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Effects of motor fatigue on cortical activation level and functional connectivity during upper limb resistance training

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Abstract— **This study aimed to clarify the effects of motor fatigue on cortical activation levels and functional connectivity during upper limb resistance training using functional near-infrared spectroscopy (fNIRS). Ten healthy college students participated in a high intensity upper limb resistance training and fNIRS was used to measure the changes of oxyhemoglobin concentration changes (HbO) in bilateral sensorimotor cortex (SMC), premotor cortex (PMC), supplementary motor area (SMA), and dorsolateral prefrontal cortex (DLPFC). The integral value (IV) of blood oxygen signal was calculated as an indicator of cortical activation level and the whole brain correlation analysis was used to calculate cortical functional connectivity. The results showed that as motor fatigue deepened, the activation levels of bilateral DLPFC and PMC in early stage were significantly higher than those in later stage ($P<0.05$), and the functional connectivity strength of the motor related cortex areas between the hemispheres was significantly reduced, which was manifested by the functional connectivity strength of LSMC-RSMC and LPMC-RSMC showed a significant decrease in middle stage compared with that in early stage ($P<0.05$) and that the functional connectivity strength of LPMC-RSMC and RSMC-SMA showed a significant decrease in later stage compared with that in early stage ($P<0.05$). In each stage, the motor related cortex areas maintained high activation levels and the cerebral cortex showed extensive functional connectivity.**

***Clinical Relevance*— The clinical relevance of this study is to deepen the understanding of the neural processes related to upper limb resistance training based on motor fatigue, and provide a clinical basis for optimizing resistance training strategies related to motor dysfunction patients with altered brain function under fatigue.**

I. INTRODUCTION

Motor function is indispensable to human production and life. Patients with motor dysfunction have serious problems in daily activities due to a partial or total loss of motor ability, especially in the upper limb motor dysfunction. Physical movements in daily life, including fine and gross movements, are inseparable from the control of the upper limbs. Researchs have shown that exercise rehabilitation training could promote the motor function of the affected limb [1]. In recent years, researchs have verified that resistance training could effectively improve motor dysfunction caused by stroke, brain injury, and other neurological diseases [2]. Resistance training, also known as "impedance exercise" or "strength training", refers to the process that the body overcomes resistance to achieve muscle growth and strength increase [3].

Continuous training can easily lead to motor fatigue, which has harmful effects on rehabilitation treatment. Functional near-infrared spectroscopy (fNIRS) indirectly monitors brain activity by measuring changes in hemoglobin concentration caused by changes in cerebral blood flow [4]. As a novel brain function imaging technology, fNIRS has the advantages of non-invasive, portable, and good head movement tolerance [5]. Recently, fNIRS has been used to dynamically monitor brain activity during fatigue [6]. The existing researchs on resistance training mainly evaluate the training effect before and after resistance training using kinematics, EMG and clinical scale [7], but few researchs focus on the changes of brain functional state caused by motor fatigue during resistance training.

The brain is a distributed network structure. In the process of performing a specific task, the cortical response is not only manifested as the activation of a specific brain area, but also as the cooperative working between different brain areas [8]. Combining cortical activation and brain network analysis is expected to more comprehensively clarify the effects of motor fatigue on cortical activation level and functional connectivity during upper limb resistance training. In this study, we used fNIRS to explore the effects of motor fatigue on cortical activation levels and brain functional connectivity in healthy individuals during resistance training. Specifically, this study mainly aimed to solve the following two questions: (1) How did motor fatigue affect the cortical activation levels ? (2) With the deepening of motor fatigue, how did the functional connection of the cortex change?

II. METHOD

A. Participants

This study was approved by the Human Ethics Research Committee of the Cancer Hospital of Chongqing University. It complies with the ethical standards set forth in the Declaration of Helsinki of 1975 and the Declaration of Helsinki as amended in 2008. The contract number was “20225901”. A total of 10 healthy college students (5 males, average age 22.15 ± 0.80 years) were recruited. Before the experiment, each participant signed an informed consent form and was familiar with the experiment operations and procedures in advance. The inclusion criteria of this study were: i) physical health, no history of mental illness, nervous system disease, motor system and other diseases; ii) Confirmed as right-handed through the Edinburgh Dominant Hands Questionnaire [9]; iii) No high-intensity exercise within 1 month before the experiment. Exclusion criteria included any previous hand or arm musculoskeletal injury, psychiatric history, major head

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injury surgery history, and special sports experience. All 10 subjects met the inclusion and exclusion criteria and were included in the experiment.

B. *Experimental design and fNIRS data acquisition*

The experimental site is located in the laboratory of School of Bioengineering, Chongqing University, where the indoor temperature and humidity are suitable. During the experiment, the room was kept quiet and dark. All participants were measured by examiners. Before the experiment, participants were briefed on the procedure.

