BOLD Deactivation Response to Hand Tapping in Multiple Sclerosis Patients

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Objective: To characterize BOLD deactivation in response to unilateral hand tapping in multiple sclerosis (MS) patients relative to healthy controls.

Background: Previous fMRI studies have shown that MS patients demonstrate functional reorganization in response to a unilateral hand tapping task (Lee et al. 2000; Reddy et al. 2002; Rocca et al. 2005). However, these observations have been based upon the positive BOLD contrast, or activation. Here we investigate functional reorganization demonstrated by the negative BOLD contrast, or deactivation, which we define as rest minus task contrast. We focus on the ipsilateral motor cortex, which has been shown to selectively deactivate during hand tapping in healthy controls (Allison et al. 2000), and has been implicated in the network of functional reorganization in MS patients.

Methods: This multi-centre FMRI study was conducted at eight European sites using 1.5 Tesla magnets. Functional MR images were obtained using the same multi-slice gradient EPI sequence at each site (echo time = 60 ms, repetition time =3000 ms, field of view 240 x 240 mm^2, matrix 64 x 64). Hand tapping was visually cued using a visual stimulus in an ABAB block design. Brain deactivation during right hand movement was assessed in 56 right-handed patients with relapsing-remitting or secondary progressive MS without hand impairment (median age 35 years, median EDSS score 2.0, median time to complete nine-hole peg test 21.0s, median disease duration 6.8 years). 55 age-matched healthy subjects served as controls.

Results: While healthy controls exhibited deactivation along the motor cortex (Figure 1), MS patients did not exhibit the same deactivation, particularly in the omega region of the precentral gyrus (Yousry et al. 1997). Subtracting MS patient deactivation from healthy control deactivation (Figure 2), MS patients showed decreased deactivation the omega region of the precentral gyrus as well as the postcentral gyrus and the superior parietal lobule.

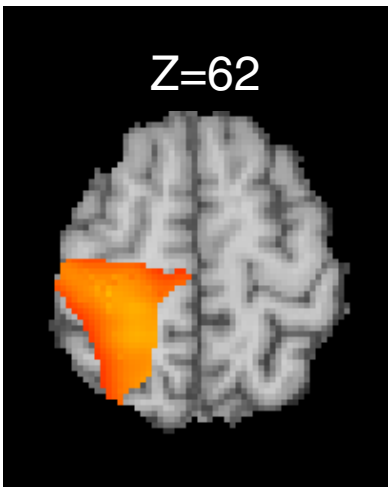

Figure 1. Healthy Control Deactivation z=2.3

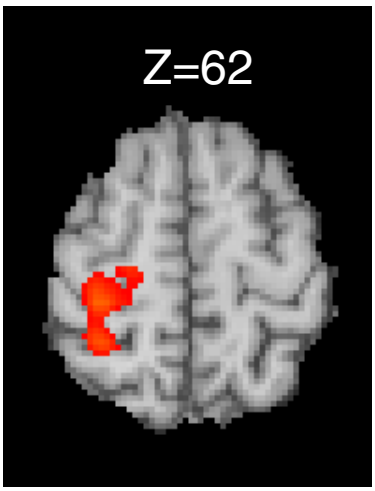

Figure 2. Healthy Control-MS Deactivation Contrast z=2.3

Discussion: We show that MS patients show less deactivation in the ipsilateral motor cortex, possibly as a compensatory measure to maintain normal hand function under the increasing burden of MS pathology. This finding is in line with results that show MS patients have increased activation in the ipsilateral motor cortex (Reddy et al. 2002). Although BOLD deactivation analysis in the motor cortex is more difficult due to inherently lower BOLD signal, we show it is possible to draw meaningful conclusions from deactivation data. Additionally, this was the first large scale multi-centre MS fMRI study. Results were consistent across centres, indicating that fMRI could potentially be added as a secondary outcome measure in clinical trials.