LTM induced by cAMP analogue was unaffected by inhibitors of NO-cGMP pathway, thereby suggesting that cAMP pathway is a downstream target of NO-cGMP pathway for the LTM formation.

P3-262 Activity of primary motor cortex correlated closely with sense of force

Yudai Takarada[1], Tomoki Haji[2], Masato Tira[2,3]
[1]Fac. of Sport Sci., Waseda Univ., Saitama, Japan; [2]Nihon Univ. Grad. Sch. of Med. Sci., Tokyo, Japan; [3]Univ. Res. Center, Nihon Univ., Tokyo, Japan

It has been suggested that a sensation of force is closely related to the motor command rather than the afferent input. However, it is not clear whether the motor cortex itself is involved in the sensation of force. We investigated relations between the sensation of force and the activity of the primary motor cortex (MI) by using fMRI. Ten healthy right-handed subjects performed a motor task: isometric handgrip contractions at four levels of force with or without arterial occlusion. The activity of M1 highly correlated with the sensation of handgrip force both in with- and without-occlusion conditions, however, the occlusion significantly increased the sensation of force and also the MI activity at all target forces. On the other hand, no changes were observed in the EMG activity and the early SEP with the median nerve stimulation in occlusion condition. These results suggest that the MI activity itself is closely involved in the sensation of force.

P3-263 Roles of the striatum in response bias and its complementary process

Yukiko Hori, Takafumi Minamimoto, Minoru Kimura
Dept. of Neurophysiol., Kyoto Prefect Univ. Med., Kyoto, Japan

Expectation of reward enhances action processing. But, in facing an unexpected situation, we must choose undesirable action for a future goal. We sought neural correlates of these processes in the striatum by recording activity of projection neurons (PANs, $n = 129$) and cholinergic interneurons (TANs, $n = 59$) of monkey performing asymmetrically rewarded GO-NOGO button press task. PANs exhibited tonic increase of activity before action request in either the GO-large reward ($n = 20$) or NOGO-large reward ($n = 10$) blocks. The tonic activation was either followed by action request-related activation ($n = 19$) or no activation ($n = 10$). Another PANs exhibited activation after either large reward- ($n = 8$) or small reward-request ($n = 24$). TANs showed decrease of tonic discharges after the action requests (47/59) which were not selective to reward and type of actions (40/47) except for TANs selective to reward and action (7/47). Our observations revealed evidence of the roles of the striatum in both response bias and its complementary process.

P3-264 Modulation of striatal neuron activity by planned action and reward expectation error

Hiroshi Yamada, Hitoshi Inokawa, Minoru Kimura
Dept. Physiol. Kyoto Prefect Univ. Med., Japan

Midbrain dopamine neurons send signals of incentive to work for reward and reward expectation error to the striatum. To examine how the striatal neuron activity is influenced by the dopamine signals, we recorded 97 striatal projection neurons during reward-based decision task of one monkey. After depressing a hold button, monkey chose one of three targets. Correct probabilities at first, second, third and repetition trials were 33, 50, 85 and 90%, respectively. Correct and incorrect choices were noticed by high- and low-tone beeps. Sixty-three neurons showed activity before and/or after the reinforcer beeps. Neuron activity was positively (3) or negatively (16) correlated with reward probability, selective to either correct (5) or incorrect beep (7), selective to whether the trial was repetition (2) or not (3), selective to the target chosen (13). Our results revealed that the striatal neuron activity is modulated by the signals of reward expectation errors and of planned actions during reward-based decision and choice of action.

