Real time BOLD functional MRI neuro-feedback affects functional connectivity

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Abstract

Functional connectivity in the resting state based on BOLD functional MRI (fMRI) has been used mainly to observe brain networks while subjects 'do nothing'. The same principle, however, can be used for any other steady-state brain condition. In this study, we compared the connectivity of the motor area during simple finger tapping with and without real time neuro-feedback of the activation in the hand motor area. The presence of the neuro-feedback not only induces correlations between the visual and motor areas, but also increases basal ganglia involvement and bilateral motor cortex connectivity.

I. Introduction

Neuro-feedback uses neurophysiological data to update the subject about his or her own performance with the goal to improve behavior. While EEG-based techniques have been used for many years [1] – [4], real-time fMRI (rt-fMRI) based neuro-feedback is a more recent technology that allows brain activity, as extracted from BOLD fMRI, to be used as the signal to feed back to the subject. This technique is implemented by reading, in real time, the BOLD images and using the intensity of activity from a region of interest as a parameter for the display the subject sees while in the MRI scanner. One main advantage of fMRI neuro-feedback is that the signal to be fed back to the subject can simply be the average of the BOLD activity in a brain area of interest, contrary to the complex pattern recognition and machine training needed in EEG based techniques. Rt-fMRI has been successfully used in motor and motor imagery tasks [5] – [7] using areas of interest in the motor cortex or supplementary motor area (SMA). This technique has also been used to modulate activity in higher cognitive areas such as the amygdala [8] and insular cortex [9].

While these studies explored the ability of the subject to modulate a particular brain area, to our knowledge, no study has yet looked at the effects the feedback has on functional connectivity. In this work, we explored the effect of the neuro-feedback signal on the functional connectivity of the motor cortex.

II. Methodology

Subjects performed a right hand finger-tapping task in the scanner with and without feedback of activity from the contralateral motor cortex. Electromyography (EMG) was used to monitor task performance. Post-hoc, we investigated changes in connectivity due to the presence of the neuro-feedback.

A. Paradigm

Task conditions were presented in a block design fashion. During the run without feedback (called GO), subjects saw the word "GO" on the screen, instructing them to tap their fingers, and a fixation cross to indicate rest. During the feedback runs (FBK), finger tapping was indicated by a red column, the height of which was modulated by the amplitude of their brain activity during finger tapping, and rest was indicated by a fixation cross. Five blocks of 20 seconds task and 20 seconds rest were collected for each condition.

B. Subjects

Five healthy subjects (3 males, 2 females; ages: 25 to 34) participated in the study after giving informed consent. All subjects were right handed and had normal neurological examination.

C. Imaging

Images were collected on a 3T GE scanner using an 8 channel head coil. After a scout image, 14 slices were selected in the axial plane, covering the motor cortex. EPI was collected using the following parameters: FOV: 22.4cm; resolution 64×64, 14 slices, slice thickness 5.0 mm, gap: 0.5mm. TR was set to 0.8 seconds, and flip angle at 50 degrees. 294 images were acquired at each run.

Full head MPRAGE was collected from all subjects and used for data normalization for group analysis.

D. Real time fMRI

BOLD signal from real-time fMRI was used to generate neuro-feedback. It was implemented using the real time plug-in in AFNI [10] and an in house program written in python [11].

The region of interest (ROI) for the neuro-feedback run was selected in the motor cortex, based on the maximum regional activations during the GO run. A second ROI was drawn in a slice distant from the motor area to correct for global effects. Each run started with a resting period for MRI signal stabilization (5 seconds). The following 20 seconds subjects were at rest, and data from this period was averaged to create reference signal 'Signal_ref'.

$$\text{Signal\_ ref} = \text{mean\_ ROI}_{\text{motor\_ ref}} / \text{mean\_ ROI}_{\text{full\_ ref}}$$

The mean value from each ROI was computed in AFNI and read by the python program. The neuro-feedback signal was computed as the relative change between the signal in both ROIs at time 't' and the reference signal:

$$Signal\_t = \frac{(mean\_ROI_{motor\_t}/mean\_ROI_{full\_t})}{Signal\_ref}$$

During the feedback blocks, subjects saw a red column on the screen with a continuously updated height that was proportional to Signal_t. Signal_t was updated after each TR and has a delay of 1 TR (0.8s) plus about 1 second. The main delay in the rt-fMRI neurofeedback comes from the hemodynamic response.

E. Electromyography

MRI-compatible electrodes were placed on the right first dorsal interosseous muscle and data measured using Brain-products system.

After removing the gradient artifact, the EMG signal was baseline corrected and rectified; finally, we computed the mean activity for the finger tapping blocks for each subject.

A two-tail paired t-test was used to compare the means of the runs with and without feedback.

