Relationship between Cerebral Activity and Movement Frequency of Maximal Finger Tapping

Naomi Kuboyama¹⁾, Teru Nabetani²⁾, Kenichi Shibuya³⁾, Keishi Machida⁴⁾ and Tetsuro Ogaki^{1,5)}

1) Graduate School of Human Environment Studies, Kyushu University

2) Department of Contemporary Communication, Shizuoka Eiwa Gakuin University Junior College

3) Department of Sports Science, Japan Institute of Sports Science

4) Hitachi Medical Co. Ltd., Tokyo

5) Institute of Health Science, Kyushu University

Abstract To examine the cerebral activity of the motor cortex during maximum movement, we measured regional cerebral blood flow (rCBF) in twelve normal volunteers, using near infrared spectroscopy (NIRS). Repetitive tapping of the right index finger was performed at 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, and 4.5 Hz, and during maximum effort (ME). The relative increase rate of rCBF during movement beginning with a resting condition was calculated for each movement condition. The left primary sensorimotor cortex showed significant activation during ME compared to the other frequencies. The rapid increase of rCBF was seen immediately after the initiation of finger tapping at all the tested frequencies but showed no increase following that. However, the rCBF during ME continued to increase until the end of the task.

Change of the integrated electromyogram (iEMG) for the frequency and change of rCBF for the frequency at all the tested frequencies showed similar tendencies. *J Physiol Anthropol Appl Human Sci* 24(3): 201–208, 2005 <http://www.jstage.jst.go.jp/browse/jpa>
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Introduction

Studies in humans through the use of positron emission tomography (PET) and rCBF signal changes as an indirect index of brain activity have explored the effect of stimulus rate on the central nervous system, particularly in the primary visual cortex (Fox and Raichle, 1984). The rCBF change in the striate cortex is proportional to the repetition rate of photic stimulation between 0 and 7.8 Hz (Fox and Raichle, 1984). In other studies, a linear relationship was also observed in the

primary auditory cortex (Wise et al., 1991; Price et al., 1992). These studies underscore the significance of the stimulus rate as a determinant of rCBF response. Moreover, research has also been conducted on the relationship between frequency and rCBF using a movement stimulus (Sadato et al., 1996; Jenkins et al., 1997).

Jenkins et al. (1997) examined the effect of joystick movement, in frequencies that ranged from 1/sec to 1 every 5.5 sec in 0.5 s steps, on cerebral activation. They observed no significant relationship between movement frequency and cerebral activation. Furthermore, Sadato et al. (1997) measured rCBF by PET and reported that the relationship between motor cortex activation and movement frequency was not significant, and tended to plateau as the frequency reached 4 Hz.

In these studies, cerebral activation showed a nonlinear increase, indicating an exponential rise. Thus, the relationship between stimulus frequency and brain activity differs in terms of the region of the brain and the type of stimulation. In brain activity studies using movement stimulus, movement was restricted by the limitations of the test equipment and was not performed with high frequency stimuli of over 4.0 Hz. Due to noise interference while the body is being measured, measurement of movements of high frequency is impossible.

For this reason, the relationship between a movement stimulus and rCBF has not been examined at high frequencies (over 4.0 Hz).

Therefore, brain activity at high frequencies is still unknown. It is important to know the reaction of rCBF for the frequency so that the mechanism of movement can be evaluated.

Changes in cerebral hemodynamics and oxygenation can be measured using several techniques. For example, positron emission tomography (PET) or tracer methods such as ¹³³Xe-single photon emission computer tomography (SPECT) have been used to measure changes in rCBF. These methods, however, are associated with the injection of radioactive

compounds, and have a low temporal resolution (Villringer, 1997). Transcranial Doppler (TCD) sonography has been used to monitor changes in blood flow velocity in the large cerebral arteries. This method has a high degree of temporal resolution, but does not provide information regarding regional changes in cerebral oxygen supply or metabolism (Hirth et al., 1997; Vernieri et al., 1999).

On the other hand, studies using NIRS and functional magnetic resonance imaging (fMRI) allow non-invasive monitoring of regional changes in cortical tissue oxygenation in response to various stimuli including visual, auditory, and exercise stimuli (Colier et al., 1997, 1999; Kleinschmidt et al., 1996; Mehagnoul-Schipper et al., 2000; Obrig et al., 1996, 2000; Rao et al., 1993; van der Kallen et al., 1998).