P3-265 Binary counting of motor performance by cells in the pre-supplementary motor area of monkey

Keisetsu Shima, Jun Tanji
Dpt. Physiol. Tohoku Univ., Sendai, Japan

We trained two monkeys to perform three different forelimb movements in two different manners. Initially, monkeys performed five trials under visual guidance, to select and respond with corresponding three movements to each cue (visual block). Thereafter, they were required to repeat the same memorized sequence either five or six trials (memory block). A flash of lights told the beginning of a new sequence. We recorded cellular activity from the SMA, pre-SMA and the primary motor cortex (M1) under this behavioral condition. We found 85 cells in the pre-SMA that exhibited two distinct levels of activity: discharges in higher-range and lower-range. What was striking was that the two levels of activity alternated in successive trials. In a majority of cases, the alternating activity level was reset when performing the first visual trial. Thus, in half of such cells activity was higher at odd number of trials, while in the other half activity was higher at even number of trials. Such binary-state property was rare in the SMA, and not found in the MI.

P3-267 Critical involvement of the lateral prefrontal cortex in suppression of both voluntary and externally-guided saccade

Mariko Kuwajima, Toshiyuki Sawaguchi
Lab. Cogn. Neurobiol., Hokkaido Univ. Grad. Sch. Med., Sapporo, Japan

Suppression of both internally driven saccade (i.e., "voluntary saccade") and externally-guided one according to a given situation is important for an appropriate behavioral control. To examine a possible involvement of the lateral prefrontal cortex (LPFC) in such functions, we locally injected muscimol at various sites in the LPFC of monkeys that performed an oculomotor Go/No-Go (OGNG) task. Muscimol injection at several sites in the LPFC induced significant increase in fixation breaks toward the contralateral visual field during the period before a cue is presented and/or false saccades toward a specific target location during the period when the monkey was required to suppress its gaze toward it. These results suggest that the LPFC is essential for suppression of not only externally-guided saccade toward an overt visible target but also voluntary saccade without such an overt target in a given situation, thereby contributing to efficient inhibitory controls of ocular behavior.

The 28th Annual Meeting of the Japan Neuroscience Society. 2005 (7/28)

Activity of primary motor cortex closely correlated with sensation of force

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Nihon Univ Grad Sch of Med Sci,
Univ Res Center, Nihon Univ

It has been suggested that a sensation of force is closely related to the motor command rather than the afferent input. However, it is not clear whether the motor cortex itself is involved in the sensation of force. We investigated relations between the sensation of force and the activity of the primary motor cortex (MI) by using fMRI. Ten healthy right-handed subjects performed a motor task: isometric handgrip contractions at four levels of force with or without arterial occlusion. The activity of MI highly correlated with the sensation of handgrip force both in with- and without-occlusion conditions, however, the occlusion significantly increased the sensation of force and also the MI activity at all target forces. On the other hand, no changes were observed in the EMG activity and the early SEP with the median nerve stimulation in occlusion condition. These results suggest that the MI activity itself is closely involved in the sensation of force.

資 料　　学会発表等 4）

宝田雄大. 重さの知覚（Sense of heaviness）.
杏林大学医学部「随意運動の調節機構とその病態生理研究会」. 2006（3/4-5）

プログラム

平成 18 年 3 月 4 日(土曜日)

9:30-10:30　杏林大学統合生理[1], 順天堂大学生理学第一[2]. 科学技術振興機構[3]

渋谷賢[1], 高橋俊光[2, 3], 北澤茂[2, 3]

(座長　杏林大学　大木紫)

片手3本指刺激の時間順序判断

10:30-11:30　国立身体障害者リハビリテーションセンター研究所

関口浩文, 河野豊, 赤居正美, 中島八十一, 中澤公孝

(座長　千葉大学　小宮山伴与志)

筋収縮様式に関する皮質脊髄路興奮性

13:00-14:00　慶應義塾大学理工学部生命情報学科, 慶應義塾大学月が瀬リハビリテーションセンター*　勝正範, 牛場潤一, 正門由久*, 富田豊

(座長　順天堂大学　遠藤隆志)

筋疲労にともなう脳波－筋電図コヒーレンスの増加

14:00-15:00　早稲田大学スポーツ科学学術院[1], 国立身体障害者リハビリテーションセンター研究所[2], 日本大学大学院医学研究科[3], 日本大学総合科学研究所[4]

宝田雄大[1], 野崎大地[2], 土師知己[3], 泰羅雅登[4]