F. MRI Data Analysis

Data processing was performed in AFNI. Five images from each run were discarded to account for MRI equilibration effects. Pre-processing included: slice timing correction, volume registration, motion correction and scale to percentage signal change. MPRAGE datasets were normalized to the Talairach standard template [12].

A seed area was selected in the motor cortex (MC), based on activation in the GO task (see figure 1a,c). This is the same area used for the neuro-feedback. We performed connectivity analysis by correlating the time-course of the MC seed during the blocks of activity with all voxels of the brain (see figure 1d).

Correlation coefficients were converted to z-scores using Fisher's transformation $(z=0.5*((1-r)/(1+r)))$. A map of the MC connectivity during finger tapping was constructed for the GO and the FBK runs by averaging the z-scores across subjects.

In order to test the differences due to the presence of the feedback signal, the GO and FBK connectivity maps were compared using a paired t-test.

For each subject, we computed connectivity during finger-tapping for the GO and FBK runs.

We defined regions of interest in the right and left hand knob, by drawing an ROI on the structural data; and in the putamen by conjunction of the t-test results and the anatomical templates provided by AFNI. For each of these ROIs, we computed the average correlation coefficient per subject and per run.

III. Results

EMG

All subjects performed the task as requested, showing EMG activity during the GO/FBK times and a quiet EMG during the resting period (see figure 1b).

There was no significant difference in EMG amplitude between the GO and neuro-feedback runs (p= 0.19)

fMRI connectivity

The MC seed, during the GO paradigm, showed less bilateral connections than what typically is seen during the resting state [13]. Notably, the right motor cortex did not demonstrate any significant correlation to the left motor cortex seed region (see figure 2).

The t-test of the connectivity maps between GO and FBK paradigms shows the strongest differences in connectivity in the basal ganglia, supramarginal gyri and insula cortex (see figure 2). The contralateral motor area and pre-motor areas showed increased connectivity. A difference is also seen in visual areas, more likely due to the increased visual stimulation during the FBK condition.

ROI analysis

The mean correlation coefficient between the seed region and the left hand motor area was 0.54 (p<0.003) for the GO and 0.74 (p<0.00013) for the FBK condition. The right hand motor area was significantly correlated to the seed (r= 0.22, p<0.0012) for the FBK condition, but did not reach significance for the GO condition (r=0.03, p>0.1). The putamen was correlated to the MC seed in both conditions, but the strength of the correlation was significantly higher in the FBK condition (Left GO: r=0.25 (p<0.015), FBK: r=0.45 (p<0.0001).; Right GO: r=0.16 (p<0.015), FBK: r=0.38 (p<0.0001). See figure 3.

IV. Discussion

Functional connectivity of the motor area has extensively been studied at rest. Less often, it has been studied as subjects perform a sustained amount of activity. Here, we showed that the connectivity is affected by the presence of neuro-feedback. Even though we studied a small sample so far, the patterns of connectivity were affected by the presence of neuro-feedback.

It has been reported that the connectivity of the motor cortex becomes more unilateral during task performance [14]. However, when feedback was present, the connectivity became more bilateral, as seen in figures 2 and 3.

The EMG level was not sufficient to account for the significant increase in connectivity between MC and putamen during the neuro-feedback runs. Ventral striatum has been related to feedback activity in monitoring performance and rewards [15]. Thus, it is possible that the motor and executive circuits of the basal ganglia are engaged during neuro-feedback, and that basal ganglia increases its connectivity with the motor cortex [16].

V. Conclusion

We showed that introduction of neuro-feedback during a simple motor task has an effect on the connectivity of the motor circuits. These results are independent of the amount of activity. Therefore, the use of rt-fMRI as a neuro-feedback tool may enable subjects to modify functional connectivity within motor circuits and could create new possibilities for clinical interventions.