The fMRI and the PET methods are vulnerable to movement artifacts and limitations in monitoring changes in cerebral oxygenation during dynamic movement. On the other hand, NIRS has an advantage in that it permits specific monitoring of changes in oxy-hemoglobin (oxy-Hb), deoxy-hemoglobin (deoxy-Hb), and total-hemoglobin (total-Hb) with high temporal resolution even during dynamic movement (Colier et al., 1997). Therefore, in order to measure brain activity at high movement frequencies, including maximum effort (ME), it is necessary to use NIRS.

In regard to the relationship between brain activity and muscle output, Dettmers et al. (1995) reported a direct relationship between the index finger flexion force and increases in cerebral blood flow in four motor-related brain regions: the contralateral sensorimotor cortex, the supplementary motor area, the cingulate cortex, and the cerebellum. Based on single-cell recordings taken in the primary motor cortex in monkeys, a direct relationship between the neuronal discharge rate and exerted force has been reported (Evarts, 1968; Hepp-Reymond et al., 1978, 1999).

These findings suggest that brain activity and cerebral blood flow are directly related to muscle output. Thus, in order to elucidate the true relationship between movement frequency and brain activity, it is necessary to measure muscle activity simultaneously.

The purpose of the present study was to observe the value of brain hemoglobin at ME which has not previously been investigated. Simultaneously, muscle activity was measured using EMG, and it was examined and compared with brain activity.

Method

Subjects

Five men and seven women, ranging in age from 22 to 37 years [25.9 ± 4.9 (mean $\pm$ SD) years] participated. All of them were right-handed as indicated by self-report. All subjects were healthy and had no known neuromuscular disorders. All subjects gave informed consent prior to participation in the study.

Motor tasks

The subjects sat in a chair and were asked to press a button on the table repetitively with their right index finger. Cerebral activation was measured by NIRS during finger tapping. To investigate the effect of movement frequency on cerebral activation, subjects were randomly divided into two groups between which there were no differences. In the low frequency group, the finger tapping frequencies were performed at 1.0, 1.5, 2.0, 2.5, 3.0 Hz, and at ME. In the high-frequency group, the finger-tapping frequencies were performed at 2.5, 3.0, 3.5, 4.0, 4.5 Hz and at ME. In both groups, the experimental order of frequencies was randomized. Finger tapping in the range of 1.0 Hz to 4.5 Hz was regulated by the sound of an electrical metronome (average achievement ratio: 89%). Each of the finger-tapping cycles lasted 20 s, followed by a 40 s rest period. Three cycles were performed. The rCBF of the left primary motor cortex was measured by NIRS throughout the three cycles.

Near infrared spectroscopy (NIRS)

NIRS, a new noninvasive optical technique, measures changes in concentrations of oxygenated and deoxygenated hemoglobin (oxy-Hb and deoxy-Hb, respectively) mainly in cerebral venous blood. Summation of the changes in oxy-Hb and deoxy-Hb indicates changes in the total hemoglobin concentration (total-Hb). The change in total-Hb can be used as a measure of blood volume changes (Delpy et al., 1988).

The 24-channel two-wavelength NIRS system (ETG-100; Hitachi Medical Corporation, Tokyo, Japan) (Koizumi et al., 1999) has eight light-incident and eight detector fibers. The light sources were 0.5 mW continuous laser diodes with wavelengths of 780 and 830 nm. Oscillators were used to modulate the intensity of each diode to within the range of 1.0 to 4.9 kHz in order to prevent cross-talk between the channels and the wave length (Maki et al., 1995). The optodes were positioned over the left motor cortex enclosing C3 according to the 10 to 20 system for standard electrode positions (American Electroencephalographic Society, 1994).

The optodes were attached to a tight elastic headband in order to press them against the scalp. Changes in total-Hb, oxy-Hb, and deoxy-Hb were sampled every 0.1 s and stored on a floppy disk for offline analysis by a computerized system. Before the beginning of the protocol, the oxygenation response was checked for 20-s 2 Hz finger tapping. If no oxygenation change could be detected, the optodes were moved, less than 1 cm, until a response was signaled (Colier et al., 1997).

