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# Progressive Muscle Fatigue Induces Loss in Muscle Force and Persistent Activation of Frontal Cortex as Measured by Multi-Channel fNIRT

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**Abstract.** The effect of fatiguing skeletal muscle exercise on brain, and in particular on ipsi- and contralateral frontal cortex (FC) has not been fully clarified. The aim of this study was to investigate by functional near-infrared topography (fNIRT) the FC oxygenation response to a prolonged fatiguing rhythmic handgrip exercise performed at the maximal voluntary contraction separately with right or left hand. fNIRT is a not harmful and non-invasive optical technique allowing the simultaneous acquisition of oxygenated and deoxygenated hemoglobin concentration ( $[O_2Hb]$ ,  $[HHb]$ ) changes on the scalp. By using a 8-channel fNIRT (NIRO-200 with multi-fiber adapter, Hamamatsu Photonics) we demonstrated a significant  $[O_2Hb]$  increase, accompanied by a smaller and delayed significant  $[HHb]$  decrease, in all measurements points of both hemispheres. A significant hemisphere x task execution modality interaction was revealed only for  $[O_2Hb]$  increase of the right FC during the right handgrip exercise ( $p=0.008$ ). A significant hemisphere x task execution modality interaction was found only for  $[HHb]$  decrease of the left FC during the left handgrip exercise ( $p<0.001$ ). These results provide further evidence that FC plays a role in maintaining strength of the forearm muscles and ensuring a correct execution of motor tasks which require a fine motor control and coordination.

**Keywords:** Near Infrared Spectroscopy; Functional Imaging; Frontal Lobe; Handgrip Exercise; Fatigue

## 1. Introduction

Neuroimaging studies have reported a proportional relationship between cortical signals and exerted joint force in humans, indicating that brain signals are positively correlated to voluntary efforts, as a high level of effort is required for exerting greater muscle force [Liu et al., 2003, 2007; Mottola et al., 2006]. The effect of fatiguing skeletal muscle exercise (involving small or large muscle groups) on brain, and in particular on ipsi- and contralateral frontal cortex (FC) has not been fully clarified.

The aim of this study was to investigate by functional near-infrared topography (fNIRT) the FC oxygenation response to a prolonged fatiguing rhythmic handgrip exercise performed at the maximal voluntary contraction (MVC) separately with right or left hand. fNIRT is a not harmful, non-invasive and safe optical technique allowing the simultaneous acquisition of oxygenated and deoxygenated hemoglobin concentration changes ( $\Delta[O_2Hb]$  and  $\Delta[HHb]$ , respectively) from an array of optical fibers on the scalp to construct maps of cortical activity [Wolf et al., 2007]. The hemodynamic response typically observed over an activated cortical area consists of a decrease in  $[HHb]$  accompanied by an increase in  $[O_2Hb]$  of two or threefold of magnitude, resulting in an increased total hemoglobin concentration ( $[tHb]=[O_2Hb]+[HHb]$ ).

## 2. Material and Methods

Mean ( $\pm$ SD) age, height, and body mass of the fifteen right-handed subjects were  $25\pm 3$  y,  $174\pm 4$  cm and  $71\pm 6$  kg, respectively. Participants completed two separate experimental sessions performed at the same time of day and separated by a minimum period of 24 hours.

In the first session each subject performed 10 MVCs with both hands (5 for each). Every MVC lasted approximately 2-s with a 120-s rest period between trials. Participants were instructed to grasp a handgrip device with either hand and to exert their maximum effort to squeeze it while staying in supine position. The reported MVC mean value for each single subject was calculated, after

eliminating the lowest and the highest MVC values, over the 3 remaining ones. In the second session, two identical rhythmic handgrip exercises (RHE) at MVC were executed; one exercise for each hand. The RHE consisted of: a 30-s rest condition, a 23-min rhythmic exercise (200 MVCs, 2-s contraction and 5-s relaxation), and a 2-min recovery. The same exercise was repeated with the other hand.

Handgrip force was measured by a system consisting of a handgrip device and a digital handgrip analyzer (MIE, Medical Research, UK). The pliers were fixed in vertical position to a rigid support and the exact point where the subject had to grasp was marked in order to standardize the testing conditions. Subjects exerted handgrip contractions looking at a visual cue figured on the ceiling by a color LCD projector connected to the PC on which the management handgrip software was running. The visual cue was a series of travelling rectangular pulses (pulse duration 2-s with a 5-s interval). The height of the pulses indicated the amplitude of the initial MVC force of the subject. The sampling rate for the force data was 33 Hz.

