A demonstration of neural plasticity in resting brain network

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INTRODUCTION: Much progress has been made recently to study the resting brain with functional connectivity MRI (fcMRI) and it is argued that understanding the resting brain activity is at least as important as that of evoked neural activity (1). Then, by the same token, we hypothesized that an important feature of the evoked activity, the plasticity of the neural response, may also be present in the resting condition and may provide critical information for understanding the nature and significance of the resting state brain activity. The goal of this study is therefore to demonstrate for the first time that the resting brain activity can be altered after repetitive stimulation of the associated brain networks. We used motor cortex as a model system since its resting connectivity is well characterized (2-4). Resting state activity is measured as the temporal correlation coefficient (CC) of low-frequency BOLD signal oscillation (<0.1Hz) between the left (LMC) and right motor cortices (RMC) (2). As a control study, we also tested whether the CC values would change without the repetitive stimulation. Resting activity in other brain networks (i.e. non-motor networks) was also assessed for possible changes. Finally, the amplitude of the BOLD fluctuation was assessed to elucidate the origin of the improved connectivity.

METHODS: BOLD fMRI data (3.4x3.4x5mm^3 voxels, TE 25ms, TR 1000ms) were acquired in 14 healthy *right-handed* adults using a 3T Philip MR scanner. All subjects (28.5±10.5yo, 8males) completed two sessions with 9 of the subjects completed a third session of control experiments. The first session includes two fcMRI runs with a 30 minute gap. During the 30 minute gap, the subject performed a unilateral (right-hand only) motor task, in which they fixated on a white crosshair and, when the crosshair occasionally changed color to grey for 1000ms, they are supposed to press a button three times with their right index finger as soon as they saw the crosshair dim. The color change occurs every 27-32 seconds with randomized intervals. The two fcMRI runs before and after the motor task were performed with the same protocol: fixation on a white crosshair, 300 image volumes covering 21 slices, duration 5 minutes. The second session (on a different day) was designed to identify bilateral primary motor cortex (M1) and only contained two motor fMRI runs. They used block-design of 20s finger tapping on both hands. This session was intentionally done separately with a minimum 24-hour gap to avoid confounding factor of motor exercise (in session 1) on the selection of motor cortex ROI. The activated voxels in the motor fMRI were ranked in descending order by their t-score and the top 400 voxels were selected as the motor area mask. Control scan: Seven 5-min consecutive fcMRI scans (300 volumes each) were conducted on nine of the 14 subjects in a third session in order to test whether the observed change was due to subject becoming sleepy/drowsy/anxious in the magnet environment. Subjects were instructed to fixate on the same white crosshair. Postprocessing: The motor cortex masks obtained from the fMRI runs was applied to the fcMRI data to obtain an averaged time course for left and right motor cortex separately. Then after respiratory correction, whole-brain fluctuation correction, low-pass filtering (<0.1Hz), baseline correction and normalization, the temporal signal remained is considered the resting state brain activity of each ROI. Correlation coefficient between the two time courses from the left/right ROIs is calculated. Coefficient of Variation (CV) of a time series is calculated as BOLD fluctuation standard deviation$_{n=300}$/temporal mean$_{n=300}$x100.

RESULTS and DISCUSSION: For each subject, once the left M1(Fig. 1B) and right M1(Fig. 1C) ROIs are identified from motor fMRI activation maps (Fig. 1A), we calculated their CC in pre-task and post-task fcMRI time courses (Fig.1D-E). Group analysis (n=14) shows that the CC increased significantly (Fig.1F). Further, the control experiments show that CC does not drift or change significantly if subjects remain rest. The CC values of run 1 were not significantly different from any of the later runs (p>0.3), suggesting that the change of CC in the task session is not due to subject settling down in the magnet. Also, the increase in CC appears specific to the M1 ROIs, as other network (DN) did not show a change in CC before and after the motor task (Fig.2). Next, we investigated whether the increased CC is because the bilateral time courses are more synchronized (with the need to change the fluctuation magnitude) or because the magnitude of the BOLD fluctuation has actually increased. Such analysis shows that the BOLD fluctuation, as assessed by CV of the time course, has increased comparing pre- and post-task fcMRI data (Fig. 3). Interestingly, this magnitude change was observed for both left and right M1, even though the task was right-hand only which supposedly only activate the left motor cortex.

To our knowledge, this is the first demonstration that fcMRI brain networks can be modified in the acute phase using a simple task. We showed that the resting state connectivity of bilateral motor cortices is strengthened after 30 minute of motor task. This change does not appear to be related to the adaptation to the magnet environment and is specific to the brain network stimulated. This method may provide a new approach to study brain plasticity in humans and may find applications in studies of aging and neurodegenerative diseases.

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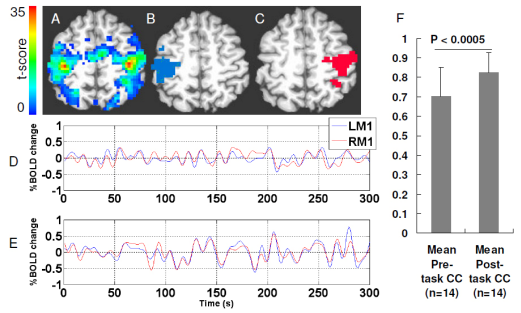

Figure 1. Motor task improved fcMRI CC in motor cortex. (A) Subject-specific t-score map showing voxels significantly activated in bilateral finger tapping scan (from a separate session). (B) Left motor cortex ROI. (C) Right motor cortex ROI. (D) BOLD time series from (B) and (C) in pre-task resting state, (E) in post-task resting state. (F) Group analysis (avg. CC of 14 subjects, std dev. error bar.)

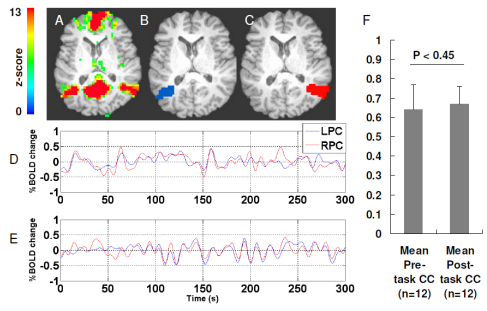

Figure 2. Motor task did not alter connectivity in a different network. (A) The Default Network during rest. (display threshold=5.4). (B) Left parietal cortex (LPC) ROI. (C) Right parietal cortex (RPC) ROI. (D) BOLD time series from (B) and (C) before the motor task, (E) after the motor task. CC between LPC and RPC did not increase after the motor task. (F) Group analysis (n=12): Average CC did not change significantly by the task.

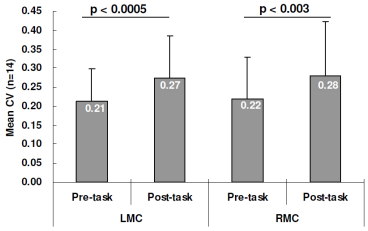

Figure 3. Magnitude of BOLD fluctuation increased significantly in post-task resting state. For both LM1 and RM1, coefficient of variation (CV) became larger after executing the motor task. Error bars reflect standard deviation across 14 subjects.