

Functional MRI Analysis of a Novel Short-Term Motor Learning Task

R. J. Cassidy¹, S. Boe^{2,3}, W. McIlroy^{4,5}, and S. J. Graham^{6,7}

¹Institute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, ON, Canada, ²School of Physiotherapy, Dalhousie University, Halifax, NS, Canada, ³Department of Psychology, Dalhousie University, Halifax, NS, Canada, ⁴Toronto Rehabilitation Institute, University of Toronto, Toronto, ON, Canada, ⁵Department of Kinesiology, University of Waterloo, Waterloo, ON, Canada, ⁶Department of Medical Biophysics, University of Toronto, Toronto, ON, Canada, ⁷Sunnybrook Health Sciences Centre, University of Toronto, Toronto, ON, Canada

Purpose

Functional MRI analyses of motor skill acquisition have the potential to inform a variety of rehabilitative treatments of neurologic insult such as stroke and traumatic brain injury. For instance, expanding our understanding of the brain regions involved as well as the time-course of motor skill acquisition in individuals with neurologic control challenges can influence the parameters of treatments used to promote recovery of function. However, the experimental tasks used in such analyses have, to date, presented two challenges: (1) they are often mastered quickly (within minutes by healthy subjects), making it difficult to elucidate short-term learning effects over fMRI examination periods (approximately 1 hour); and (2) they are often difficult to generalize to performance of other tasks, such as those associated with activities of daily living. As short-term learning and generalization are fundamental components of robust, long-term skill acquisition, which is the basis of neuro-rehabilitation, we have developed a novel experimental task for initial investigation of these aspects of motor learning. In the present work, we present initial fMRI results and discuss the significance of our findings.

Methods

For this visuomotor task, participants held MR-compatible squeeze-bulbs to control cursor movement toward a 2-dimensional target. The grip pressure of the right and left hand determined the horizontal and vertical extent of the cursor motion, respectively. Task difficulty was introduced by the requirement that grip force be asymmetric (i.e., non-45° cursor deflection), and the use of a short time interval for grip force measurement. For each participant, the experiment consisted of four phases: (1) pre-training, (2) training (not scanned), (3) post-training (all trials of phases 1-3 with the same fixed target), and (4) testing involving a different target (representing generalization of the initially learned skill). Each scanning phase consisted of 20 trials, each of 20 s duration, with 600 trials for the unscanned training phase. After each trial, participants were given a visual indication of their achieved cursor location, distance to the target, and an indicator of 'success' if cursor location was within 1 cm of the target, all of which were recorded as behavioral measures. Sixteen healthy participants (8 female, aged 24.8±3 yrs) were scanned in a research-dedicated 3T system (TIM Trio, Siemens, vbl5 software) using multislice axial oblique acquisition with a 12-channel head coil and TR=2 s.

fMRI preprocessing and analysis was performed with AFNI [1]: participant data was preprocessed using physiologic noise correction, slice time correction, rigid motion correction, and spatial smoothing with a 5 mm FWHM Gaussian kernel. In the process, 2 participants were excluded due to errors in physiologic measurement and excessive motion, respectively. In this event-related analysis, individual subject general linear model (GLM) analyses were conducted using the 4.0 s of each trial corresponding to the interval of measured bilateral gripping. GLM analysis included estimation of a data-dependent hemodynamic response function (HRF) over lags of 0 to 6 TR, along with detrending using a 3rd order Legendre polynomial. Univariate group analyses were conducted for phases (1),(3) and (4) described above, yielding an activation map for each phase contrasting event-related gripping with baseline BOLD activity (measured during presentation of a visual fixation point). Maps were thresholded at a significance level given by $p < 0.001$. Lastly, to quantify the level of activation seen in brain regions of interest, the number of activated voxels was computed for each of a set of regions commonly associated with sensorimotor control and learning: the cerebellum, the thalamus, the middle frontal gyrus (MFG), both the ventro-lateral pre-frontal and pre-motor cortices (Brodmann areas 9 and 6, respectively), the supplementary motor area (SMA), and the primary motor cortex (M1). Regions were obtained via a union of Talairach-Tourneau areas using atlases by (1) Lancaster and Fox [5], and (2) Eickhoff et al. [4]