Electromyography (EMG) signal

Surface EMG was recorded from the extensor digitorum and flexor carpi radialis during finger tapping. Bipolar electrodes (4 mm in recording diameter) were attached to the skin overlaying the muscle in the forearm with a reference electrode. The muscles were identified by palpating the skin surface while the subject moved the index finger. The EMG signal was recorded during finger tapping at different

frequencies. The EMG signal was digitized at a rate of 1000 samples/s and saved onto the hard disk of a personal computer for off-line analysis. The EMG was rectified and averaged over a 500-ms period when the EMG was greatest.

Statistical analysis

All parameters are described by mean $\pm$ SD. The NIRS time trend was analyzed by repeated measures ANOVA, with the Bonferroni correction for post-hoc tests. $p<0.05$ was considered statistically significant.

Results

There were no significant differences in maximal finger tapping scores between the low frequency group and the high frequency group subjects.

The finger-tapping task at ME was 5.7 ± 0.5 Hz in the low frequency group, and was 6.6 ± 0.9 Hz in the high frequency

group. The finger tapping caused activity in the motor cortex in all frequencies.

In the low frequency group, no significant increases in total-Hb, oxy-Hb, and deoxy-Hb were seen from 1.0 Hz to 3.0 Hz. In the high frequency group, no significant increases in total-Hb, oxy-Hb, and deoxy-Hb were seen from 2.5 Hz to 4.5 Hz.

As for the total-Hb during ME, both groups (high: 0.386 ± 0.049 mmol*mm, low: 0.301 ± 0.048 mmol*mm) showed significantly high values compared with those at other frequencies ($p<0.01$). Oxy-Hb (high: 0.343 ± 0.037 mmol*mm, low: 0.300 ± 0.021 mmol*mm) also showed similar trends. In the low frequency group, deoxy-Hb showed no significance. In the high frequency group, deoxy-Hb (0.023 ± 0.015 mmol*mm) at ME showed significantly high values compared with those at other frequencies ($p<0.05$). Table 1 and Fig. 1 summarize the results of the increase of oxy-Hb, deoxy-Hb, and total-Hb in relation to their baseline values in the low frequency group and the high frequency group.

Table 1 Average changes in oxy-hemoglobin ([oxy-Hb]), deoxy-hemoglobin ([deoxy-Hb]), and total hemoglobin ([total-Hb]) concentrations as measured from their baseline values by NIRS over the left motor cortex, and average changes in electromyographic (EMG) over muscle of extensor digitorum (ED) and muscle of flexor carpi radialis (FCR) at 1.0, 1.5, 2.0, 2.5, 3.0 Hz and ME (5.7 Hz) during 20 s finger tapping task in the low frequency group.

	Δ total-Hb	Δ oxy-Hb	Δ deoxy-Hb	extensor digitorum communis	superficial finger flexor
2.5 Hz(#1)	0.049 ± 0.011	0.045 ± 0.009	0.009 ± 0.017	0.008 ± 0.005	0.027 ± 0.015
3.0 Hz(#2)	0.052 ± 0.014	0.037 ± 0.005	0.001 ± 0.006	0.008 ± 0.005	0.030 ± 0.021
3.5 Hz(#3)	0.042 ± 0.017	0.039 ± 0.009	0.005 ± 0.008	0.007 ± 0.005	0.027 ± 0.016
4.0 Hz(#4)	0.045 ± 0.016	0.035 ± 0.014	0.002 ± 0.012	0.009 ± 0.006	0.030 ± 0.015
4.5 Hz(#5)	0.045 ± 0.034	0.036 ± 0.020	0.005 ± 0.007	0.011 ± 0.007	0.029 ± 0.015
max(6.6 Hz)(#6)	0.364 ± 0.105	0.303 ± 0.094	0.083 ± 0.091	0.051 ± 0.028	0.071 ± 0.035
<i>p</i> -value	$9.10\text{E}-40$	$1.29\text{E}-37$	$1.38\text{E}-27$	$2.1\text{E}-06$	$5.0\text{E}-03$
significant	#6>#1.2.3.4.5	#6>#1.2.3.4.5	#6>#1.2.3.4.5	#6>#1.2.3.4.5	#6>#1.2.3.4.5

The increase of [total-Hb] and [oxy-Hb] at ME from their baseline values were significantly higher than other frequencies ($p<0.01$). EMG at ME were significantly higher than other frequencies ($p<0.01$). Data are presented as mean $\pm$ SD. ** Significantly changes from base line value ($p<0.01$).