Acknowledgments

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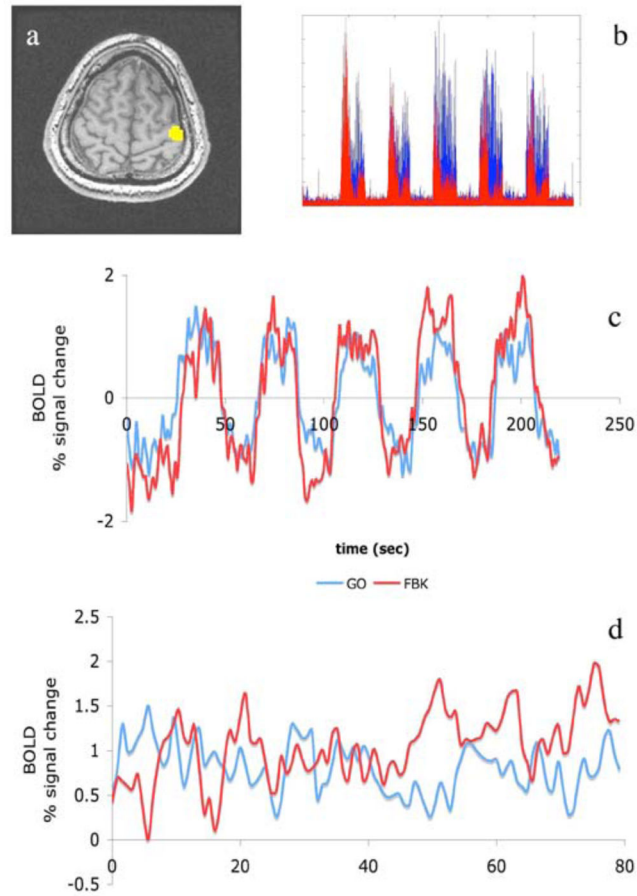
Figure 1.
Single subject data. a) Motor Cortex seed; b) EMG activity measured over 5 blocks; c) BOLD signal time courses during the GO (blue) and FBK (red) runs; d) BOLD signal time course for the blocks of motor activity.
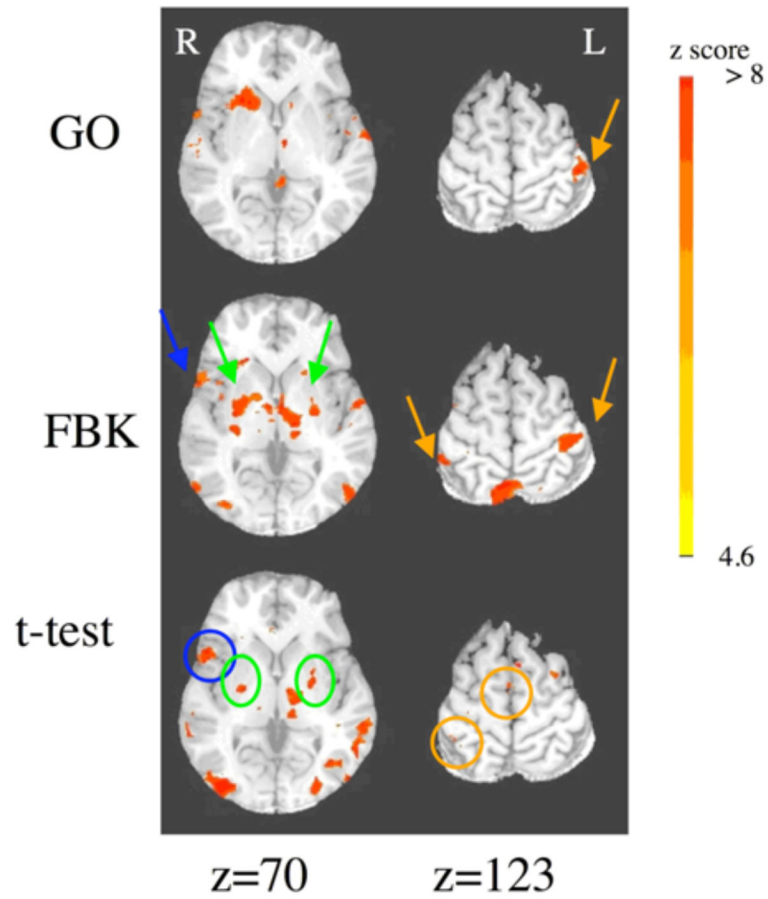
Figure 2.
Connectivity maps with the MC seed, data from five subjects. Orange arrows signal motor cortices, green putamen and blue insula cortex. Circles indicate the same areas in the t-test map.
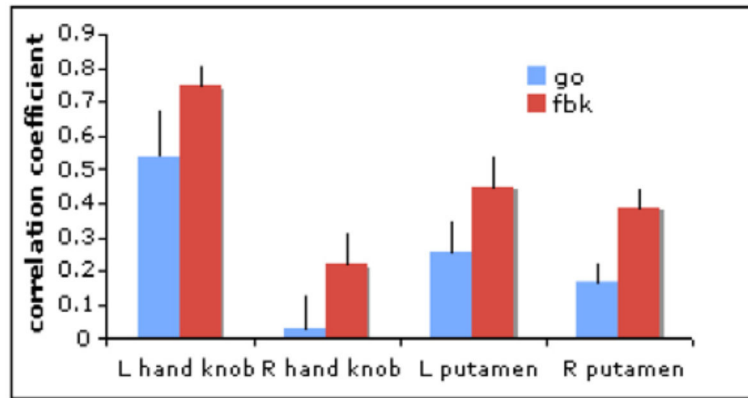
Figure 3.
Mean correlation for selected ROIs