Cortical Activation Volume During a Bilateral Motor Task in Multiple Sclerosis Patient: A Study of the Effect of Subject Motion and Task Performance

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Introduction: Previous fMRI studies in multiple sclerosis (MS) have reported increased cortical sensory and motor activation following performance of a unilateral hand motor task[1-3]. This has been attributed to cortical motor reorganization in the patient population. It is well-known that gross head motion and variations in task performance can affect fMRI studies of the motor system. When comparing populations with motor impairment to control subjects it can be particularly important to ensure that the affect from these factors is normalized across both groups. To assess the confounding effects of head motion and task performance on the fMRI cortical activation volume in MS, we employed a complex bilateral finger tapping paradigm and employed strict quality control measures to ensure that comparisons were made across groups with similar head motion and task performance profiles.

Methods and Materials: Gradient echo EPI fMRI exams at 3T were performed on 25 MS patients and 20 approximately age and gender matched controls. The multiple sclerosis functional composite (MSFC) examination was administered to all subjects prior to MR scanning. One hundred-sixty volumes of 31-4mm thick axial slices (TE/TR/flip=29ms/2000m/90°, matrix=64x64, 256mm x 256mm FOV, receive bandwidth=125KHz) were acquired. Subjects performed a bilateral finger tapping task in an interleaving 32s "rest"/32s "tapping" block paradigm. Fingers were tapped sequentially in the following order: thumb, middle, pinky, index and ring finger. Subjects were instructed to repeat the sequence as fast as possible without making mistakes, and task performance was recorded with a data glove (Fifth Dimension Technologies, Irvine, CA). The data glove timeseries were analyzed and errors were assigned for all finger taps occurring out of the proscribed sequence. The error rate was defined as total number of errors/ total number of finger taps. Head motion was monitored using a prospective motion correction methodology[4]. FMRI timeseries data were spatially filtered with a Hamming filter[5] and analyzed for activation by least-squares fitting the timeseries for each pixel to a boxcar reference function plus a slope[6]. The resulting student t maps were overlaid onto high resolution T1-weighted images. For each subject, anatomic ROIs were defined bilaterally around the primary sensorimotor cortex, supplementary motor area, premotor cortex, secondary and supplementary sensory regions. Volume of activation, mean t-value, and mean percent signal change were determined for each ROI for a range of thresholds from t>3.5 to t>12. To quantitate the effect of head motion on activation volume, the mean head displacement[7] was calculated from the motion parameters for each time point and correlated with the first and second harmonics of the reference function. Each correlation was plotted against the total number of non-motor (i.e. outside all ROIs) activated voxels within the entire 31-slice volume for each subject to determine if there was significant motion-related cortical activation.

Results: MSFC scores were 0.3907 +/- 0.4387 for patients and 0.5880 +/- 0.4167 for controls (p=.0393). The task error rates for patients (0.0985 +/- 0.0722) and controls (0.0939 +/- 0.0738) were similar. MSFC and task error rate were significantly correlated across all subjects (r = -0.5709, p = 4.2168e-05). For all thresholds, the number of activated voxels, mean student t value and mean percent signal change were not significantly different in controls when compared to MS patients. The mean peak head displacement was 1.13 +/-0.63mm for MS patients and 0.86 +/- 0.43mm for controls (p<0.12). When quality control measures were applied to the motion data, 13/25 MS patients and 6/20 controls had significant motion related brain activation. When the data were reanalyzed excluding subjects with significant motion effects, control subjects had a significantly greater activation volume within the sensory-motor system (i.e. inside the ROI's) than MS patients for all thresholds (Fig. 1). A further analysis of task performance revealed that poor performing control subjects had activation volumes that were statistically similar to MS patients, indicating the need to control for task performance in both populations.

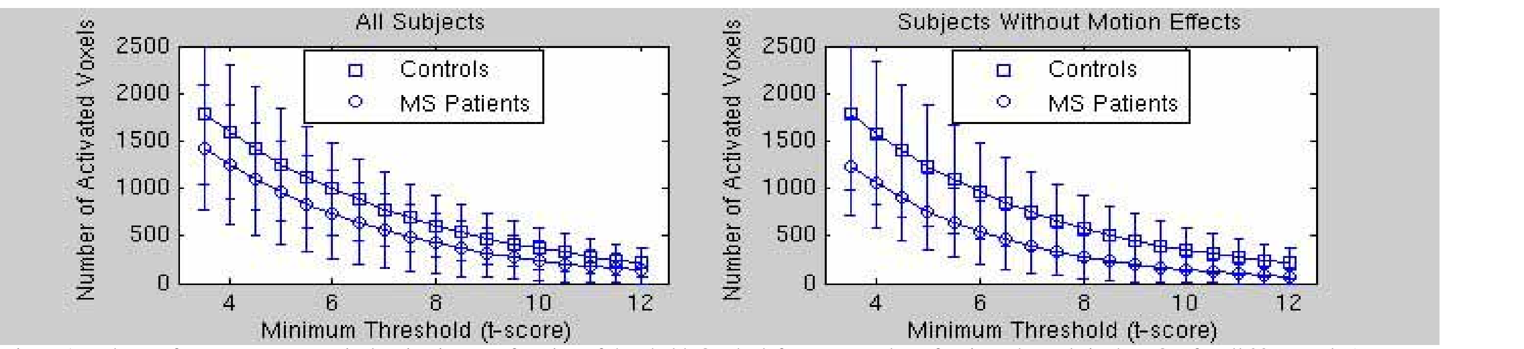

Figure 1. Volume of sensory-motor cortical activation as a function of threshold. On the left, mean number of activated voxels in the ROIs for all 20 controls (top curve) and all 25 MS patients (bottom curve). The difference was not significant. On the right, the mean number of activated voxels in the ROIs for the 14 controls (top curve) and 12 MS patients (bottom curve) that did not have significant false positive activation caused by motion artifact. The difference was significant (p<.05) at all thresholds. This effect is due to the fact that in our study, MS patients exhibited greater amounts of head motion then control subjects, resulting in artifacts that could not be corrected by standard prospective and retrospective motion correction techniques.

Conclusion: Many factors affect the volume of cortical activation seen during fMRI examination, including the clinical severity of disease in the patient population, the specific task being performed, and individual task performance. In addition we have shown that false positive activation resulting from head motion can differentially affect control and patient populations. In this study of relatively healthy MS patients, when head motion was carefully controlled for, the degree of activation seen in the sensory-motor cortex during performance of a complex bilateral finger tapping task was greater in control subjects compared to MS. Additionally, careful assessment of task performance suggests that activation in control subjects who perform the task poorly is similar to that seen in subjects with MS. These findings illustrate the need to carefully account for head motion and task performance in assessment of fMRI data.

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