

Beta Changes Induced by Acute Hand Loss Model during NMES*

Yun Zhao, Guang H. Xie, Ren Q. Yang, Hai Y. Qin, Yu P. Yang, Xiao Y. Wu, and Wen S. Hou

Abstract— Neuromuscular electrical stimulation (NMES) has been demonstrated to effectively modulate cortical activities by evoking muscle contraction in upper limb and generating joint movements, which showed an excellent performance in motor rehabilitation. However, due to hand loss and cortical function reorganization induced by hand amputation, how neural activities in sensorimotor cortex response to NMES-evoked muscle contraction in the end of an amputation stump is not clear. In this paper, Ischemic nerve block (INB) technique was used to build an acute hand loss model, and 64-channel EEG signals were recorded from 11 healthy subjects to perform a 2×2 factorial design protocol, with the INB state and the current intensity as factors. The changes of NMES-evoked sensorimotor cortical activities were quantified by computing Beta-band event-related desynchronization (Beta ERD) patterns and the time-varying functional connectivity using adaptive directed transfer function (ADTF) before and during INB. The acute hand “loss” resulted in ipsilateral dominance of Beta ERD induced by NMES with two current intensities in the topographic maps, that is, ipsilateral Beta ERD was significantly higher than that the contralateral one ($p < 0.05$). However, before INB, Beta ERD in the contralateral sensorimotor cortex induced by NMES above motor threshold was significantly higher than that in the ipsilateral area ($p < 0.01$). Meanwhile, whatever before or during INB, clustering coefficients of the ADTF network in sensorimotor cortex showed temporal dynamics during two NMES tasks. During INB, NMES above motor threshold-evoked lower clustering coefficients of the time-varying network in sensorimotor cortex than that before INB ($p < 0.05$). The present results suggest that the loss of the hand proprioception will degrade cortical activities in the contralateral area, and increase cortical activities in the ipsilateral area compensatively responding to NMES. This finding may be particularly important to improve the reconstruction of the proprioception function of hand prosthesis.

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I. INTRODUCTION

Neuromuscular electrical stimulation (NMES) has been reported to evoke phantom limb sensations used in sensory feedback of hand amputees by activating afferent fibers at the end of the stump. Generally, electrocutaneous evoked by NMES below motor threshold sensation has been widely used in sensory feedback of hand prosthesis [1], while few studies focused on the electric proprioception evoked by NMES above motor threshold. Proprioceptive feedback plays a key role in various daily flexible movements of human hands [2]. Exploring the physiological mechanism of neural response to NMES-evoked proprioception will promote precise and dexterous control of hand prosthesis.

For NMES studies, healthy subjects are often recruited to ensure the successful implementation of the experiment. However, most NMES patterns for sensory feedback designed from healthy subjects could not apply to prosthesis control used in amputees due to the anatomical structure of the hand and the neural changes [3]. Therefore, how to erase the gap between healthy subjects and amputees should be explored for improving the effectiveness of sensory feedback schemes with NMES based on healthy subjects.

Therefore, many researchers focused on exploring acute functional hand loss model through a lot of techniques, one of which is ischemic nerve block (INB). INB could block sensory afferents from the limb by a blood pressure cuff to model an acute limb loss, which has been used in studies on amputation rehabilitation [4]. Recent INB studies mainly focused on sensory degeneration and phantom limb sensation over time [5], and the changes of cortical activities during INB [6]. Therefore, exploring the changes of cortical activities in sensorimotor cortex may provide some physiology knowledge to further understand how to design NMES patterns for sensory feedback of the hand prosthesis.

Brain activities are usually from different spatial regions forming various functional networks to modulate human behavior, which provides important physiological information for understanding cortical function on limb movement [7]. Brain functional connectivity has been recently used to evaluate dynamical information interactions among cortical regions [7]. Several algorithms of brain connectivity can be used to quantify the information interactions among different brain regions, such as Granger causality (GC) [8], directed transfer function (DTF) [9], and Adaptive directed transfer function (ADTF) [10]. ADTF has been reported to usefully extract the time-varying network patterns in various information processing stages of a cognitive task [11].

In this paper, we utilized INB technique to build an acute model of the hand loss, and then recorded 64-channel EEG data using Beta ERD and time-varying network with ADTF method in sensorimotor cortex from 11 healthy subjects

during NMES tasks before and during INB respectively, aiming to investigate the functional changes of sensorimotor cortical activities induced by the acute hand loss.

II. MATERIALS AND METHODS

A. Subjects

Eleven healthy right-handed subjects (4 females and 7 males, 25±4 years old) were recruited in this experiment. Inclusion criteria for the subjects included: no history of former cardiovascular disease, neurological disorders or orthopedic problems in arms, the dominant right hand, free of upper limb resistance training in the past 6 months. All protocols and recruitment procedures were approved by the ethical committee of Chongqing Cancer Hospital. All subjects signed the informed consent before the experiments.