(座長　杏林大学　小川潤)

重さの知覚

15:00-16:00　杏林大学整形外科　滝徳宗, 宝亀登, 相川大介, 里見和彦

頸髄症患者の定量的運動機能評価の試み

(座長　長野病院　進藤政臣)

16:00-　特別講演

杏林大学統合生理, 東京都神経科学総合研究所システム生理研究部門*

平井直樹, 佐々木茂人*

(座長　東北文化学園大学　田中勵作)

18:30-　懇親会

平成 18 年 3 月 5 日(日曜日)

9:00-10:00　杏林大学整形外科, 統合生理*

佐野秀仁, 渋谷賢*, 小川潤, 里見和彦, 大木紫*

(座長　東京学芸大学　中島剛)

Corticospinal tract を中継する脊髄固有ニューロンに見られる左右差

10:00-11:00　東京学芸大学連合学校教育学研究科　田添歳樹

(座長　広島大学　高橋真)

足関節背屈による上肢筋運動野の抑制低下

時間は暫定的なものであり、変更される可能性があります。

5 日は、12:30 頃の終了を予定しています。

演者の方へ:

発表は原則として、パソコンプロジェクターを用いて行います。パソコン、もしくは発表ファイル(Power Point 限定、媒体:USB メモリ、CD-R)をご持参ください。

資 料　　学会発表等 5）

宝田雄大. 力の知覚に一致した一次運動野の活動性 ーfMRIによる研究ー.
早稲田大学人間総合研究センター 「スポーツと脳機能」. 2006 (3/17)

プログラム

◇挨拶：12:30～12:40
山崎勝男　スポーツ科学学術院長

◇教育講演：12:40～13:15
司会：渡邉丈夫
佐々木由香
MRIを用いた脳機能研究のテクニック
早稲田大学人間総合研究センタープロジェクト研究員
ハーバード大学医学部

◇特別講演：13:20～14:20
司会：宝田雄大
丹治　順
アクションをもたらす脳の高次機能
玉川大学学術研究所脳科学研究施設

◇シンポジウム第1部
司会：大築立志、彼末一之
誉田雅之　(14:30～14:50)
感覚タスクに基づく動作プラニング機構
早稲田大学人間総合研究センタープロジェクト研究員
宝田雄大　(14:50～15:10)
力の知覚に一致した一次運動野の活動性 ―機能的MRIによる研究―
早稲田大学人間総合研究センタープロジェクト研究員
彼末一之　(15:10～15:30)
複数肢協調動作の制御機構
早稲田大学人間総合研究センタープロジェクト研究員
大築立志　(15:30～16:10)
熟練スポーツ動作の脳制御
東京大学大学院総合文化研究科

◇Coffee break　(16:10～16:25)

◇シンポジウム第2部

司会：中島八十一、内田 直

内田　直　(16:25～16:45)

脳画像研究とスポーツ

早稲田大学人間総合研究センタープロジェクト研究員

正木宏明　(16:45～17:10)

事象関連電位によるアクションモニタリング機能の研究

早稲田大学人間総合研究センタープロジェクト研究員

中島八十一　(17:10～17:50)

スポーツから脳を護る ―高次脳機能障害との闘い―

国立身体障害者リハビリテーションセンター研究所

◇総合討論　(17:50～18:20)

■懇親会　18:40～

場所：大隈ガーデンハウス

立食形式

力の知覚に一致した一次運動野の活動性
ー機能的 MRI による研究ー

宝田雄大[1]、土師知己[2]、泰羅雅登[2,3]
[1]早稲田大学スポーツ科学学術院、[2]日本大学大学院医学研究科、[3]日本大学総合科学研究所

重さあるいは力の知覚に、運動指令が重要であることは以前から指摘されている (McCloskey, 1978)。実際、任意のレベルの力を発揮しているときに、脊髄の運動ニューロンの興奮性を変化させて、必要とする運動指令の大きさを変化させると知覚される重さが変化することが知られている (Aniss, 1987) 。

