fMRI Neurofeedback of Kinesthetic Motor Imagery

Mark Chiew[1,2], Stephen M LaConte[3,4], and Simon J Graham[1,5]

[1]*Medical Biophysics, University of Toronto, Toronto, Ontario, Canada,* [2]*Rotman Research Institute, Toronto, Ontario, Canada,* [3]*Virginia Tech Carilion Research Institute, Virginia Tech, Roanoke, Virginia, United States,* [4]*Virginia Tech – Wake Forest University School of Biomedical Engineering and Sciences, Virginia Tech, Blacksburg, Virginia, United States,* [5]*Imaging Research, Sunnybrook Research Institute, Toronto, Ontario, Canada*

Introduction: Functional MRI neurofeedback (fMRI NF) is an emerging technique that trains subjects to regulate their brain activity by manipulating representations of their fMRI signals in "real-time". Using this methodology, feedback loops can be generated that have latency on the timescale of seconds. One fMRI NF application that is actively being explored is the access and control of motor network regions using motor imagery [1,2]. As kinesthetic motor imagery (kMI) holds promise as a tool to improve stroke rehabilitation [3], it is of interest to explore how fMRI NF training in young healthy adults can influence the brain activity associated with kMI. Here we report an fMRI NF study of brain activity in the left and right primary motor areas associated with kMI, analyzed using partial least squares (PLS) methods.

Methods: Eighteen young, healthy, right-handed adult subjects performed kMI involving each hand separately, with NF training targeting regions of interest (ROIs) in the left and right primary motor cortex (M1). Throughout, subjects attempted to maximize a laterality index (LI) of brain activity - the difference in activity between the contralateral ROI (relative to the hand involved in kMI) and the ipsilateral M1 ROI - while receiving real-time updates of the LI values on a visual display. Thirteen subjects in the experimental group received true NF, which accurately reflected the subject's brain activity, while 5 subjects in the control group received sham NF, which were recorded LI values from a randomly selected experimental subject.

Real-time imaging was performed on a 3.0 T Magnetom TIM Trio system (VB15 software, Siemens Healthcare, Erlangen, Germany), using a modified gradient echo echo-planar imaging sequence with 3x3 mm^2 in-plane resolution on a 64x64 matrix, 16x5mm slices, 30 ms TE and 1 s TR. The image reconstruction software was modified to provide real-time data transfer to an external computer running AFNI, which delivered ROI signal averages to a computer dedicated to visual stimulus presentation. The 5x5x2 voxel ROIs were drawn manually over the left and right M1 areas, guided by a functional localizer fMRI scan prior to the NF experiment.

The NF experiment consisted of four consecutive 9 min runs, with 6 left-handed (LH) and 6 right-handed (RH) trials per run. Each trial consisted of a 20 s rest period, a 5 s cue presentation, 15 s real-time feedback, and a 5 s reward screen. Subjects were cued for LH or RH trials with 2 different visual cues, and commenced kMI as soon as the cue was presented. During the 15 s of real-time feedback, subjects viewed a horizontal arrow whose length scaled with the instantaneous amplitude of LI and direction changed with polarity (contralateral > ipsilateral, or vice versa). A vertical green line that shifted in the left-right direction also indicated the cumulative time-averaged LI value. After the 20 s of kMI, subjects were presented with a reward screen indicating trial success or failure, depending on whether the trial averaged LI value exceeded a hidden threshold that increased based on improved NF performance.

The fMRI data were processed offline using PLS analysis software [4], a multi-variate method for determining spatial patterns of activity based on covariances between neuroimaging data and external measures. In this study, behavioural-PLS was used to identify patterns based on performance measure covariates. All subject data were pre-processed using a conventional pre-processing pipeline, including rigid body motion correction, physiological noise correction, spatial smoothing (6 mm Gaussian kernel), and spatial normalization to the Montreal Neurological Institute template.

