Neurofeedback real-time fMRI for the regulation of motor areas in chronic stroke patients

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Introduction: The goal of physical rehabilitation for the stroke patients is to enable patients to re-acquire important fundamental motor skills. Real-time feedback of physiological signals, such as proprioceptive feedback necessary for motor learning, helped stroke patients to set a performance goal or to supplement damaged cortical functions during (attempted and executed) physical locomotion. However, these methods provide only information pertaining to the activities associated with peripheral neuromuscular function, not the functional recovery/reorganization processes at the very level of the brain where the direct damage occurred. Therefore, the method enabling the monitoring of the local CNS activation was warranted for the feedback application toward potential neuro-rehabilitation. We developed real-time fMRI (rtfMRI) neurofeedback method to chronic stroke patients with unilateral hand motor deficits, with an aim to demonstrate that real-time feedback of an individual's regional brain activation [1], especially from the motor-related areas that are affected by a stroke, will help the patients to gain a degree of voluntary regulation of the activation from the same areas.

Method: The study was approved by the local Institutional Review Board. The fMRI data were acquired in a 3-Tesla clinical scanner (Signa VH, GE Medical System) using a single-channel standard birdcage head coil. Two volunteers (Table for description; both right-handed before stroke) were participated in the neurofeedback experiments via rtfMRI. Prior to the fMRI examination, the recruited patients underwent locomotor assessment of the affected hand. The assessment of the upper extremity motor control was measured using the Fugl-Meyer Assessment (FMA) scale (upper extremity portion). Spasticity was measured using the Modified Ashworth Scale (MAS). The primary motor scale was the FMA because it is a well-designed, widely-used clinical examination method for the stroke population.

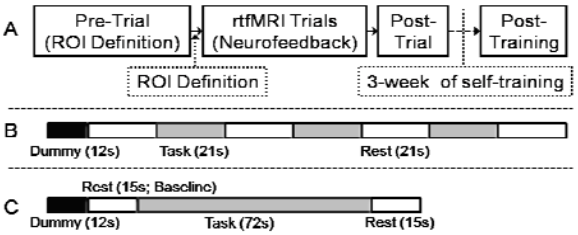

Fig. 1 *Illustrations of the (A) flow diagram of the study design, (B) designed paradigm during the pre-, post-trial, and post-training, and (C) designed paradigm during rtfMRI trials.*

The flow of the study is illustrated in Fig. 1. A gradient echo planar imaging (EPI) sequence was applied to obtain BOLD fMRI data and 24 axial slices were acquired to image most of a brain volume including the cerebellum (TE/TR=35/1500ms, FA=90°, 64×64 in-plane voxels, 5mm thickness, 1mm gap, field-of-view=24×24cm^2). After the acquisition of the fMRI data, diffusion tensor imaging (DTI) sequence was applied using a standard 8-ch head coil in order to quantify the integrity of white matters before and after the 3-week self-practice. The 32 volumes including one T_2-weighted baseline volume and diffusion-weighted volumes in 31 gradient directions were acquired (TE/TR=76.9/7300ms; FA=90°; 256×256 in-plane voxels; 4mm slice thickness; no gap). After applying the anatomical registration [2], the anatomical areas of the participant's EPI volumes were automatically labeled from an automated anatomical labeling (AAL) map and Brodmann's area (BA) to help the identification of the ROI. Since we targeted on the feedback of the hand-motor related BOLD activations, the CC values within the primary motor and sensory areas (*i.e.* M1 & S1) on both hemispheres were measured and a voxel showing a maximum CC value along with four neighbor voxels (*i.e.* anterior/posterior/left/right) in the same slice were selected as the ROI from each hemisphere. The feedback information, BOLD signal originating from the ROI, was shown as a line plot to the subjects.

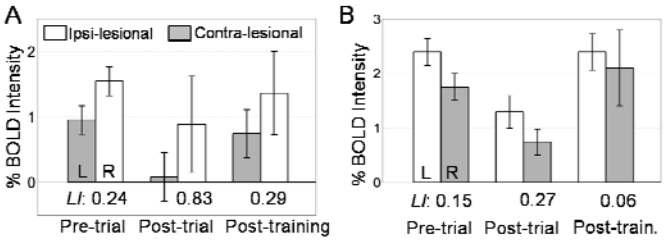

Fig. 2. *The results of the average percent BOLD intensities (bar) during task-related periods along with standard deviation (whisker) within two ROIs on both hemispheres from the (A) subject 1, and (B) subject 2 (L: left hemisphere; R: right hemisphere; LI: laterality index). Note that the LI values were increased after rtfMRI training for both subjects.*

Results & Discussion: During the rtfMRI trials, a male subject showed the ability to modulate the desired level of activation pattern at the 6th trial while a female subject showed the ability in the 4th trial. The overall performance on the enhancement of ipsi-lesional neuronal activities along with the reduction of the contra-lesional activities was measured as Laterality Index (*LI*;[3]) based on the averaged percent BOLD activations during task-period of the pre-, post-trials, and post-training fMRI data (Fig. 2). The white and gray bar graphs indicate the mean percent BOLD intensities corresponding to the ipsi- and contra-lesional areas, respectively (L: left-, R: right-hemisphere). After the rtfMRI trials, the *LI* values from the post-trials were substantially increased for both subjects compared to these of the pre-trials (subject 1: from 0.24 to 0.83, subject 2: from 0.15 to 0.27). The slightly reduced percent BOLD intensities of the post-trials common for both subjects may be due to decreased processing demand associated with motor skill learning. A female subjects (Fig 2B), who was not able to follow the designated practice routine, showed that training did not helped to maintain the elevated *LI* value, which suggests the importance of self training after the neurofeedback trials. Both subjects showed the improvement in speed of affected hand movement (Table I). In summary, this preliminary data indicates that fMRI neurofeedback may help chronic stroke patients to gain voluntary regulation of stroke-affected regional brain function.

Subject #1 Male, 56 year old, right subcortical hemorrhaging, hemiperetic; MMSE=29/30	
FMA_pre=19/66; speed* L/R=9.15/2.5 s	FMA_post=22/66; speed L/R=8.80/2.4 s
Subject #2 Female, 63 year old, left subcortical ischemia, hemiperetic; MMSE=28/30	
FMA_pre=28/66; speed L/R=3.91/13.7 s	FMA_post=29/66; speed L/R=3.2/12.0 s

Table 1. Subject information and functional assessment results before and after the neurofeedback session ('FMA_pre' versus 'FMA_post')

Reference: [1] Yoo et al. Neuroreport (2002) 13:1377-81. [2] Lee et al. Hum Brain Mapp. 2008; 29(2):157-66 [3] Yoo et al. Neurosci Lett. (2005)383(1-2):1-6.