A 8-channel fNIRT system (NIRO-200 with multi-fiber adapter, Hamamatsu Photonics K.K., Japan) was used to measure frontal changes in  $[O_2Hb]$  and  $[HHb]$ . Two optical fiber bundles (2.5 m length; 3 mm diameter) carried the light to the left and the right FC; whereas eight optical fiber bundles of the same size (4 for each lobe) collected the light emerging from the frontal areas. The two illuminating bundles and the collecting ones were assembled into a specifically designed flexible probe holder ensuring that the position of the 10 optodes, relative to each other, was fixed. The 8 fNIRT measurement points (channels) were defined as the midpoint of the corresponding detector-illuminator pairs (distance set to 3 cm). The channels 8, 5, 4, and 1 corresponded to Fp1, AF3, Fp2, and AF4 respectively, according to the extended international 10/10 system of electrode placement. The quantification of concentration changes, expressed in  $\Delta\mu M$ , was obtained by including an age-dependent constant differential pathlength factor ( $5.13+0.07\times\text{age}^{0.81}$ ). Data were acquired at 1 Hz and transferred online from the NIRO-200 monitor to a computer.

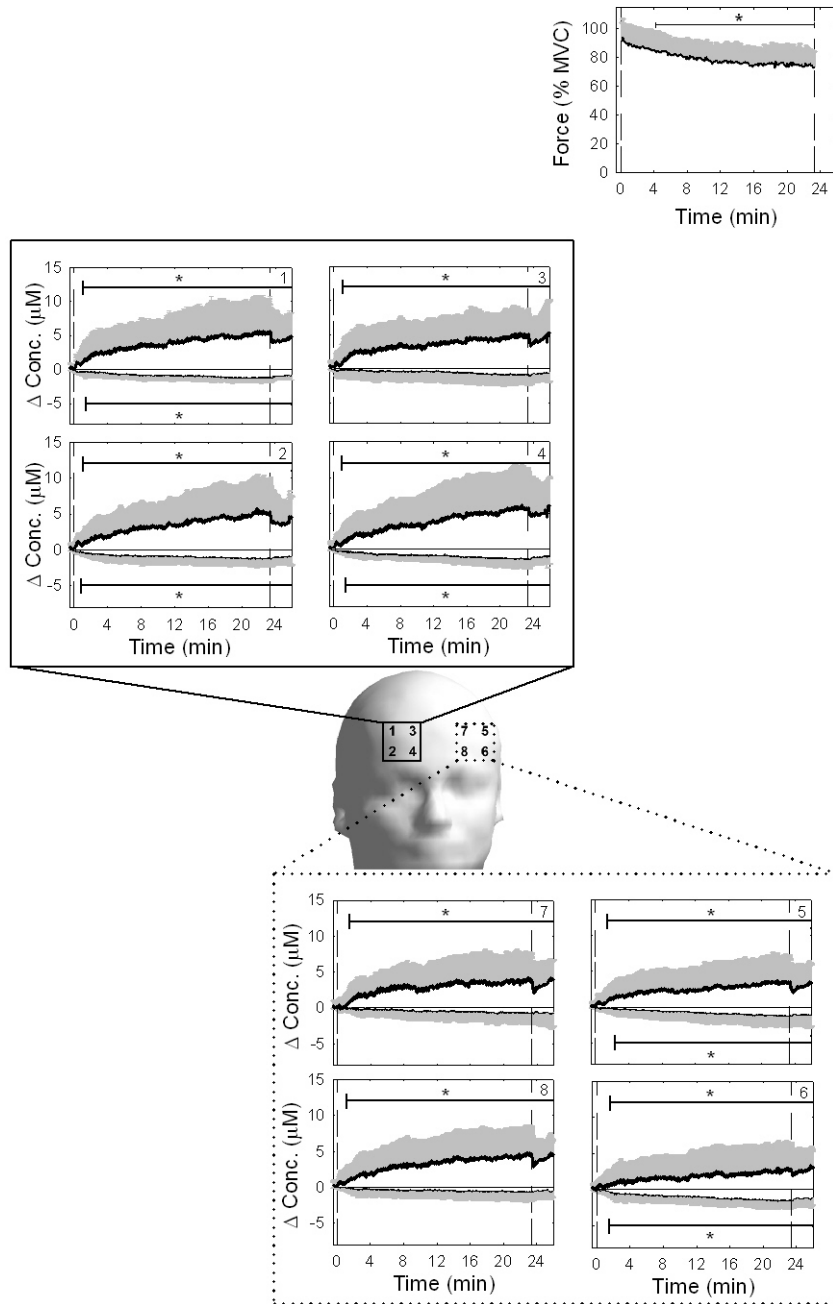
In order to determine the significance of  $[O_2Hb]$ ,  $[HHb]$  and force changes, one way repeated measures analysis of variance (one-way RMANOVA) and post-hoc Tukey test were performed. To examine the effect of the task on  $[O_2Hb]$  and  $[HHb]$  changes, areas under the curve (AUCs) were computed using the curves over the time associated with the exercise. AUC data were analyzed by using a three-way analysis of variance model using post-hoc Tukey test to determine the significance of individual changes between three experimental factors [hemisphere (2) $\times$ channel (4) $\times$ condition (2)]. In order to determine left/right asymmetry of FC activity during the handgrip task, a laterality index (LI) for the  $[O_2Hb]$  concentration changes was calculated using the formula  $(R-L)/(R+L)$ , where R and L indicated the sum of the AUC values of the right side (channels 1,2,3,4) and the left side.  $LI > 0$  indicates greater activity of the right FC, whilst  $LI < 0$  indicates greater activity of the left FC. When the activation of one side was 1.4 times greater than that one found on the other side, the absolute value of LI became greater than 0.15. One side predominance was arbitrarily defined as the absolute LI greater than 0.15.

