Abstract  The purpose of the present study was to investigate the effect of the repetition rate of a simple movement on the magnitude of neuronal recruitment at maximal effort in humans. Nine right-handed healthy subjects [age: 27.4±4.8 yr, stature: 174.5±12.2 cm, body-weight 74.3±16.6 kg (Mean±SD)] participated in this study. We measured the regional cerebral hemodynamics using 24-channel near infrared spectroscopy (NIRS). An auditory-cued, repetitive flexion movement of the right index finger against a button was performed as the finger-tapping task at maximal effort (ME), at 25% of maximal effort (25% ME) and at 50% of maximal effort (50% ME). The increase of the left primary motor cortex hemodynamics during movement relative to the hemodynamics under the resting condition was calculated for each pair of movement conditions. The frequency of finger-tapping was 1.61±0.18 Hz (25% ME trial), 3.23±0.36 Hz (50% ME trial), and 6.46±0.72 Hz (ME trial). The left primary motor cortex showed significant activation under all conditions. The change in total hemoglobin ([tHb]) between the ME trial and the resting value (1.19±0.93 mmol · mm) was significantly higher than those between the resting value and the 25% ME trial (0.04±0.04 mmol · mm) or the 50% ME trial (0.08±0.11 mmol · mm) (p<0.05). There was a 29.8-fold increase of the [tHb] value between the 50% ME trial and the 25% ME trial, but only a 2-fold increase of the [tHb] value between the 25% ME trial and the 50% ME trial. These results demonstrated that the rate of change in regional cerebral hemoglobin at a maximal effort finger-tapping task was much higher than that at a low frequency finger-tapping task. J Physiol Anthropol Appl Human Sci 23 (4): 105–110, 2004 http://www.jstage.jst.go.jp/browse/jpa

Keywords: near infrared spectroscopy, cerebral hemodynamics, cerebral oxygenation, motor cortex, movement stimuli, frequency

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Introduction

In contrast to many other organs, the human brain is characterized by a unique dependence on continuous and uninterrupted oxidative metabolism for the maintenance of its functional and structural integrity. Since the amount of oxygen stored in the brain is extremely small compared with its rate of utilization (Kastrup et al., 2002), the brain requires adequate delivery of oxygenated blood at rest as well as during focal activation. The concept of a tight coupling of regional cerebral blood flow (rCBF) to brain activity was originally postulated by Roy and Sherrington (1890) over 100 years ago and was initially confirmed by Ingvar and Risberg (1965). Because regional brain metabolism and regional cerebral blood flow are closely coupled, it is possible to use cerebral hemodynamics as an index of activation for motor cortex centers during motor activity (Lassen et al., 1988). The change of regional cerebral hemodynamics and oxygenation can be measured by several techniques that allow non-invasive monitoring. For example, positron emission tomography (PET), functional magnetic resonance imaging (fMRI) and near infrared spectroscopy (NIRS) have been used to measure the change in regional cerebral blood flow (rCBF) (Fox et al., 1984; Seiz et al., 1990; Price et al., 1992; Sabatini et al., 1993.). However, PET and fMRI have a limitation in that monitoring changes in cerebral oxygenation is difficult during dynamic movement. In contrast, NIRS is a widely available technique that permits specified monitoring of changes in oxy-hemoglobin ([O2Hb]), deoxy-hemoglobin ([HHb]) and total-hemoglobin ([tHb]) with high temporal resolution even during dynamic movement (Colier et al., 1997). In previous studies that investigated cerebral functional activation using NIRS, a variety of stimuli have been used, including visual stimuli (Kato et al., 1993; Meek et al. 1998; Colier et al., 1999), auditory stimuli (Hoshi et al., 1993), and exercise (Colier et al. 1999). The exercise stimulation included was foot movement (Colier et al., 1999),
finger-opposition and finger-tapping (Rao et al., 1996). In the motor system, some previous studies investigated the effect of the movement repetition rate on rCBF. For example, Jenkins et al. (1997) examined the effect of joystick movement, in frequencies ranged from 1/sec to 1 every 5.5 sec in steps of 0.5 s, on cerebral activation. They reported that there was no significant relationship between the movement frequency and cerebral activation. In that study, they did not examine the motor cortex activity in frequencies of over 1 Hz due to the restrictions of the measurement equipment. Further, Sadato et al. (1997) measured rCBF during repetitive flexion movement of the right index finger against the thumb by PET, and reported that the motor cortex activation was not significant, and tended to plateau as the frequency reached 4 Hz. The movement frequency used in the studies of Jenkins et al. (1997) and Sadato et al. (1997) was not the maximal frequency. In general, finger-tapping with maximal effort reached a frequency of over 4 Hz in healthy adults. The relationship between cerebral activation and movement frequency at above 4 Hz was not made clear in previous studies. In order to clarify the relationship between the movement frequency and cerebral activation, it is necessary to investigate this relationship at the frequencies near and at the maximal frequency. We investigated the frequency-related [tHb] changes that occur over the left motor cortex. The purpose of this study was to investigate the relationship between the cerebral activation and the repetition rate of finger-tapping, including finger-tapping at maximal effort.