Fig. 1 A: In the low frequency group, change in total hemoglobin [total-Hb] concentrations as measured by NIRS over the left motor cortex in healthy subjects (n=6) during a 20-sec contralateral finger tapping task. Total-Hb at ME (5.7 ± 0.5 Hz) shows significantly high values compared with those at other frequencies ($p<0.01$). ** Significantly changes from base line value. Data are presented as mean $\pm$ SD. B: In the high frequency group, change in total hemoglobin [total-Hb] concentrations as measured by NIRS over the left motor cortex in healthy subjects (n=6) during a 20-sec contralateral finger tapping task. Total-Hb at ME (6.6 ± 0.9 Hz) shows significantly high values compared with those at other frequencies ($p<0.01$). ** Significantly changes from base line value. Data are presented as mean $\pm$ SD.

In a change of rCBF with time course during finger tapping for 20 seconds, an increase of rapid rCBF was seen in the frequency range of 1.0 Hz to 4.5 Hz immediately after the initiation of the finger-tapping task. However, it did not increase afterwards. The total-Hb during ME increased immediately after the initiation of motion. This increase continued to the end of the finger-tapping task.

Table 2 and Fig. 2 summarize the results of iEMG in the low frequency group and the high frequency group.

The iEMG was not significant in the range of 1.0 Hz to 4.5 Hz. The iEMG during ME, (extensor digitorum communis: low frequency group 0.026 ± 0.007 mV, high frequency group 0.051 ± 0.028 mV, superficial finger flexor: low frequency group 0.054 ± 0.026 mV, high frequency group $0.071 \pm$

0.035 mV) showed values comparable to other frequencies and was significantly high ($p < 0.05$).

Discussion

We found that the relationship between brain activity and movement frequency was not exponential. The increased rCBF during ME was significantly higher than at other frequencies, and the increased rCBF during ME differed from the exponential nature that the relationship between tapping frequency and brain activation had been reported (Jenkins et al., 1997; Sadato et al., 1996).

Some studies have investigated the relationship between brain activity and movement frequency. In studies using visual

Table 2 Average changes in oxy-hemoglobin ([oxy-Hb]), deoxy-hemoglobin ([deoxy-Hb]), and total hemoglobin ([total-Hb]) concentrations as measured from their baseline values by NIRS over the left motor cortex, and average changes in electromyographic (EMG) over muscle of extensor digitorum (ED) and muscle of flexor carpi radialis (FCR) at 2.5, 3.0, 3.5, 4.0, 4.5 Hz and ME (6.6 Hz) during 20 s finger tapping task in the high frequency group.

	Δ total-Hb	Δ oxy-Hb	Δ deoxy-Hb	extensor digitorum communis	superficial finger flexor
1.0 Hz(#1)	0.064 ± 0.008	0.041 ± 0.010	0.008 ± 0.009	0.013 ± 0.006	0.027 ± 0.016
1.5 Hz(#2)	0.054 ± 0.016	0.030 ± 0.004	0.002 ± 0.007	0.013 ± 0.009	0.024 ± 0.014
2.0 Hz(#3)	0.050 ± 0.011	0.043 ± 0.018	0.003 ± 0.011	0.013 ± 0.007	0.026 ± 0.014
2.5 Hz(#4)	0.054 ± 0.017	0.043 ± 0.008	0.009 ± 0.003	0.018 ± 0.010	0.031 ± 0.017
3.0 Hz(#5)	0.065 ± 0.035	0.045 ± 0.021	0.010 ± 0.003	0.014 ± 0.007	0.030 ± 0.018
max(5.7 Hz)(#6)	0.221 ± 0.108	0.202 ± 0.029	0.028 ± 0.071	0.026 ± 0.007	0.054 ± 0.026
<i>p</i> -value	$6.78E-42$	$4.75E-47$	$7.86E-13$	0.048	0.060
significant	#6>#1.2.3.4.5	#6>#1.2.3.4.5	#6>#1.2.3.4.5	#6>#1.2.3.4.5	N.S

The increase of [total-Hb] and [oxy-Hb] at ME from their baseline values were significantly higher than other frequencies ($p < 0.01$). EMG at ME were significantly higher than other frequencies ($p < 0.01$). Data are presented as mean $\pm$ SD. ** Significantly changes from base line value ($p < 0.01$).