B. Experimental Setup

The acute hand loss model was built using a commercial blood pressure cuff (Yuwell hemopie-zometer, Yuwell Medicine, China) applying to right fore-arm near the wrist with rapidly inflating to a pressure of 260 mm Hg to block the whole right hand, as shown in Fig.1(A). Above the cuff, the stimulation electrodes were placed on the top of index finger extensor to evoke extension movement or the tactile sensation. Programmable Stimulator (Master-9, AMPI, Jerusalem, Israel) with isolated cables (ISO-Flex, AMPI, Jerusalem, Israel) delivered the stimulation current with the stimulation frequency of 40Hz and the bipolar pulse width of 1 ms, and two stimulation levels: one was set as the intensity to evoke fully extension of index finger with 1.5s (NMES-aMT), another was set as the amplitude to evoke maximal sensation of index finger without extension movement (NMES-bMT). Scalp 64-channel EEG was recorded according to the International 10–20 system using a multi-channel neural data acquisition system (Cerebus 128; Cyberkinetics Neurotechnology Systems, USA) with a low-pass of 500 Hz, sampled at 1 kHz and grounded with an electrode placed over the middle between FPz and AFz.

C. Experimental Protocol

Subjects sat comfortably in a chair with their right arm placed at a customized wood platform on the right side of the chair. The elbow joint was constrained with a bandage to immobilize the forearm.

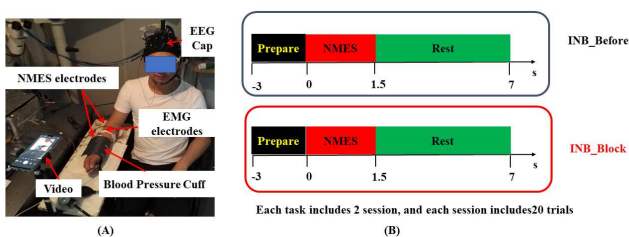


Fig.1 Experimental paradigm of each trial

Each subject was asked to perform 4 tasks: NMES-aMT-evoked index finger extension, NMES-bMT-evoked somatic sensation of index finger before INB (INB_Before) and during fully INB (INB_Block). Each trial was performed as shown in Fig.1(B). There was a 5s rest for subjects between two trials. Between two conditions, a 5 min rest was set for subject to avoid muscle fatigue. All tasks were firstly performed in the INB_Before condition.

During INB, cuff pressure was maintained constant through this whole experimental condition. Before achieving complete block of large fiber sensory afferents, the experimenter conducted psychophysical evaluation every 5 min for the first 20 min and then did every 2 min. The evaluation was performed to test the light touch position, sensation intensity of hand using a cotton swab. The movement sensation of fingers was measured with a plastic rod to pull certain finger, and subjects were required to rate the sensation of finger movement and position, and the effort to extend fingers voluntarily by a numerical rating scale (NRS), with the left end ‘0’ representing ‘not affected’ and ‘7’ representing ‘inability to extend fingers’. While subjects cannot correctly report their sensations of light touch and finger movement, the hand was completely blocked.

D. EEG data processing

EEG data preprocessing were performed in EEGLAB [12], including resampling with 200Hz, Butterworth bandpass filtering of 2~40Hz, interpolating the bad channel using the CleanLine plugin, removing power line interferences and electrooculogram artifacts by the independent component analysis (ICA) method, segmenting the EEG data into the trials from -3 to 7s, with 0s aligned to the onset of NMES tasks, and correcting it using the baseline of -2.5s to -0.5s.

Event-Related Spectral Perturbation (ERSP) was utilized to inspect the spectral power changes of the preprocessed EEG data in time-frequency domain for ERD evaluation using wavelet transform with Morlet wavelets of 7 cycles applied in EEGLAB [12]. Beta ERD values were calculated as ERD_{mean} through averaging the power spectrum across trials at Beta band and the duration of delivering the stimulation current. ERD_{mean} values of EEG data in 21 channels (FC5, FC3, FC1, FCz, FC2, FC4, FC6, C5, C3, C1, Cz, C2, C4, C6, CP5, CP3, CP1, CPz, CP2, CP4, CP6) associated with the sensorimotor cortex were used to draw the brain topographic map. The averaged ERD_{mean} values at the electrodes of FC3, C3 and CP3 were used as the activity level of the contralateral sensorimotor cortex, while that at the electrodes of FC4, C4 and CP4 as the activity level of the ipsilateral area.