Participants participated in a bilateral upper limb resistance training experiment, and the upper limb training device used could help participants complete upper limb rotation movements. Fig. 1 shows the experimental task design process. Repetition Maximum (RM) is usually used to measure the resistance exercise intensity, and it is also the simplest method to determine the appropriate intensity of exercise training [10]. Before resistance training, 10RM was defined as the maximum resistance level that the subject could rotate 10 consecutive circles, and the resistance strength of 70% 10 RM was recorded as the resistance load of subsequent resistance training. The formal experiment consisted of multiple blocks, each block was composed of a 40s task period and a 30s rest period. Participants were required to resist 70% 10RM resistance load to perform uniform circular rotation movement during the task period, and completely relax during the rest period. This process was repeated until the participant failed to complete the experiment due to exhaustion. Before the formal experiment, participants were asked to practice briefly to get familiar with the experiment content. During the experiment, the participants concentrated and sat in a comfortable position on the wooden chair, a long distance from the arm of the handle of the upper limb training device, participants' arms were restrained using the experimental bandage. At the same time, participants were required to keep the pelvis as upright as possible and let the lower back away from the backrest. The early stage of resistance training was defined as the first 5 blocks after the beginning of the experiment, the later stage was defined as the 5 blocks before the end of the experiment, and the middle stage was defined as the blocks between the early stage and the later stage.

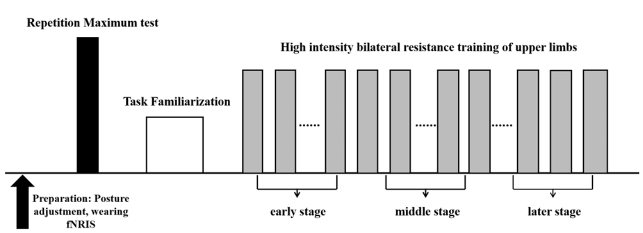


Fig. 1 Experimental task design

During the resistance training process, fNIRS signals were collected using a multi-channel near-infrared spectral brain function imaging system produced by Danyang Huichuang Company, and the sampling frequency was set at 11Hz. According to the international 10-20 system standard, the position of Cz point is used as the reference point. We mainly focused on the following regions of interest (ROIs): left and right primary sensorimotor cortex (LSMC; RSMC), left and right premotor cortex (LPMC; RPMC), supplementary motor area (SMA), left and right dorsolateral prefrontal cortex (LDLPFC; RDLPFC). Therefore, we used a total of 39 channels. Fig. 2 showed the arrangement of fNIRS channels. The areas enclosed by the circle were our regions of interest (ROIs).

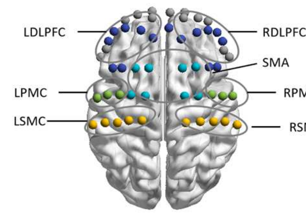


Fig. 2 Arrangement of functional near-infrared spectrum (fNIRS) channels

C. *Data preprocessing and analysis*

In this study, the Homer2 toolbox was used to preprocess fNIRS data [11]. (1) Convert the original light intensity signal to optical density signal. (2) Moving standard deviation combined with cubic spline interpolation to remove motion artifacts in the signal. (3) In order to remove high-frequency physiological noise and low-frequency baseline drift in the signal, including respiration and heartbeat, etc. [12], a 5th-order infinite impulse response Butterworth filter was used to perform 0.01~0.1Hz bandpass filtering on the signal. (4) Based on the modified Lambert-Beer law [13], the optical density signal was converted into hemoglobin concentration value. Because oxygenated hemoglobin (HbO) signal is the most sensitive marker reflecting regional cerebral blood flow changes in fNIRS detection, and its signal-to-noise ratio and amplitude are higher than those of deoxyhemoglobin hemoglobin(HbR), this study mainly analyzed HbO signal.

In this study, the characteristic parameter of HbO change duration - integral value (IV) - was extracted to characterize the cortical activation level. Researchs have shown that [14], IV, the area surrounded by the positive change of oxygenation hemoglobin concentration and the time axis during the task period reflects the supply state of cerebral blood flow during the brain nerve activity, and can describe the size of the hemodynamic response during the task, the larger the response volume, the richer the cerebral blood flow supply, and the higher the cortical activation level. The activation level of each ROI corresponding to the early, middle, and later stages was defined as the average of the multiple task periods of IV in the included channel.

Functional connectivity (FC) refers to the temporal correlation or dependence of neural activities between various regions of the cerebral cortex. It is a method to measure the degree of functional coupling between brain regions [15]. Functional connectivity analysis was performed using the open-source software FC_NIRS, and whole brain correlation analysis was used to calculate the correlation between all channel time series. Firstly, the Pearson's correlation was used to calculate the correlation coefficient between ROIs, and then the Pearson R value was converted to Fisher's z-score. Based on the principle of graph theory, each ROI was regarded as a node, and the connection between each ROI was represented by an edge. Finally, 21 edges were constructed and the threshold to determine whether the edge between two nodes had functional connections was set to 0.4.