Fig. 2 A: In the low frequency group, change in electromyography (EMG) signal over muscle of extensor digitorum (ED) and muscle of flexor carpi radialis (FCR) in healthy subjects ($n=6$) during a 20-sec right finger tapping task. EMG at ME [ED(●): 0.054 ± 0.026 mV; FCR(○): 0.026 ± 0.007 mV] shows significantly high values compared with those at other frequencies ($p < 0.01$). ** Significantly changes from base line value. Data are presented as mean $\pm$ SD.
B: In the high frequency group, change in electromyography (EMG) signal over muscle of extensor digitorum (ED) and muscle of flexor carpi radialis (FCR) in healthy subjects ($n=6$) during a 20-sec right finger tapping task. EMG at ME [ED(●): 0.071 ± 0.035 mV; FCR(○): 0.051 ± 0.028 mV] shows significantly high values compared with those at other frequencies ($p < 0.01$). ** Significantly changes from base line value. Data are presented as mean $\pm$ SD.

stimuli, Fox and Raichle (1984) reported the rCBF change was proportional to the repetition rate of photic stimulation between 0 and 7.8 Hz in the primary visual cortex. Wise et al. (1991) and Price et al. (1992), who used auditory stimuli, also observed a linear relationship in the primary auditory cortex. Thus, the relationship between visual and auditory stimuli and brain activity was seen to be linear.

The present study used a movement stimulus. The increased rCBF-related frequency range from 1.0 Hz to 4.5 Hz was not significant. The rCBF during ME showed a significantly higher value than at other frequencies. The relationship between movement frequency and brain activity was not seen to be linear. Thus, the relationship between movement stimulus and brain activity and that of visual and auditory stimulus differ. That means that the reaction to stimulus is different in terms of brain region.

Some researchers have reported the relationship between movement stimulus frequency and brain activity. Jenkins et al. (1997) observed that the relationship between brain activity and movement frequency is exponential during movement under 1.0 Hz. Sadato et al. (1997) reported that the change in motor cortex activation was not significant, and increased rCBF tended to plateau during movement as the frequency reached 4.0 Hz. On the basis of the above studies ranging from 1.0 Hz to 4.0 Hz, a range increase of rCBF was seen immediately after the initiation of movement but showed no increase following that during movement in each frequency. And there was no significant difference in cerebral activation. In the present study in the range from 1.0 Hz to 4.5 Hz, the results showed that the relationship between movement frequency and brain activity is in agreement with the results reported by Jenkins et al. (1997) and Sadato et al. (1997). In the other words, a range increase of rCBF was seen immediately after the initiation of movement but showed no increase following that during movement in the range from 1.0 Hz to 4.5 Hz. And there is no significant difference of cerebral activation compare with in each movement frequency. However, change of rCBF in ME is clearly different from change of rCBF under 4.5 Hz. ME has not been previously studied. In ME, rCBF during movement (20 sec) continued to increase till movement was over. And increased rCBF in ME has a significantly high value as compared with increased rCBF in other movement frequencies. It could be considered that the reason for the rCBF during ME being higher than at other frequencies is due to the difference of muscle activity. In the present study, NIRS and EMG measurements were performed simultaneously. The results showed no difference in the muscle activity range of 1.0 Hz to 4.5 Hz.

Some researchers have investigated the relationship between muscle activity and brain activity (Dettmers et al., 1995; Dai et al., 2001; Evarts, 1968; Hepp-Reymond et al., 1978, 1999; Siemionow et al., 2000). Dai et al. (2001) determined the relationship between fMRI-measured brain activation and handgrip force, and between fMRI-measured brain signals and the iEMG of finger muscles. They reported that in the primary

motor and sensory cortex, the signal intensity and the iEMG increased linearly across the entire range of the force levels tested. Thus, the muscle activity is also equivalent, if the brain activity is equivalent. Because iEMG data from 1.0 Hz to 4.5 Hz has no significant difference, muscle activity from 1.0 Hz to 4.5 Hz is the same. And cerebral activity from 1.0 Hz to 4.5 Hz shows no significant difference. In other words, muscle activity and cerebral activity indicate almost the same though movement frequency increases. The results from 1.0 Hz to 4.5 Hz of the present study were agreement with those reported by Dai et al. (2001). However, the iEMG showed significantly higher value at ME than the results of them did at other frequencies. De Luca et al. (1982) reported that a hand and finger muscular main control mechanism were neural discharge rate, and most motor units are mobilized by 50% of maximum muscle output. Muscle output in ME may increase slightly as compared with other frequencies. But it is hard to consider an increase in muscle output as remarkable when dealing with an increase in finger tapping frequency. Therefore, we considered that the neural discharge rate mainly affects the increase of iEMG in ME than the number of motor units.