Subject

Nine healthy subjects [male 7, female 2, stature: 174.5±12.2 cm, age: 27.2±4.8 yrs, body-weight: 74.3±16.6 kg (Mean±SD)] recruited in this study. All subjects were right-handed. None of the subjects were taking any medications and had any history of cardiovascular or neurological disorders. They were fully informed of any possible risk or discomfort associated with these experiments before participate in this study, and they gave their written informed consent.

Protocol

Subjects sat on a chair and were asked to press a button on the table repetitively with their right index finger while the cerebral activation was measured by NIRS. The finger-tapping frequencies were performed at the maximal effort (ME), 25% of the ME (25% ME) and 50% of the ME (50% ME). First, to determine the frequency at an individual’s maximal effort, all subjects underwent the ME trial. Then they performed the tapping in frequency constituting 25% and 50% of the ME trial. The 25% ME trial and 50% ME trial were randomized. The frequency of tapping in the 25% ME trial and 50% ME trial was regulated by the sound of an electrical metronome. Each of the finger-tapping cycles lasted 20 s, followed by a 40 s rest period. Three cycles were performed. The motor cortex hemodynamics was measured by NIRS throughout three cycles. The laboratory was kept at 21–24°C and was kept very quiet. All subjects had their caffeine intake restricted for at least 8 h before the experiment and their alcohol intake restricted of at least 24 h before the experiment, and did not eat for 2 h before the experiment.

Measurement

The NIRS method is based on near-infrared light absorption changes that depend on concentration changes of the chromophores [O₂Hb] and [HHb] in the tissue under investigation. We used 24-channel two-wavelength NIRS systems (ETG-100; Hitachi Medical Corporation, Tokyo, Japan) (Koizumi et al., 1999) with eight light-incident and eight detector fibers. The depth of the measuring point depends on the distance between the transmitting and the receiving probes, it is reported that the NIRS signal reflects the absorption at a depth of 1.2–2.0 cm from the scalp when the inter-probe distance is 2.7 cm (Raichle et al., 1994). As the human cerebral cortex usually lies about 1.0–2.0 cm deep from the scalp, the suitable inter-probe distance should be about 2.5–3.0 cm, to measure the activities of the cerebral surface. According to the above discussions, the inter-probe distance was decided to be 3.0 cm in the present study. 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 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 skin. The change in [tHb], defined as the sum of the changes in [O₂Hb] and [HHb], can be used as a measure of blood volume changes (Delpy et al., 1988). Changes in [tHb], [O₂Hb] and [HHb] 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 to a 20-s 2 Hz finger opposition task was checked. If no oxygenation change could be detected, the optodes were moved, less than 1 cm, until a response was found (Colier et al., 1997).

Statistics Analysis

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

Result

The frequency of finger-tapping was 1.61±0.18 Hz (25% ME trial), 3.23±0.36 Hz (50% ME trial), and 6.46±0.72 Hz (ME trial). Table 1 and Figures 1, 2 and 3 summarize the results of the increase of [O₂Hb], [HHb] and [tHb] from their baseline values at 25% ME trial, 50% ME trial and ME trial. In all of the trials for each subject, [tHb], [O₂Hb], and [HHb]...
increased from their baseline values. The increases of \([tHb]\), \([O_2Hb]\), and \([HHb]\) from their baseline values in the 50% ME trial were not significantly different from the increases in the 25% ME trial \((p>0.05)\). In the ME trial, the increases of \([tHb]\), \([O_2Hb]\), and \([HHb]\) from their baseline values were significantly higher than those in the 25% ME trial and the 50% ME trial \((p<0.01)\).

### Table 1  Average changes in oxy-hemoglobin \([O_2Hb]\), deoxy-hemoglobin \([HHb]\), and total hemoglobin \([tHb]\) concentrations as measured from their baseline values at 25% ME, 50% ME and ME by NIRS over the left motor cortex during 20 s finger tapping task

<table>
<thead>
<tr>
<th></th>
<th>25% ME (#1)</th>
<th>50% ME (#2)</th>
<th>ME (#3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(\Delta [O_2Hb] ) (mmol·mm)</td>
<td>0.04±0.03</td>
<td>0.06±0.07</td>
<td>0.96±1.02 ** #1, #2&lt;#3</td>
</tr>
<tr>
<td>(\Delta [HHb] ) (mmol·mm)</td>
<td>-0.005±0.04</td>
<td>0.01±0.04</td>
<td>0.29±0.48 ** #1, #2&lt;#3</td>
</tr>
<tr>
<td>(\Delta [tHb] ) (mmol·mm)</td>
<td>0.04±0.04</td>
<td>0.08±0.11</td>
<td>1.19±0.93 ** #1, #2&lt;#3</td>
</tr>
</tbody>
</table>

The increase of \([tHb]\), \([O_2Hb] \), and \([HHb] \) at ME from their baseline values were significantly higher than at these at 25% ME and 50% ME \((p<0.01)\). Data are presented as mean±SD. ** Significantly changes from base line value \((p<0.01)\).