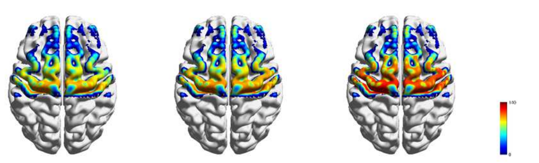
D. *Statistical analysis*

The K-S test was used to evaluate the normality of the data, and all variables satisfied the normal distribution. Therefore, all data were allowed for parameter statistical analysis. A single-sample t-test was used to determine whether there was a functional connectivity between ROIs in the early, middle, and later stages of resistance training (test value was set at 0.4). The paired sample t-tests were used to compared whether there were significant differences in activation levels and functional connectivity strength between different stages of the same ROI, with an FDR (false discovery rate) multiple comparison correction for statistical analysis. IBM SPSS Statistics 23.0 (IBM, Germany) was used for statistical analysis, and the significance level was set at P<0.05.

III. RESULTS

A. *Comparison of cortical activation level in each stage*

Fig. 3 showed the cortical activation map corresponding to different stages under resistance training, and a~c represented the early, middle and later stages in turn. The results showed that motor related cortex areas including SMC, PMC, and SMA were consistently highly activated during all stages of resistance training. The activation levels of ROIs showed a similar change trend in different stages, which was manifested by the activation levels of each ROI increased with the deepening of motor fatigue.



(a) early stage **(b) middle stage** **(c) later stage**

Fig. 3 Cortical activation map in different stages under resistance training; a ~ c represent the early, middle, and later stages, respectively;

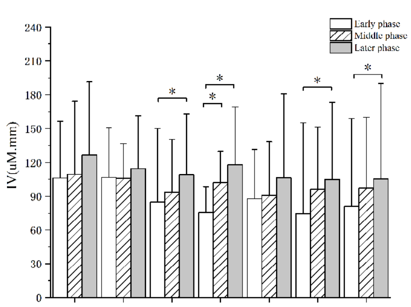
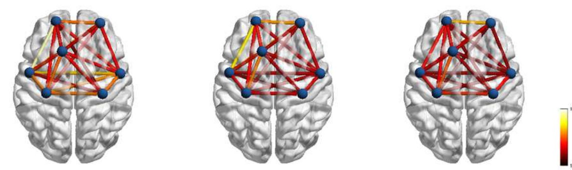


Fig.4 Changes of the activation level of regions of interest (ROIs) at different stages of resistance training; *: P <0.0.5;

As shown in Fig. 4, we further analyzed the changes in cortical activation levels of ROIs during different stages of resistance training. The results of paired sample t-test showed that the activation level of bilateral PMC in early stage was significantly lower than that in later stage (P<0.05), the activation degree of RPMC in early stage was significantly lower than that in middle stage (P<0.05), and the activation degree of bilateral DLPFC in early stage was significantly lower than that in later stage (P<0.05).

B. *Comparison of functional connectivity in each stage*

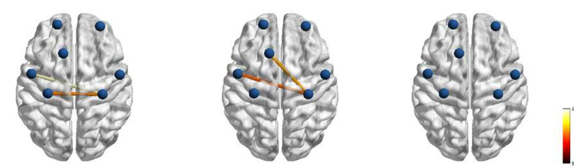
Fig. 5 showed the functional connectivity map at different stages under resistance training. The results of single-sample t-test showed that the cerebral cortex exhibited extensive functional connectivity at each stage. Except that RSMC-RDLPFC didn't have functional connectivity at each stage (P>0.05), and that RSMC-LDLPFC didn't have functional connectivity at middle stage (P>0.05), other ROIs have functional connectivity at each stage.



(a) early stage **(b) middle stage** **(c) later stage**

Fig. 5 Functional connectivity map at different stages under resistance training. The significance t value (P <0.05) indicates that the functional connectivity between each ROI is drawn with different colored lines; a-c represent early, middle and later stages respectively. Seven regions of interest (ROI) are drawn by blue circles;

Fig. 6 showed the difference in functional connectivity strength between different stages under resistance training. The results of paired-sample t-test showed that the functional connectivity strength of LSMC-RSMC at early stage was significantly greater than that at middle stage (P<0.05), the connectivity strength of LPMC-RSMC at early stage was significantly greater than that at middle and later stages (P<0.05), and the connectivity strength of RSMC-SMA in early stage was significantly greater than that at later stage (P<0.05), There was no significant difference in functional connectivity strength between ROIs at middle and later stages (P>0.05).