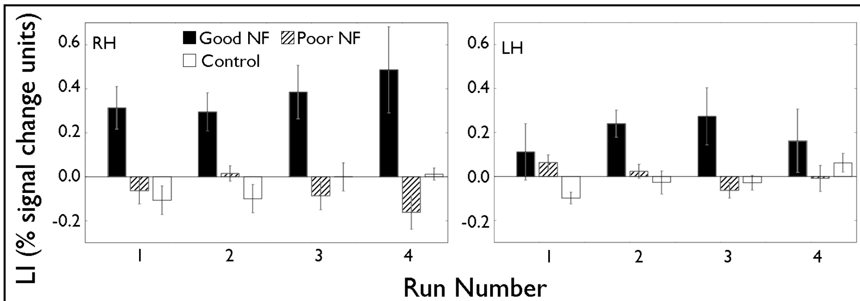

Figure 1 (above) – LI values for good NF responders, poor NF responders and control subjects averaged across subjects and within runs, with RH and LH trials separated. Error bars are standard error of the mean.

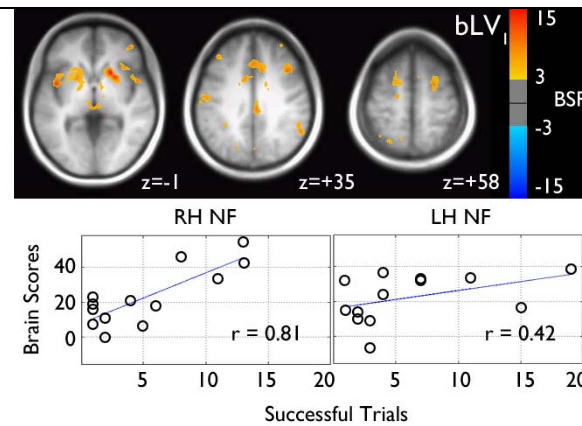

Figure 2 (right) – Behavioural PLS results, showing 3 slices of a bootstrap ratio map of brain activity of the first latent variable bLV$_1$. Below, plots showing the brain scores for RH and LH trials separately, plotted against the number of successful trials. The brain scores reflect expression of the bLV$_1$ activation pattern, and are significantly positively correlated to task performance in both RH and LH trials.

Results: Subjects displayed variable results when performing the NF task, with 7/13 subjects performing similar to control group subjects, classified as "poor" NF responders, and 6/13 performing better than controls, classified as "good" NF responders. When reorganized into these groupings, the difference in performance is clearly evident, as seen in Fig. 1. Looking into the ROI-specific contributions to the LI for the good NF group indicated that suppression of ipsilateral M1 activity, rather than upregulation of contralateral M1 activity, was the primary factor driving the positive LI values. In the poor NF and control groups, no consistent differential pattern of activity across the ipsilateral and contralateral ROIs was observed. In the behavioural PLS results, significant correlations were present between a particular spatial pattern of brain activity and performance, measured by the number of successful trials, for both LH and RH conditions. Some of the regions highlighted in this pattern can be seen in Fig. 2, including the bilateral insula regions, dorsolateral prefrontal regions, and pre-motor (frontal eye fields) areas, a subset of the regions commonly identified as part of the task-positive network [5].

Discussion: Previous examinations of fMRI NF using a motor imagery task have presented results with varied success [1,2]. This study reports approximately half (6/13) of the experimental group subjects performing above the level of the controls, which is consistent with the previous literature. Identification of potential task-positive network expression significantly correlated with task performance suggests that this network should be a target for future investigations of NF efficacy and engagement across subjects, and possibly as a marker for receptiveness to NF training. The novel observation of ipsilateral M1 suppression driving NF success suggests that differential ROI approaches to NF like the one employed here have potential to access alternative mechanisms for self-regulation of BOLD activity, beyond simply modulating signal in a single ROI. Prior evidence suggests suppression of ipsilateral motor activity can enhance motor skill learning [6]. The results presented here may be useful for identifying potential subjects that are likely to benefit from kMI NF, as well as developing new NF training methods that may result in tangible changes in motor behaviour following stroke.

References

1. Bray, S. et al., *J Neurosci* 2007; 27(28): 7498-507
2. Yoo, S.S. et al., *Int J Imaging Sys Tech* 2008; 18(1): 69-78
3. Braun, S.M. et al., *Arch Phys Med Rehabil* 2006; 87(6): 842-52
4. McIntosh, A.R. et al., *Neuroimage* 1996; 3(3 pt. 1): 143-57
5. Fox, M.D. et al., *Proc Natl Acad Sci USA* 2005; 102(27): 9673-8
6. Kobayashi, M. et al., *Eur J Neurosci* 2009; 29(4): 833-6