Altered basal ganglia activation during complex finger tapping tasks in patients with MS

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Introduction: Multiple sclerosis has been studied extensively using MRI. Recently, investigators have applied functional MRI to the evaluation of multiple sclerosis.[1-3] The most common finding of fMRI during motor paradigm performance is a relative increase in the extent of activation within the primary sensorimotor cortex (SMC) as well as the supplementary motor area (SMA). Additionally authors have reported new areas of cortical activation in MS subjects in comparison to controls during motor task performance.[1-3] These studies have largely focused on changes in the degree of cortical activation with little or no information regarding the effect of MS on deep gray matter structures. The present study evaluates the extent of activation in deep gray matter structures in patients with multiple sclerosis performing a complex finger tapping task unilaterally and bilaterally.

Methods: GE EPI fMRI was performed at 3T (Siemens Trio, Erlagen Germany) on 21 MS and 15 right-handed subjects, approximately age and gender matched controls with the following parameters: slice thickness 4mm, TE/TR/flip=29ms/2000m/90°, matrix=64x64, 256mm x 256mm FOV, receive bandwidth=125KHz. Subjects performed a unilateral lateral left, unilateral right and bilateral complex finger tapping tasks in an interleaving 32s "rest"/32s "tapping" block paradigm. Task performance was recorded with a data glove (Fifth Dimension Technologies, Irvine, CA) and analyzed for tapping rate, error rate and mirror movements. Head motion was rigorously monitored and data was discarded if motion corruption was present in one or more of the fMRI scans. Time series data was analyzed and student t maps were generated and overlaid onto high resolution T1-weighted images. For each subject, anatomic ROIs were drawn bilaterally around the SMC, SMA, basal ganglia BG (putamen and globus pallidus) and thalamus. Student's t maps and ROIs for each subject were transformed into Talairach space. Talairach transformed Student's t maps were averaged voxel-by-voxel to generate composite maps for each group For each individual subject, activation volume was determined for each ROI for a range of thresholds from t>2.0 to t>12 and the xyz coordinates of the maximally activated voxel in each ROI were determined. Correlations between the subcortical and cortical activation volumes at threshold of t>3.5 were determined for MS patients and controls.

Results: 10 control subjects and 8 MS subjects demonstrated adequate task performance without mirror movements and no significant head motion. Similarly to our previously reported results[4], no significant difference in the extent of activation was seen in the SMC and SMA in control subjects compared to MS subjects. MS subjects demonstrated significantly decreased volume of activation in comparison to controls (Figure1) within the left BG during bilateral finger tapping (control = 509 +/- 366, MS = 201 +/- 167, $p < 0.04$), right BG during bilateral tapping (control = 577 +/- 418, MS = 243, $p < 0.06$) and left BG during right hand tapping (control = 839 +/- 735, MS = 185 +/- 283, $p < 0.03$). No significant difference was identified within the left BG during unilateral left or right finger tapping or within the right BG during right sided finger tapping. Control subjects demonstrated a very strong correlation between the size activation within the ipsilateral SMA and BG for all tapping conditions with correlations ranging from r=0.61, p<.06 to r=0.94, p<.00005. Similarly, significant correlations were identified for the ipsilateral BG and SMC nearly all of the tapping conditions ranging from r = 0.69, $p < 0.03$ to r = 0.85, $p < 0.002$. Interestingly, findings were not significant within the left hemisphere during right-handed finger tapping or within the right hemisphere during left-handed tapping. No significant correlations between the volume of ipsilateral BG and SMA or BG and SMC were identified in MS subjects.

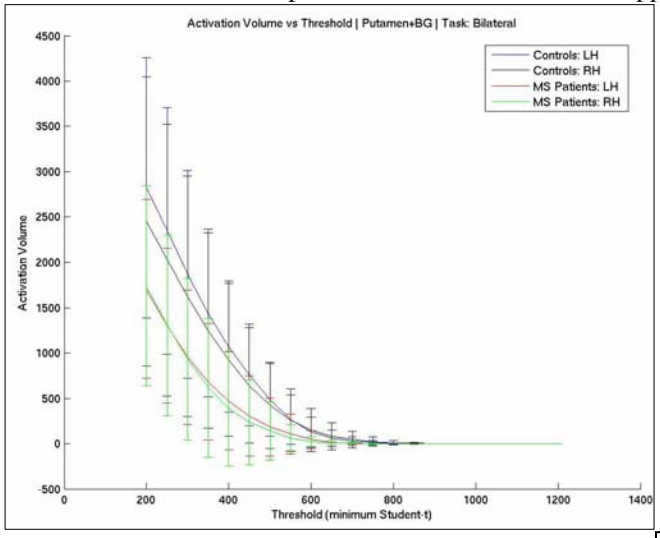

Figure1. Activation volume in the BG as a function of theshold demonstrating decreased activation in the MS subjects (green and red) compared to controls (black).

Discussion/Conclusion: Previous fMRI evaluations of multiple sclerosis have focused on cortical areas of activation with little or no data regarding the effect of MS on deep brain structures. The present study suggests that patients with MS demonstrate significantly reduced activation during motor tasks within the basal ganglia. Further, there is a loss of the strong correlation in the volume of activation between the BG and SMA as well as the BG and SMC seen in control subjects. Findings suggest potential disconnection/disruption of motor pathways involved in complex motor task performance. Note this disconnection is apparent even though subjects maintain an adequate level of task performance.

References: 1.Reddy et al., Brain, 2000. **2.** Rocca et al., Ann Neurol,2002 **3.** Filippi et al., Hum Brain Mapp, 2004. **4.** Lowe et al. Proc ISMRM 2006.