最近我々は、虚血 (動静脈阻血) がハンドグリップ力の知覚を増大させることを両側の重量合わせの実験により確かめた (Takarada and Taira, 2005)。またこの実験では、虚血の末梢神経の伝導に対する影響を調べるために、自然血流下と虚血下での正中神経刺激に対する体性感覚誘発電位 (SEP) とM波の比較をおこなった。SEP の EP と N20 の潜時及び最大振幅とM波の積分値を両条件で比較したが変化はみられなかったことから、虚血中の力の知覚の増大には中枢性の運動指令が強く関与していることが示唆された。

そもそも、脊髄の運動ニューロンへの運動指令の起源は皮質運動野であり、重さあるいは力の知覚にこの領域の活動が深く関与することが考えられる。しかし、これまでの研究は末梢レベルでの研究がほとんどであり、重さあるいは力の知覚と大脳皮質との関連についての研究は行われていない。そこで、本研究では、重さあるいは力の知覚に関する中枢神経機構を明らかにする目的で、虚血による重さあるいは力の知覚の変化と皮質の一次運動野(MI)の活動との関連について機能的 MRI を用いて調べた。

各被験者 (右利きの健常者 10 名) が、自然血流下と虚下で、最大随意等尺性筋力の 20%, 40%, 60%, 80%の筋力で等尺性ハンドグリップ運動を行っているときの脳活動を機能的 MRI によって測定し、さらに、左右の前腕屈筋の筋電図、及び発揮筋力を同時に測定した。また、被験者の力の知覚の指標として、各運動直後に CR-10 scale によって発揮した筋力の評価をおこなった。皮質の活動性については個人レベルにおいて解析をおこない、1x 1x1mm で撮像した個人の T1 画像に activation 画像を重ね合わせ、活動領域が MI にあることを確認したのち、relative BOLD signal change でその活動性を評価した。

上腕基部への虚血は運動中の筋活動に何らの変化も与えなかった。被験者の力の知覚は被験者の発揮筋力と比例関係にあり、虚血下では自然血流下に比べ、いずれの発揮筋力レベルでも有意に増加していた。MI の活動も、虚血の有無にかかわらず、筋力に比例して増加し、被験者の力の知覚にも比例していた。しかし、虚血下の MI の活動は、被験者の力の知覚と同様に、自然血流下に比べ全ての発揮筋力レベルで有意に増加した。重さあるいは力の知覚と MI の活動が密接に関与していることを示す以上の結果は、重さと力の知覚の形成に大脳皮質からの出力自体が強く寄与している可能性を示唆している。

〔略歴 : 65 年生まれ、01 年東京大学大学院 博士課程修了 (学術博士)、専門は運動神経生理学。〕

資 料　　学会発表等 6)

Yudai Takarada, Tomoki Haji, and Masato Taira.
Activity of primary motor cortex closely correlated with sensation of force.
12th Annual Meeting of the Organization for Human Brain Mapping. 2006 (6/11-15)

COGNITION AND ATTENTION
Perception, Imagery, Spatial

12th Annual Meeting of the Organization for Human Brain Mapping. 2006 (6/11)

Activity of primary motor cortex closely correlated with sensation of force

Yudai Takarada, Tomoki Haji, and Masato Taira
Fac of Sport Sci, Waseda Univ.,
Nihon Univ Grad Sch of Med Sci,
Univ Res Center, Nihon Univ

It is a common experience that muscular fatigue produce perception of an increased effort to achieve a given force. In such a case, the force perception has been well known to depend more on motor command required to achieve the muscular force than afferent sensations signaling the muscular force achieved (McCloskey, 1978).

Recently, we reported that a tourniquet-induced arterial occlusion elevates the perceived magnitude of a handgrip force by using the contralateral limb-matching method (Takarada and Taira, 2005). In that study, we also examined SEPs and the M response under the arterial occlusion, and found that there was no serious effects on the median nerve function per se. These results strongly suggest that the centrally generated motor command is contributed to the overestimation of force during arterial occlusion.