Results and Discussion

The activation of regions associated with sensorimotor control and learning is readily apparent in group maps for each of the three scanned task phases shown in Fig. 1a-c. Widespread activation is seen in the cerebellum, thalamus, SMA, and M1, consistent with the large body of literature supporting their role in motor behaviour and control (e.g., via cerebello-thalamo-cortical circuits). Additionally, activation was observed in the dorsolateral prefrontal cortex, which is implicated in working memory and attention, consistent with a participant's introspective evaluation of prior grip effort in order to modulate future behavior.

Qualitatively, the approximate size of the activation clusters shown confirms the hypothesized effect of (1) increased activation during pre-training, (2) decreased activation post-training, and (3) an intermediate level of activation for the test phase using a different target. Quantitative analysis of this learning effect is provided in Table 1. While the thalamus shows a trend of increasing activation pre-post training, activation size in the SMA and M1 is progressively reduced, reflecting trends (1) and (2) of the above hypothesis. Voxel counts for the cerebellum and MFG demonstrate all three hypothesized trends, including an intermediate level of activation for the test phase with a different target. In a separately conducted pilot study (N=7), behavioral performance corresponded to the observed pattern of brain activation, with cursor-target error of 8.3±1.4 cm pre-training, 2.2±0.3 cm post-training, and 4.0±0.7 cm with a new target location.

In general, the results confirm the applicability of the task to the study of robust short-term learning. The difference between activation in the pre-training phase and post-training phase is consistent with the behavioural analysis indicating a gradual learning process and more efficient recruitment of neural resources. Moreover, the intermediate level of activation observed in the testing phase supports the hypothesis that exposure to different 2-D targets gives a natural generalization of the initially learned task. Future work will focus on studying the evolution of the above motor learning-related brain activation pre- and post-training, along with multivariate analysis to correlate brain activity with behaviour. In addition, EEG data has been collected separately using the same experimental paradigm, creating the opportunity for future multi-modal data analysis.

Figure 1 – Group maps showing cerebellar, thalamic, dorsolateral prefrontal, SMA, pre-motor, and motor activity for (a) pre-training, (b) post-training, and (c) test with different target.

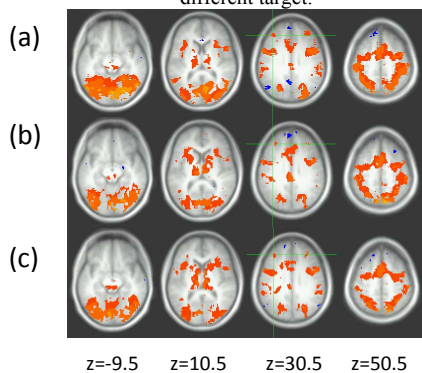


Table 1 – Number of activated voxels in sensorimotor and learning regions across imaging conditions

Region	Pre-Train	Post-Train	Test
Cerebellum	7558	5108	5777
Thalamus	487	685	840
MFG	901	574	749
SMA	1282	1114	984
M1	2212	1726	1647

¹R.W. Cox, *Comput Biomed Res*, 29(3): 162-173, 1996. ²R. Cabeza & L. Nyberg, *J Cog Neurosci.*, 12(1): 1-47, 1996. ³A. Floyer-Lea & P.M. Matthews, *J Neurophys.*, 94: 512-518, 2004. ⁴S. B. Eickhoff, K. E. Stephan, H. Mohlberg, C. Grefkes, G. R. Fink, K. Amunts, K. Zilles, *NeuroImage*, 25(4): 1325-1335, 2005. ⁵J. L. Lancaster, M. G. Woldorff, L. M. Parsons, M. Liotti, C. S. Freitas, L. Rainey, P. V. Kochunov, D. Nickerson, S. A. Mikiten, & P. T. Fox, *JHBM*, 10(3):120-131, 2000.