Performance related brain differences in real-time fMRI neurofeedback of imagined hand motor activity

M. Chiew[1,2], S. M. LaConte[3], and S. J. Graham[1,4]
[1]Medical Biophysics, University of Toronto, Toronto, Ontario, Canada, [2]Rotman Research Institute, Toronto, Ontario, Canada, [3]School of Biomedical Engineering, Virginia Tech, Blacksburg, Virginia, United States, [4]Imaging Research, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada

Introduction Neurofeedback (NF) is a training technique supporting self-regulation of brain activity, based on appropriate sensory stimuli that index mental processing performance in "real-time". Functional magnetic resonance imaging (fMRI) can be used to implement NF through real-time acquisition of blood oxygenation level dependent (BOLD) signals that can provide feedback on the timescale of seconds. The use of fMRI for NF is of increasing interest, with applications ranging from pain management [1] to brain-computer interfaces [2]. Recently, fMRI NF in motor imagery experiments using operant conditioning was successfully demonstrated [3]. Here, NF is applied in a similar approach with hand motor imagery to increase lateralized BOLD activation in primary motor areas. Distinct from previous work, however, the brain activity that mediates successful NF in the motor system is investigated by accounting in multivariate analysis for an anticipated wide spectrum of NF performance. This approach is statistically more powerful than simply comparing group differences with and without NF. The results of this study ultimately will help to elucidate the neuronal mechanisms that underlie NF and self-regulatory processes, to develop improved NF techniques and to triage subjects who will or will not be receptive to NF training.

Methods Data were acquired at 3.0T on a Magnetom TIM Trio system using a 32-channel phased array head coil. Real-time fMRI was performed using a modified 16 slice (5mm) gradient echo T2*-weighted echo-planar imaging (EPI) acquisition, with 3x3mm^2 in-plane resolution, 192mm field-of-view, 30ms TE, 1000ms TR. A specially adapted image export module provided real-time data transfer to a computer running AFNI over a local network. Mean BOLD activation amplitudes were computed from regions of interest (ROIs) over the left and right primary motor areas and sent to a display computer that relayed visual stimuli to the subjects via projector. ROIs were identified from a block design "functional localizer" using motor imagery and overt hand clenching (15s on/off, 10 blocks) and were defined using 3x3 voxels in-plane and 2 voxels in the z-direction, centrally located on the regions corresponding to peak left and right imagery.

Eleven young (27 ± 3.4 years), healthy right-handed subjects (6 male) volunteered for a series of 4 NF training runs. Each run consisted of 12 trials of 45s duration, 6 per hand. In the trials, subjects were instructed to maximize a laterality index, computed as the difference in %BOLD activation between the targeted and opposite ROIs. After a 5s cue, subjects performed motor imagery while viewing a horizontal bar and vertical line displaying the instantaneous and time-averaged laterality index, continuously updated with a single TR lag. This was followed by a 5s assessment period which compared the block averaged laterality index to a success threshold, and then 20s of rest. Thresholds changed after 4 consecutive successful or failed trials, either increasing to the minimum index of the previous 4 successful trials, or resetting to the previous threshold. The initial threshold was 0%.

The fMRI data were analyzed using behavioural partial least squares (PLS) [4], a multivariate method for determining spatial patterns or networks in brain activity that maximize correlations between behavioural and neuroimaging data. The behavioural performance measure used for each subject was the total number of successful (above threshold) right-hand imagery trials. Only two experimental conditions were included in the analysis: cue presentation and real-time neurofeedback during right-handed trials. The data were pre-processed using rigid body motion correction, physiological noise correction, and spatial smoothing (6 mm Gaussian kernel). All subject data were spatially normalized using the Montreal Neurological Institute atlas for group comparison.

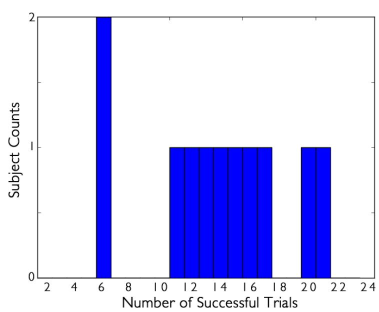

Figure 1 - Histogram showing the broad distribution of the number of successful right handed trials across all subjects.

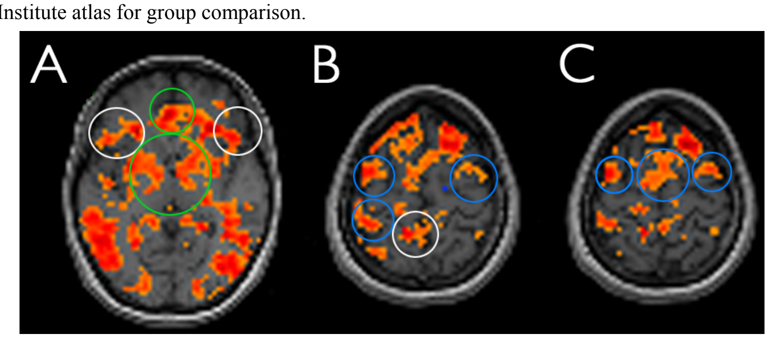

Figure 2 - Three slices from a group averaged behavioural PLS analysis, showing the spatial distribution of latent variable 1. Regions highlighted in green correspond to feedback processing, in white to self-awareness and imagery, and in blue to motor control.

Results Fig. 1 shows the spread of NF performance values across all subjects, indicating that subjects varied widely in their ability to perform NF trials successfully.The behavioural PLS results produced one significant latent variable (LV1, p=0.04) which accounted for 66% of the data cross-block covariance. For the regions in LV1, the correlation between the number of successful right hand trials and the average BOLD activity during the real-time NF condition was 0.40. This implies approximately 16% of the variance in NF performance is associated with the spatial distribution of activity defined by LV1.The resultant group averaged spatial map of brain scores is shown in Fig. 2, with 3 representative slices highlighting some of the regions that are associated with successful motor imagery NF. In A, activity can be seen in bilateral basal ganglia, thalamus, insula, anterior cingulate, and middle temporal gyrus. Left primary motor, precuneus and bilateral premotor activity can be seen across B and C, and supplementary motor area activity is evident in C.

Discussion Previously we have shown successful up-regulation of BOLD signal in primary motor ROIs due to motor imagery NF, without looking at the underlying neuronal mechanisms [5]. The brain regions described here contribute to these aspects of mental processing: self awareness and imagery, feedback processing, and motor control. Prior work in brain-computer interfaces identified cortico-basal ganglia-thalamic circuits that were integral to mediating NF techniques [6], as well as the anterior cingulate cortex and ventral striatum and midbrain [7], which are confirmed in Fig. 2. Activation of the insula has not previously been reported in this context, although studies have found increased activity in insular regions following 2 weeks of self-practice motor imagery [8]. The insular cortex is known to be involved in motor control, as well as self-awareness and interoception (the act of sensing internal state). The precuneus is associated with motor co-ordination and imagery, although it has been previously reported to be more active in NF control subjects (receiving sham feedback) than those subjects receiving true NF [8]. The pre-motor, supplementary motor and primary motor regions are involved in motor planning and execution, and are all involved in motor imagery. The low 16% variance explained by LV1 is likely due to temporal averaging during the analysis, collapsing all the temporal information into a grand mean, which can be remedied in the future with an event-related PLS analysis. Additional future work will address the spatiotemporal separation of the distinct networks involved in these three tasks, as well as their interaction and relative contributions to successful NF.

References

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