The activity of the primary motor cortex (MI) is a strong candidate for the centrally generated motor command involved in the force perception; however, there has been no study on the force perception in reference with a function of MI. We investigated relations between the sensation of force and the activity of MI by using fMRI.

Ten right-handed volunteers (seven men and two women; aged 20.3 ± 0.82 years old, mean ± SD) with no history of neurological or other disease participated in the study. All of the subjects were previously informed well about the experimental procedure to be utilized as well as the purpose of this study, and their written informed consent was obtained. We measured the brain activity with fMRI during unilateral isometric handgrip contractions at the predetermined target level of muscular force [20%, 40%, 60%, and 80% of maximal voluntary contraction (MVC)] with or without the tourniquet-induced arterial occlusion. During the fMRI scans EMG

activities were, also, recorded from the skin surface of wrist flexor muscles. Subjects were asked to numerically assess the perceived magnitude of exerted forces immediately after the handgrip contractions.

The activity of MI estimated by the relative BOLD signal change highly correlated with the sensation of force both in with- and without-occlusion conditions, however, the occlusion significantly did not increased the force sensation ($p < 0.01$, Student's paired *t*-test) (Figure 1), but also the MI activity at all target forces ($p < 0.05$, Student's paired *t*-test) (Figure 2) with no changes of the somatosensory cortex (SI) activity. On the other hand, no changes were observed in the EMG activity between those two conditions. These results suggest that the MI activity itself is closely involved in the force perception.

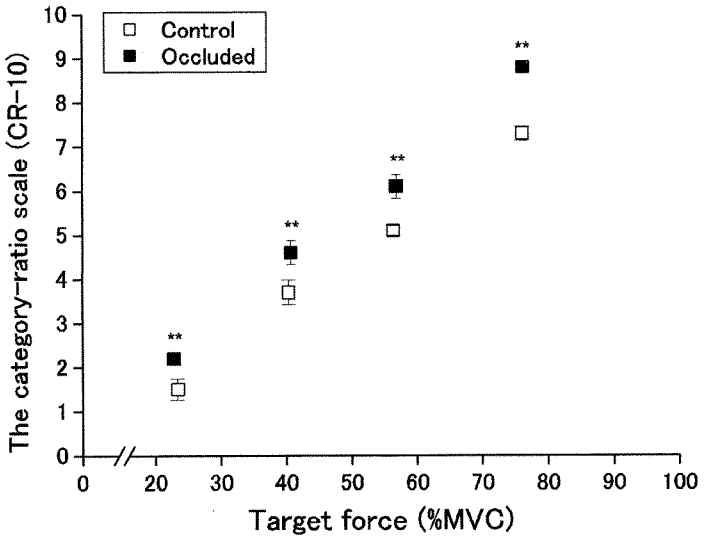

Figure 1. Effects of arterial occlusion on numerical estimation of the perceived handgrip force. Values of exerted handgrip force were normalized to those during the maximal voluntary contraction (MVC) in each subject. All values are shown as means ± SE (n = 9). **Statistically significant difference between values during handgrip contractions with no arterial occlusion and those during contractions with that at the almost same target force ($p < 0.01$, Student's paired t-test).