### 3. Results

Figures 1 and 2 show the grand average of the force,  $[O_2Hb]$  and  $[HHb]$  changes over the eight FC measurement points during the right and left exercise, respectively. In both exercises, force declined significantly after the first 37 contractions. During the task period, a significant increase in  $[O_2Hb]$ , accompanied by a smaller and delayed significant decrease in  $[HHb]$ , was observed in all measurements points of both hemispheres. Particularly, during the execution of the right exercise,  $[HHb]$  decreased significantly except for the measurement points # 3, 7 and 8. Interestingly,  $[O_2Hb]$  increased significantly at  $76\pm 14$  and  $73\pm 19$  s after the onset of the task in the right and left exercise, respectively; conversely  $[HHb]$  decreased significantly at  $92\pm 33$  and  $74\pm 16$  s afterward. Based on the tight coupling between neuronal activity and oxygen delivery, this oxygenation pattern can be interpreted as an indicator for cortical activation. The three-way analysis of variance revealed a significant hemisphere  $\times$  task execution modality interaction only for the  $[O_2Hb]$  increase of the right FC during the right handgrip exercise ( $p=0.008$ ).

The three-way analysis of variance revealed a significant hemisphere  $\times$  task execution modality interaction only for the  $[HHb]$  decrease of the left FC during the left handgrip exercise ( $p<0.001$ ).

The laterality index for  $[O_2Hb]$  changes (the most sensitive parameter to cortical blood flow changes) is reported in Figure 3. In the FC ipsilateral to the exercising hand, the laterality index was found significant in 12 and 7 subjects during the right and left exercise, respectively. In the FC contralateral to the exercising hand, the laterality index was found significant in 2 subjects during the right and the left exercise, respectively.