The primary motor cortex at maturity represents the contralateral limb muscles through direct spinal projections and indirect projections through the brain stem (Porter and Lemon, 1993). Classic stimulation studies (Porter and Lemon, 1993) have shown that limb movement representations have a basic somatotopic organization, with distinctive arm and leg areas. Within these areas, there appears to exist a relatively complex organization because an individual muscle can be represented at multiple sites as well as at a single site (Armstrong and Drew, 1984; Donoghue et al., 1992; Sato and Tanji, 1989). These findings suggest that small regions of the primary motor cortex could represent motor synergies (Donoghue et al., 1992; Sanes et al., 1995).

The rCBF measured by NIRS reflects the rCBF of the cortex under the scalp between probes (30 mm in the present study). Therefore, in this study it was not possible to confirm the difference of the number of detailed motor units. However, the difference in activation areas is difficult to determine in vivo since almost identical points are activated during muscle cooperation. In the present study, the results of iEMG analysis showed that changes in the activity of the common digital extensor muscle agreed almost completely with the changes in rCBF. We assume that the value of rCBF during ME being higher than during other frequencies is affected by the increase of iEMG due to the increase in the neural discharge rate.

The high frequency group tended to have a higher rCBF during ME than the low frequency group. Also, the high frequency group tended to have a higher iEMG than the low frequency group. This is due to the neuronal discharge rate of finger flexor and extensor muscles in the low frequency group being lower than that of the high group (De Luca et al., 1982).

Roland et al. (1980) found the same rCBF for the same frequency (1 Hz) when the subjects flexed their index fingers

against a 5.88 N/cm spring as when they flexed their index fingers with no power output after having been injected with ^{133}Xe in the internal carotid artery. They suggested that the increase of rCBF in the motor cortex depended less on the increase of muscle power output than on the increase of movement frequency. Because the neural discharge rate and number of mobilization of motor unit become high with an increase of power output, muscle does activity. Compared with no power output, power output is clearly high for muscle activity in the same frequency. That is to say, we consider that degree of muscle activity is a main factor of brain activity. Therefore, muscle output alone is not a factor of brain activity.

As stated earlier, some studies have reported that auditory stimulus increases brain activity (Wise et al., 1991; Price et al., 1992). In the present study, the frequency of finger tapping in the range of 1.0 Hz to 4.5 Hz was regulated by the sound of an electrical metronome. It is possible that increased rCBF in the range of 1.0 Hz to 4.5 Hz includes an increased volume of rCBF from the effect of auditory stimulus. Even if rCBF is increased by an auditory stimulus, there will be little effect. There is not only because the region of measurement is the motor cortex and not the auditory cortex, but also because there is no significant difference of increased rCBF in the range of 1.0 Hz to 4.5 Hz. In a study of audio-initiated hand movement by monkeys, Gemba and Sasaki (1987) found that the field potentials in the prefrontal cortex were relatively small after repeated training, but increased temporarily when the frequency of the auditory stimulus was changed. Those researchers suggested that when the monkey devoted intensive attention to auditory stimuli, a large potential appeared in the prefrontal cortex. In a human study using PET (Pardo et al., 1991), the prefrontal cortex area on the right appeared to be related to sustained attention to sensory input. The cingulate cortex has a reciprocal connection with the prefrontal cortex (Pandya et al., 1981). Paus et al. (1993) speculated that the anterior cingulate gyrus may contribute to the funneling of cognitive commands from the prefrontal cortex to the motor cortex, facilitating the execution of the appropriate responses and suppressing inappropriate ones. However, in the present study, we did not adopt an external auditory stimulus during ME. The apparent rise in cerebral activity during ME was not affected by the auditory cue.

As a subject for further research, it is necessary to examine the relationship between movement frequency and the extent of the region activated in the brain.

Conclusion

We conclude that during maximum effort, the level of neuron discharge of the muscle is high, and that the regional brain blood flow volume is also high in the motor cortex.

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Correspondence to: Naomi Kuboyama, Graduate School of Human Environment Studies, Kyushu University, Kasuga-koen 6-1, Kasuga, Fukuoka 816-8580, Japan

Phone: +81-92-583-7555 (ext. 7357)

Fax: +81-92-592-2866

e-mail: kuboyama-n@students.ihs.kyushu-u.ac.jp