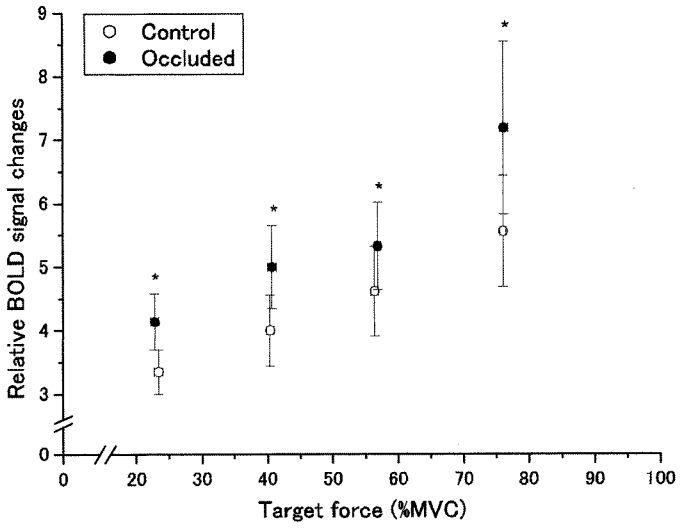

Figure 2. Effects of arterial occlusion on fMRI-measured activation of the primary cortex (MI). The fMRI-measured activations of MI were shown as relative BOLD signal changes. All values of exerted handgrip force were normalized to those during the maximal voluntary contraction (MVC) in each subject. All values are shown as means±SE (n = 9). *Statistically significant difference between values in handgrip contraction with arterial occlusion and those in contraction without that at the almost same intensity ($p < 0.05$ Student's paired t-test).

資 料　　学会発表等 7）

宝田雄大. 虚血が引き起こす筋肥大と力の知覚の増大.
防衛医科大学校「バイオを論じる会」. 2007 (1/26-27)

防衛医科大学校「バイオを論じる会」. 2007（1/26）

①演題名

Ischemia-induced muscular hypertrophy and force overestimation

虚血が引き起こす筋肥大と力の知覚の増大

②演者と所属

Yudai Takarada

Fac. of Sport Sci., Waseda Univ., Saitama,

宝田雄大

早稲田大学　スポーツ科学学術院　スポーツ医科学科

③抄録

ヒト骨格筋では、通常筋肥大を伴った筋力の改善には最大筋力の約 65%以上の運動強度が必要とされてきた。しかし、極端に低強度な運動においても虚血下で運動をおこなうと、顕著な筋力と筋断面積の増加が生じることが明らかにされている。この効果には虚血による筋内環境の変化が深く関係していることが確認され、結果的に骨格筋の適応が運動強度の機械的刺激により一義的に決定されるわけではないことが分かった。

一方、虚血は発揮筋力の大きさに対する知覚を顕著に増大させる。すでに短時間の上腕基部への局所的な圧迫は末梢神経機能を阻害しないことが分かっているので、この知覚の増大は発揮筋力に注がれる中枢性の要因に起因する可能性が高い。実際、力の知覚は一次運動野（MI）の活動と相関が高い。また、MI 活動と知覚の増大には何らの運動出力の変化もともなわなかったことから、MI の神経活動自体が力の知覚を生み出している可能性が示唆された。

資 料　　学会発表等 8）

Takarada, Y.

Activity of primary motor cortex closely correlated with force perception.

The 340th HBRC Seminar. Kyoto University Graduate School of Medicine Human Brain Research Center. 2007 (1/31)

The 340th HBRC Seminar

updated on 2007/01/24

日時：平成19年1月31日（水）　午前9時00分～午前10時00分
31st. Jan. (Wed), 2007　9:00～10:00

演者：宝田雄大　Yudai Takarada
早稲田大学　スポーツ科学学術院　助教授
Fac. of Sport Sci., Waseda Univ., Saitama

タイトル：力の知覚と相関している一次運動野の活動
Activity of primary motor cortex closely correlated with force perception

場所：旧産科病棟3階　高次脳機能総合研究センター　カンファレンス室
Old Gynecology Bldg. 3F Human Brain Research Center
Conference room

京都大学大学院医学研究科附属高次脳機能総合研究センター
「第340回 高次脳機能総合研究セミナー」. 2007 (1/31)

抄録

虚血は発揮筋力の大きさに対する知覚（力の知覚）を顕著に増大させる。すでに短時間の上腕基部への局所的な圧迫は、正常な末梢神経機能を阻害しないことが分かっているので、この知覚の増大は発揮筋力に注がれる中枢性の要因に起因する可能性が高い。実際、力の知覚は一次運動野（MI）の活動と相関が高い。また、MI活動と知覚の増大には何らの運動出力の変化もともなわなかったことから、MIの神経活動自体が力の知覚を生み出している可能性が示唆された。