Deterioration of cortical functional connectivity due to muscle fatigue

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Introduction

How the brain controls a fatiguing muscle is not well known. This question is fundamental in motor control and a better understanding of it is important for gaining insights into prevailing clinical fatigue that frequently involves impairments of the central nervous system. Recent studies have shown that brain activation level measured by functional MRI (fMRI) in healthy subjects increases during muscle fatigue induced by submaximal-force tasks [1]. This occurs in multiple sensorimotor-related cortical regions, including the primary motor (M1) and sensory (S1) cortices and the higher-order cortices such as the frontal lobe (FL) and supplementary motor area (SMA). However, whether or not muscle fatigue affects the strength of functional integration in the neural network has not been studied yet. The purpose of this study was to evaluate effects of muscle fatigue on functional connectivity (FC) among sensorimotor-related cortical regions using fMRI data obtained during a fatigue motor task [2].

Methods

Subjects and Fatigue Task

Ten healthy young subjects (men, age = 32.8±8.4 yrs, all right-handed) participated in the study. Each subject performed 120 handgrip contractions at 50% maximal voluntary contraction (MVC) level. Each trial lasted 3.5 s, followed by a 6.5-s rest period. Visual cues were generated by a computer and displayed to the subjects via the visual monitor system that was installed with the MR system. Subjects followed the visual cues to time the contraction and rest. Handgrip forces during the experiment were recorded using a hydraulic pressure transducer system [3]. MVC forces were measured before and immediately after the fatigue task.

Image Acquisition

Both functional and anatomical MR brain images were acquired on a 3T Siemens Trio scanner. For the fMRI data collection, TR = 2 s, TE = 30 ms, image matrix = 64 x 64, and in-plane resolution = 3.44 mm x 3.44 mm. For the T1-weighted anatomical images, TR = 300 ms, TE = 12 ms, image matrix = 256 x 256, and in-plane resolution = 0.9 mm x 0.9 mm. For both types of images, the same 30 slices (thickness = 4 mm) along the anterior-posterior commissure were collected. 3D anatomical images covering the whole brain were also collected in the sagittal planes using the TurboFlash sequence, TR = 2600 ms, TE = 3.9 ms, image matrix = 256 x 256, and voxel size = 1 mm x 1 mm x 1 mm.

Data Analysis

(1) The fMRI data were processed using the BrainVoyager software. Motion detection and correction were performed on all fMRI data using the AIR algorithm. Data of 2 subjects were excluded from further analysis because the overall head motion exceeded 2 mm. Slice scan time correction was applied. Linear trends and nonlinear drifts were also removed from the data. (2) The fMRI data were first registered to the T1-weighted anatomical images, then to the 3D anatomical images, and finally to the Talairach space. (3) The 120 handgrip contractions were divided into 12 blocks of data with 10 trials in each block. (4) The activation maps were generated by correlating the fMRI signal timecourse of each voxel with the motor task performance waveform (hemodynamic delay was considered). Any cluster with a correlation coefficient > 0.4 and cluster size >125 was considered significantly activated in relation to the task. (5) For FC maps, the average timecourse of the activated voxels in the contralateral M1 area (Brodmann area 4, the left side) was selected as the reference for cross-correlation analysis. Any cluster in the brain with a correlation coefficient > 0.6 and cluster size >125 was considered significantly functionally connected to M1. (6) The number of activated voxels in the activation maps (N_A) and the number of voxels that were functionally connected to M1 in the FC maps (N_{FC}) were counted in each region of interest (ROI). (7) Repeated measures ANOVA analysis was applied to determine whether changes in N_A and N_{FC} along the course of fatigue were significant (P<0.05).

Results

1. MVC handgrip force decreased substantially. The handgrip MVC force decreased to about 60% of the initial MVC value after 120 contractions, indicating significant muscle fatigue.

2. Brain activation volume increased with muscle fatigue. The volumes of activated brain parts increased along with muscle fatigue in motor-related cortices including M1, S1, FL, SMA, and cerebellum, which is consistent with former results [1].

3. Functional connectivity among cortices decreased with muscle fatigue. Functional connectivity to the contralateral M1 decreased significantly in S1, SMA, FL, and cerebellum, indicating deteriorated communication of motor and sensory information among the cortices due to fatigue (Fig. 1).

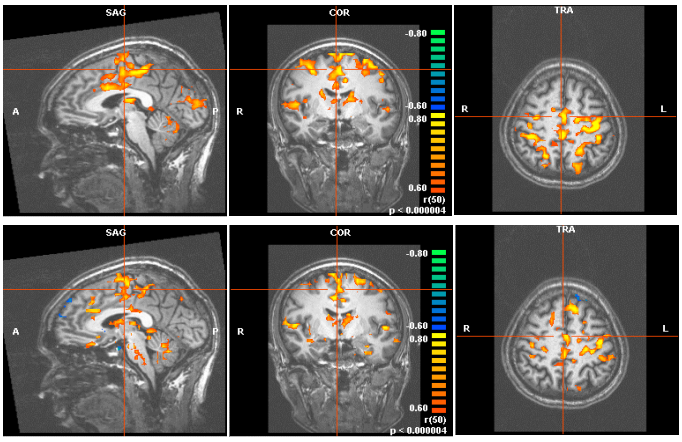

Fig. 1: Functional connectivity (FC) map. The upper and lower rows show FCs to the contralateral M1 before and after muscle fatigue, respectively. Colorbar indicates the strength of FC.

Conclusions & Discussion

The results indicate that during a sub-MVC muscle fatigue task, the individual task-related brain areas try to increase their levels of involvement to compensate for the fatigue effect, however, the reduced ability of information exchanging among them due to fatigue prevents them from more effective integrated effort to maintain the task performance. At the neuron level, in response to fatigue, more neurons need be recruited to strengthen the descending motor command and process increasing peripheral sensory information, leading to increased activation in individual cortices. However, the fatigue effect reduces the efficiency of the neural network and the synchronization among the neurons, leading to decreased FC.

References

[1] Liu JZ, Shan ZY, Zhang LD, Sahgal V, Brown RW, Yue GH. Human brain activation during sustained and intermittent submaximal fatigue muscle contractions: an fMRI study. *J Neurophysiol* 90:300-312, 2003.

[2] Lowe MJ, Mock BJ, Sorenson JA. Functional connectivity in single and multislice echoplanar imaging using resting-state fluctuations. *Neuroimage* 7:119-132, 1998.

[3] Liu JZ, Zhang LD, Yao B, Yue GH: Accessory hardware for neuromuscular measurements during functional MRI experiments. *Magn Reson Mat Phys Biol Med* 13: 164-171, 2001.

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