Learning Effects of Neurofeedback-fMRI on Neural Substrates Involved in Motor Imagery

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Introduction: Recent bodies of evidence have shown that feedback of region-specific brain function, characterized by functional MRI (fMRI), can help individuals voluntarily modulate cortical activities. These include the regulation of activity in somatomotor areas during hand motor tasks [1], in rostral-ventral/dorsal parts of the anterior cingulate cortex associated with the regulation of affective states and pain [2,3]. Posse et al. [4] studied an active process of induced emotion by measuring the MR signal changes associated with self-regulation. Recently, modulation of auditory areas was reported from the selective auditory attention task using fMRI-enabled neurofeedback [5]. deCharms et al. [6] have shown that the performance strategy can be learned and retained (even after the trial sessions) to enhance activation in the somatomotor cortex during hand imagery tasks. However, the investigation regarding the long-term effects (more than 2 weeks) of neurofeedback training, factoring in the comparison subject population, was warranted. We were motivated to systematically examine the effect of neurofeedback on motor imagery tasks, which was augmented by repeated daily self-training, based on the task-strategy learned through neurofeedback.

Method: **Study Procedure:** The study was approved by the local Institutional Review Board. A total of 24 right-handed healthy participants were divided into two groups (one group undergoing real neurofeedback and the other a placebo comparison group undergoing 'sham' neurofeedback). The two groups were matched in terms of gender (M:F=7:5 in each group), basic cognitive ability (tested via sequential number memorization tasks [6]; p>0.05) and age (24.8±4.67 yr; p>0.05). The study was conducted in a 3 Tesla clinical scanner (Signa VH, GE) using a standard birdcage head coil for RF detection. An EPI sequence (TR/TE=1000/40ms, 64x64, 5mm slice thickness, 24cm square field-of-view) was used. After brief instruction, subjects performed a motor imagery task of the right hand. All subjects practiced the task 2-3 times prior to scanning in order to reduce variant activation patterns. An overall schematic of the study is shown in Fig.1. Three sets of pre-trial fMRI sessions were administered to establish the baseline signal level. Each task lasted 60s, with the task occurring at 20s and stopping at 25 s. Subsequently, seven sets of neurofeedback sessions employing real-time fMRI (each 1min 51 sec long) were administered where the subjects were shown their own BOLD signal activities, originating from the left motor areas as a line graph, via MR compatible goggles. For the comparison group (all subjects were blinded to the session and believed that they were undergoing a neurofeedback session), the BOLD signal was sampled from non-activated sites and scrambled in sequence to create sham contents to the subjects. Consequently, three sets of post-trial fMRI were conducted using the same paradigm as the pre-trial task. The subjects were given a PDA device (HP Pocket PC, iPAQ 4150) implemented with the same task paradigms for use in self-practice of the same task for two weeks (once everyday) before the 2nd study visit. Using the learned and practiced task-strategy, the subjects again underwent the last 3 sets of fMRI sessions as post-train sessions.

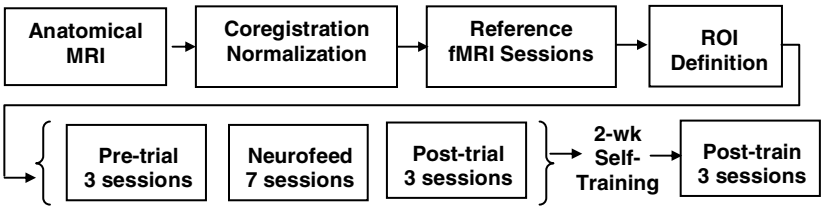

Fig. 1. Schematics of overall experimental procedure.

Data Analysis: The data was processed with SPM2 after data reconstruction and preprocessing (slice timing correction, motion-correction, normalization to MNI space and spatial smoothing of 8mm FWHM kernel). Individual effects were estimated using a General Linear Model, examining the effect of neurofeedback (Post-Trial> Pre-Trial) and the effect of self-training over a 2 week period (Post-Training > Post Trial). A paired *t-test* was conducted to compare two groups (n=12 each, d.f.=11) with a thresholded of p<0.05 (T-score>1.8), focusing on the sensorimotor areas. Self-evaluation of each subject's performance was obtained (1 through 10; 1 being unable to perform, 10 being best performance) based on the results during the neurofeedback sessions.

Results & Discussion: The proposed method of automated real-time processing and display of cortical activities was successfully implemented for all subjects. As shown in Fig.2A, control (placebo) subjects' perception toward the training was indifferent from the pre-trial session, but the neurofeedback group performed better after the neurofeedback trial and its corresponding training (paired-t; p<0.05). Data analysis showed that the contralateral region-of-interest (ROI) from the neurofeedback group has shown a greater increase of BOLD signals as compared to the matched comparison groups (Fig.2B in yellow arrow) and were even consolidated via the training sessions. It was interesting to find that the motor area ipsilateral to the tasks (right hemisphere) also showed an equivalent and even stronger degree of signal enhancement through PDA-training (Fig.2B in blue arrow). The results indicate that neurofeedback and subsequent training enhance the cortical activity associated with a motor imagery task to a greater extent than placebo-training sessions. The clinical implication of the engagement of ipsilateral hand motor areas via neurofeedback and subsequent training may have future ramification on motor rehabilitation.

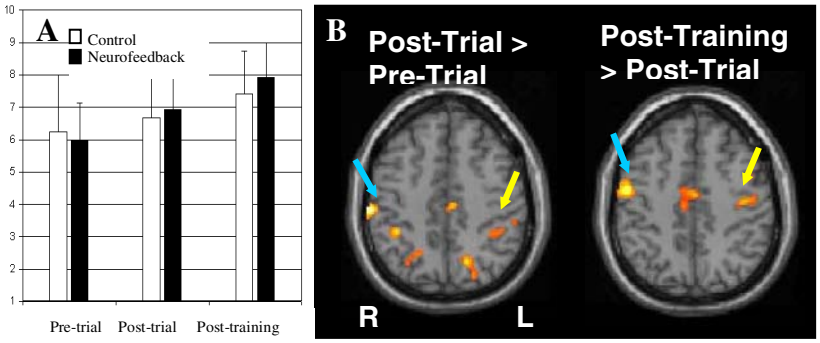

Fig. 2. (A) Results of subject self-evaluation and (B) The group effects from comparing the effects of trial and effects of training upon neurofeedback

Reference: **[1]** Yoo et al. Neuroreport. (2004) 15(10):1591-5. **[2]** Weiskopf et al. IEEE Trans Biomed Eng. (2004) 51(6):966-70. **[3]** deCharms *et al.* Proc Natl Acad Sci U S A. (2005) 102:18626-18631. **[4]** Posse et al. Neuroimage (2003)18(3):760-8. [**5**] Yoo et al. Neuroreport. (2006) 17(12):1273-8. [6] deCharms et al. Neuroimage (2004) 21(1):436-43.

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