(a) early stage vs middle stage **(b) early stage vs later stage** **(c) middle stage vs later stage**

Fig. 6 Plot of significant functional connectivity strength differences during resistance training. The significance t-value (P <0.05) of the paired sample t-test indicates the significant functional connectivity strength difference between each ROI and is plotted with different colored lines.(a) significant functional connectivity strength differences at early stage compared with middle stage. (b) significant functional connectivity strength differences at early stage compared with later stage. (c) significant functional connectivity strength differences at middle stage compared with later stage.

IV. DISCUSSION

No matter in continuous or intermittent exercise training, continuous repeated exercise will lead to motor fatigue, and motor fatigue will cause functional reorganization of brain function, manifested by changes in the activation level of specific brain areas and the functional connectivity between different cortical areas. The purpose of this study was to use fNIRS to explore the effects of motor fatigue on cortical activation levels and functional connectivity during upper limb resistance training. Our results showed that with the deepening of motor fatigue, there were significant differences in cortical activation levels and functional connectivity strength between different stages.

In this study, the integral value (IV) of HbO was used to evaluate cortical activation levels during different stages of resistance training. Participants were required to perform a high-intensity bilateral upper limb resistance training at a constant speed. High-intensity motor needs to increase the activation level of the cerebral cortex functional areas to activate more motor neurons, so as to achieve the purpose of regulating muscle contraction and power output [16]. Therefore, as the main cortical areas in the cerebral cortex that induced motor control, motion-related cortical areas including SMC, PMC and SMA, were highly activated at each stage of resistance training (Fig. 3).

PMC was in front of SMC, and PMC was mainly involved in the planning and preparation of exercises. Research have shown that [17], during motor fatigue, it becomes difficult to regulate muscle output, and PMC is involved in the regulation of muscle output. As shown in Fig. 4, bilateral PMC had a significantly higher activation level at later stage than that at early and middle stages of resistance training. This may be due to the involvement of PMC in the regulation of muscle output during resistance training. During exercise training, the DLPFC is related to attention levels, cognition, control, and higher power output [18]. Research have shown that [19], high levels of control movements require higher attention to maintain motor performance. Part of the explanation for the significantly higher activation level of DLPFC at later stage than that at early stage may be that with the deepening of motor fatigue, participants needed higher attention to maintain certain sports performance.

In this study, whole-brain correlation analysis (SCA) in functional connectivity analysis was used to calculate functional connectivity between different cortex areas during resistance training, aiming to further explore how brain functional connectivity changed in resistance training with the deepening of motor fatigue. As shown in Fig. 5, the functional connectivity range of the cerebral cortex at different stages was similar, showing a wide range of functional connectivity states. Bilateral upper limb resistance exercise belongs to the coordinated movement of wrist, elbow and shoulder joints of upper limbs. Compared with traditional fine movement of the hands or fingers and point-to-point task-oriented training, more muscle groups are activated and the range of activity is wider during upper limb resistance movement, and the task difficulty is more complex [20]. Therefore, more brain areas were needed to strengthen functional connectivity to maintain motor performance during the process of performing task in this study,

As shown in Fig. 6, there existed significant functional connectivity strength differences between the different stages. Compared with early stage, the functional connectivity strength of motor related cortex areas between hemispheres was significantly reduced at middle and later stages. Specifically, the functional connectivity strength of LSMC-RSMC at early stage was significantly greater than that at middle stage, the functional connectivity strength of LPMC-RSMC at early stage was significantly greater than that at middle and later stages, and the functional connectivity strength of RSMC-SMA at early stage was significantly greater than that at later stage. High intensity resistance training could easily lead to acute fatigue. Some researchers have used EEG to explore changes in functional connectivity related to acute motor fatigue. The results showed that the connectivity between the hemispheres of the motor area decreased after fatigue [21], which was consistent with the results of this study.

V. CONCLUSION

Our study initially explored changes in cortical activation and functional connectivity associated with motor fatigue in healthy adults performing high intensity upper body resistance training. Our results showed that the activation levels of DLPFC and PMC were significantly increased and the strength of functional connectivity in motor-related cortical regions between hemispheres was significantly decreased with the deepening of motor fatigue. At each stage, motor-related cortical regions maintained high levels of cortical activation, and the cortex exhibited extensive functional connectivity. As we all know, rehabilitation exercise training can promote the recovery of limb function in patients with motor dysfunction. Among them, motor fatigue can easily lead to muscle soreness and reduced flexibility, and the thinking ability such as judgment and reaction is significantly reduced, thereby reducing the rehabilitation effect. The results of this study have deepened the understanding of the neural processes related to upper limb resistance training based on motor fatigue, and provided clinical basis for the optimization of resistance training strategies related to motor dysfunction patients with changes in brain function under fatigue.

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