**Fig. 1** Change in total-hemoglobin \([tHb]\) concentrations as measured by NIRS over the left motor cortex in healthy subjects \((n=9)\) during a 20-sec contra-lateral finger tapping task. The individual changes were time-locked averages over three cycles of finger tapping. Data are presented as mean±SD.

**Fig. 2** Change in oxy-hemoglobin \([O_2Hb]\) concentrations as measured by NIRS over the left motor cortex in healthy subjects \((n=9)\) during a 20-sec contra-lateral finger tapping task. The individual changes were time-locked averages over three cycles of finger tapping. Data are presented as mean±SD.
Discussion

The main finding in the present study was that the level of [tHb] at ME trial was apparently higher than the level at 25% ME and 50% ME trial.

In the present study, there was no significant difference between the change of increase rate from resting value of [tHb] in the 25% ME trial and that in the 50% ME trial. Executing voluntary exercise requires activity of the cerebral neuron cell. The changes in the hemodynamic response to finger-tapping have been described as a result of regional brain activation presumably reflecting the degree of neuronal activity (Fox and Raichale., 1984; Zhu et al., 1998; Price et al., 1992). Therefore, it is considered that the level of the cerebral neuronal activity in the 25% ME trial is approximately equal to that in the 50% ME trial. On the other hand, the results of the ME trial obviously differ from those of the 25% ME trial and the 50% ME trial. The ME frequency was 6.46±0.72 Hz, which was 4-fold the level in the 25% ME trial and 2-fold the level in the 50% ME trial, and more than the level show in previous studies of Jenkins et al. (1997) and Sadato et al. (1997). [tHb] in the ME trial was 1.19±0.93 mmol·mm, which 29.8-fold the level in the 25% ME trial and 14.9-fold the level in the 50% ME trial, which reflected a significant increase over the levels in the 25% ME and 50% ME trials. In the present study, we adopted an external auditory cue. 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 devotes intensive attention to auditory stimuli, a large potential appears in the prefrontal cortex. In human study using PET (Pardo et al., 1991), the prefrontal cortex area on the right appeared to be related to the sustained attention to sensory input. The cingulated cortex has a reciprocal connection with the prefrontal cortex (Pandya et al., 1981). Paus et al. (1993) speculated that the anterior cingulated gyrus may contribute to the funneling of cognitive commands from the prefrontal cortex to the motor structures, facilitating the execution of the appropriate responses and suppressing the inappropriate ones. However, in the present study, we did not adopt an external auditory stimulus at ME. The apparent rise in cerebral activity at ME was not affected by the auditory cue.

Roland et al. (1980) found the same rCBF when the subjects flexed their index fingers against a 5.88 N/cm spring as when they flexed their index fingers in the same frequency with no power output after having been injected with $^{133}$Xe in the internal carotid artery. Those researchers suggested that the increase of rCBF in the motor cortex depended less on the increase of muscle power than the increase of exercise frequency (Roland et al., 1980). On the other hand, the previous studies reported that there was a positive relationship between the percentage of the maximum force of voluntary contraction (%MCV) and the motor area of fMRI signals, and the relationship was a logarithmic function during isometric exercise (Dettmers et al., 1995; Thickbroom et al., 1998). Dettmers et al. (1995) reported that their electromyographic recording (EMG) data confirmed this phenomenon that increasing the force exerted by the finger was associated with successive activation of the muscles acting at the wrist, elbow and shoulder. By increasing the movement frequency, the subjects contracted their shoulder muscles without their awareness. Thus, the automatic use of the arm and shoulder muscles to stabilize joints would be under cortical control. On the basis of the results of Dettmers et al. (1995), we considered that the result of our study, which indicated higher increase of cerebral activity from 50% ME to ME than from 25% ME to 50% ME, indicate the mobilization of addition muscle at ME than at 25% ME and 50% ME. The mechanisms of the relationship between the repetition rate and cerebral activity remained unclear in the present study. Further studies are

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**Fig. 3** Change in deoxy-hemoglobin [HHb] concentrations as measured by NIRS over the left motor cortex in healthy subjects (n=9) during a 20-sec contra-lateral finger tapping task. The individual changes were time-locked averages over three cycles of finger tapping. Data are presented as mean±SD.
needed to evaluate the effect of the repetition rate of a simple movement on cerebral activity.

Conclusion

Our results demonstrated that the rate of change in regional cerebral hemoglobin at maximal effort finger tapping was much higher than that at low frequency finger tapping tasks.

Reference


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