The preprocessing EEG data of 21 electrodes described above were selected for time-varying connectivity analysis using adaptive directed transfer function (ADTF), calculated as the following:

$$A(f, t)X(f, t) = E(f, t) \quad (1)$$

$$X(f, t) = A^{-1}(f, t)E(f, t) = H(f, t)E(f, t). \quad (2)$$

where, $X(f, t)$, $A(f, t)$, and $E(f, t)$ are the transformations of EEG data $X(t)$, the coefficient matrices $A(i, t)$ of multivariate adaptive autoregressive model, and the multivariate independent white noise $E(t)$ in frequency domain. $H(f, t)$ is the system transfer function.

ADTF value is calculated:

$$ADTF_{ij}(f, t) = |H_{ij}(f, t)|^2 \quad (3)$$

$H_{ij}(f, t)$, as each element of $H(f, t)$, represents the directed information flow from the j th to the i th node at the frequency f and the time t .

Then, the ADTF values were normalized and integrated in the interested frequency band from f_1 to f_2 :

$$\gamma_{ij}^2(f, t) = \frac{|H_{ij}(f, t)|^2}{\sum_{m=1}^N |H_{im}(f, t)|^2}. \quad (4)$$

$$\theta_{ij}^2(t) = \frac{\sum_{k=f_1}^{f_2} \gamma_{ij}^2(k, t)}{f_2 - f_1}. \quad (5)$$

Finally, ADTF values were averaged in 11 segments including one segment before NMES onset (-200~0ms), and 10 segments after NMES onset (each segment with the time window of 150ms). The first segment was taken as the reference value to detect significantly different networks in other segments during NMES tasks. Graph-theoretical analysis was used to measure the time-varying brain network property of the clustering coefficient based on the BCT toolbox (<https://sites.google.com/site/bctnet/Home>).

D. Statistical analysis

Paired t test was used to compare ERD_{mean} values and the clustering coefficients between contralateral and ipsilateral sensorimotor cortex during NMES tasks. The clustering coefficients over time were divided into three stages: initial phase (0~150ms, Stage1), changing phase (151~750ms, Stage2) and stable phase (751~1500ms, Stage3). Friedman M test was used to analyze the significant difference of the clustering coefficients among the three stages, and then paired t test was used to compare the values between any two stages with FDR correction. IBM SPSS, version 22 was used for statistical analysis, and the significance level was set at $p < 0.05$ for all procedures.

III. RESULTS AND DISCUSSION

A. Effect of INB on Beta ERD Values between Bilateral Sensorimotor Cortex induced by NMES

The topographic map based on ERD_{mean} values of 21-channel EEG data showed the cortical activities in sensorimotor cortex during four tasks (Fig. 2). INB resulted in ipsilateral dominance phenomenon in the Beta ERD distribution of the topographic maps for both NMES_aMT and NMES_bMT tasks, which was opposite to that induced by NMES-evoked muscle contraction in normal state, that is, a contralateral dominance phenomenon of Beta ERD in topographic map, indicating that INB caused the acute functional plastic changes in the sensorimotor cortex.

According to the effect of INB on the spatial distribution of Beta ERD in bilateral sensorimotor cortex shown in Fig. 2, we further compared the difference of Beta ERD values between bilateral sensorimotor cortex, as shown in Fig.3. For INB_Before, ERD_{mean} values in the contralateral sensorimotor cortex were significantly lower than that in the ipsilateral hemisphere ($p < 0.05$), while for INB_Block, ERD_{mean} values in the contralateral sensorimotor cortex showed significant increase than that in the ipsilateral hemisphere ($p < 0.05$) during NMES_aMT task. NMES_bMT-evoked ERD_{mean} values in the contralateral sensorimotor cortex were also significantly higher than that in the ipsilateral hemisphere ($p < 0.05$).

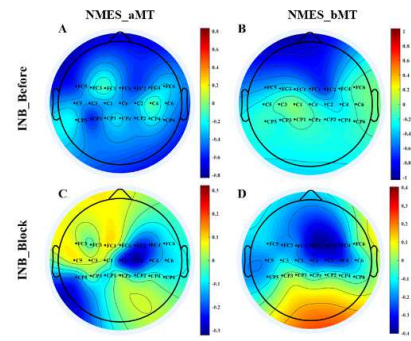


Fig. 2 The averaged topographical distributions of Beta ERD (ERD_{mean}) of sensorimotor cortex for all subjects in two conditions (INB_Before and INB_Block) during NMES_aMT and NMES_bMT. Notes: the blue color indicates the magnitude lower than zero, representing ERD