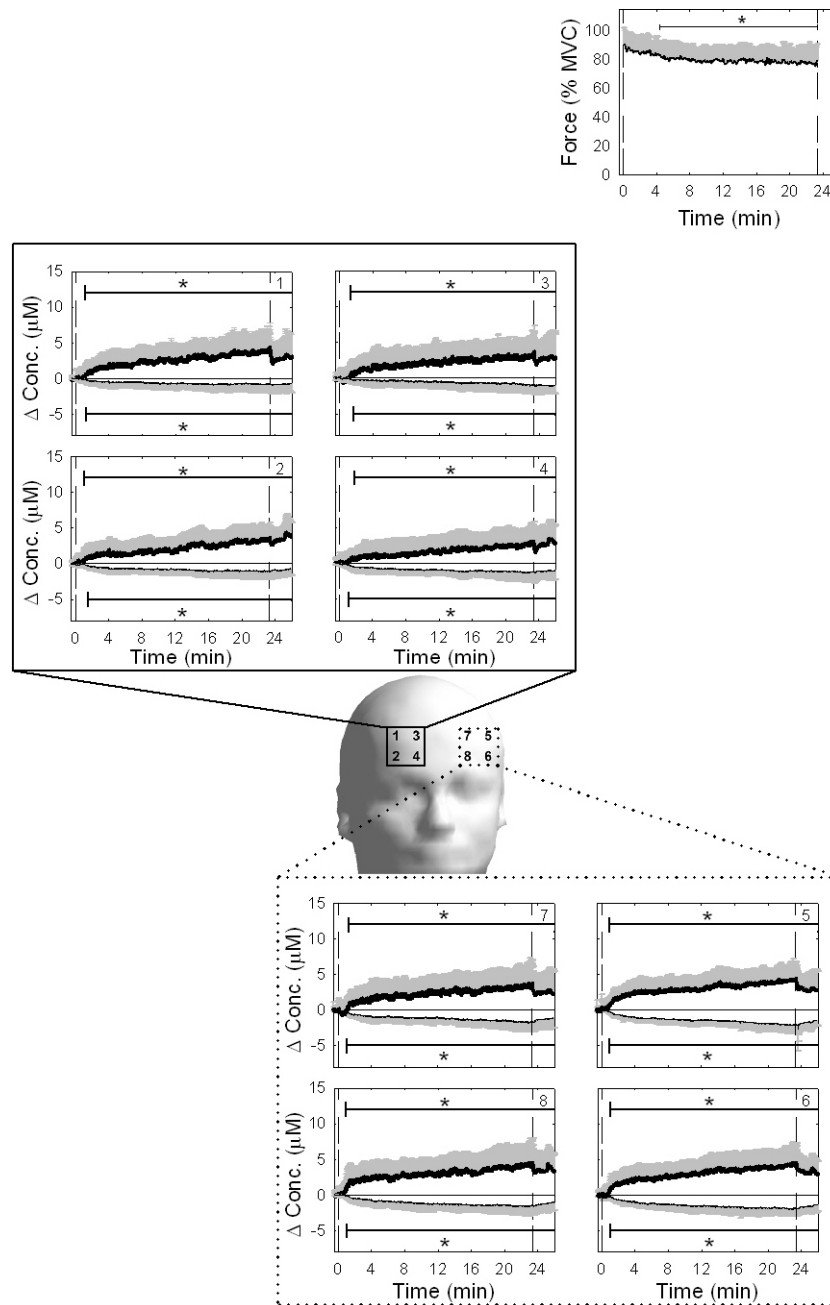


**Figure 1.** Force tracing and cortical oxygenation changes during right handgrip exercise in 4 measurement points of the right and left frontal region (upper and lower boxes, respectively). Although the force was decreasing during the exercise period, frontal cortex was found activated (increase in  $[O_2Hb]$  and a concomitant decrease in  $[HHb]$ ) throughout the investigated frontal region. The highest activation was found in the frontal cortex ipsilateral to the exercising hand. The vertical dashed lines indicate the period of the exercise; the horizontal lines indicate the significance interval. ( $N=15$ ; means $\pm$ SD;  $p<0.05$ ).

## 4. Discussion

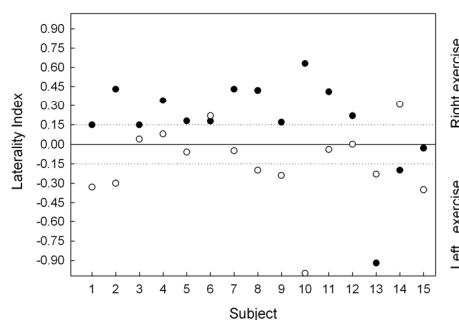
The results of the present study confirm the previous ones obtained by others using fMRI [Liu et al., 2003, 2005, 2007], and provide further evidence for supporting the hypothesis that FC plays a role in maintaining strength of the forearm muscles and ensuring a correct execution of motor tasks which require a fine motor control and coordination. During RHE, the so-called cortical activation of both FC areas (ipsi and contralateral to the exercising hand) characterized by a specific hemodynamic pattern

(see Fig. 1 and 2) which is representative of a localized increase in regional blood flow, was observed in all subjects. Concomitantly, the force declined progressively up to about 18 and 12% for the right and left exercise, respectively.



**Figure 2.** Force tracing and cortical oxygenation changes during left handgrip exercise in 4 measurement points of the right and left frontal region (upper and lower boxes, respectively). Although the force was decreasing during the exercise period, frontal cortex was found activated (increase in  $[O_2Hb]$  and a concomitant decrease in  $[HHb]$ ) throughout the investigated frontal region. The highest activation was found in the frontal cortex ipsilateral to the exercising hand. The vertical dashed lines indicate the period of the exercise; the horizontal lines indicate the significance interval. ( $N=15$ ; means $\pm$ SD;  $p<0.05$ ).

The lateralized FC activation during the right RHE confirms the results by Liu et al., [2007] who found, adopting the same protocol and EEG, a shifting of the activation center. The present study and others [Harada et al., 2007; Kikuchi et al., 2007; Leff et al., 2008; Mihara et al., 2008; Mottola et al., 2006; Okamoto et al., 2004; Suzuki et al., 2004, 2008] confirm the potentiality of using fNIRS for investigating and clarifying the cortical topography activity patterns during progressive muscle fatigue and precision/coordination tasks.



**Figure 3.** Laterality index for the  $[O_2Hb]$  changes in the 15 subjects for the right (filled circle) and left (empty circle) hand exercises. The two dashed lines indicate the significant thresholds for both exercises.

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