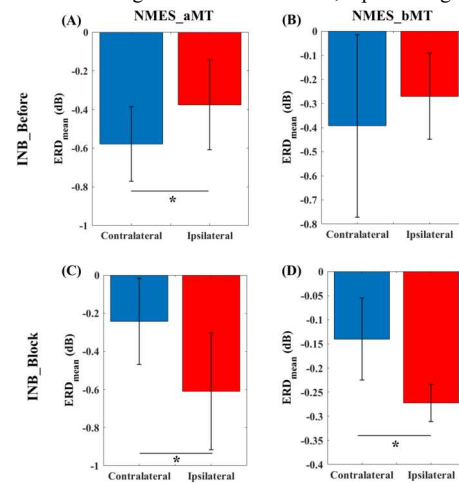


Fig. 3 The difference of ERD_{mean} values between two bilateral hemispheres in two conditions (INB_Before and INB_Block) during NMES_aMT and NMES_bMT. * denotes significant difference ($p < 0.05$)

B. Beta Time-varying Network Properties Induced by NMES in the Sensorimotor Cortex

ADTF values of the links among the channels in sensorimotor cortex displayed in Fig. 4. As shown in Fig. 4(A), the electrode C3 was a main source sending information flow to other area during NMES_aMT task before INB, indicating a contralateral domain of the network connectivity, while transferred to the ipsilateral area (FC4) during NMES_aMT task after INB (Fig. 4B). The similar changes were observed in the network connectivity for NMES_bMT before and during INB (Fig. 4D). Those results further revealed cortical function reorganization during INB, which was also observed in previous fMRI study that during INB, the excitability of the ipsilateral sensorimotor cortex was stronger than that in contralateral region [13]. This is because INB caused a decrease of GABA in the sensorimotor cortex [14], resulting in the cortical excitability increase in the adjacent blocked hand sensorimotor area. Therefore, it suggests that the loss of sensory and motor information in the hand will induce a plasticity function changes in sensorimotor cortex observed during NMES, and the ipsilateral sensorimotor cortex will increase its contribution to the response to the current stimulation.

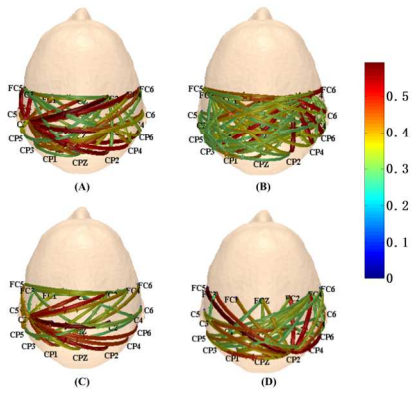


Fig. 4 Color-coded 3-D directed graphs representing the grand-mean information flow during NMES in beta band before and during INB respectively, (A) NMES_aMT before INB, (B) NMES_aMT during INB, (C) NMES_bMT before INB, and (D) NMES_bMT during INB.

Fig.5 showed the statistical results of the difference of the time-varying brain network properties in sensorimotor cortex before and after INB during NMES tasks. Compared with before INB, the clustering coefficients of the time-varying networks in sensorimotor cortex during NMES_aMT tasks were significantly lower in different time periods (151~300ms, 451~600ms, 751~900ms, 901~1050ms, 1051~1200ms, and 1351~1500ms) during INB ($p < 0.05$), see Fig. 5(A). Those results revealed that acute hand loss significantly decreased the efficiency of the functional segregation in sensorimotor regions [15]. However, no significant difference of the clustering coefficients was observed for NMES_bMT tasks between before and during INB ($p > 0.05$), as shown in Fig. 5(B). The clustering coefficient has been shown to be related to the functional efficiency of the brain induced by limb movements, that is, movement-related information processing efficiency [16], which is influenced by proprioceptive afferent information. Therefore, we assumed that the loss of proprioceptive information from the INB-blocked hand was the main reason to reduce the functional segregation efficiency of the sensorimotor cortex during NMES-evoked muscle contraction.

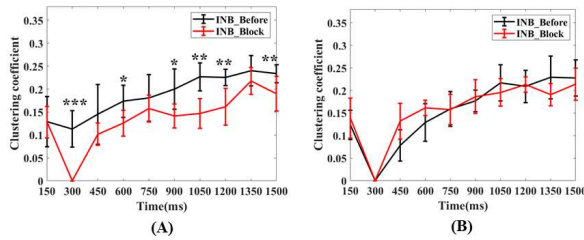


Fig.5 Time-varying network properties of sensorimotor cortex during (A) during NMES_aMT, and (B) during NMES_bMT. * indicates $p < 0.05$, ** indicates $p < 0.01$, and *** indicates $p < 0.001$

IV. CONCLUSION

In conclusion, our study highlighted that INB resulted in the acute sensorimotor cortical plasticity which could be observed from the results of Beta ERD and ADTF values in sensorimotor cortex. However, regardless of INB, NMES-evoked forearm muscle contraction could modulate the functional efficiency of the time-varying networks in

sensorimotor areas, revealing the important role of proprioceptive information on modulating sensorimotor cortical response to NMES, which will promote further exploration of artificial sensory feedback using NMES for prosthesis control.

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