Resting State Fluctuation Amplitude Indicates Impaired Cerebrovascular Reactivity in Multiple Sclerosis

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Target audience: This information will be of interest to researchers using fMRI to study multiple sclerosis.

Purpose: It is known that multiple sclerosis results in decreased cerebral metabolic rate of oxygen and blood flow(1, 2). Both of these are critical elements in cerebrovascular reactivity (CR) to neuronal activation. It has been shown that resting state fluctuation amplitude (RSFA) can be a surrogate to hypercapnic challenge as a measure of cerebrovascular reactivity(3). We show that the correlation between BOLD activation and RSFA is much weaker in MS patients than in healthy controls, indicating that CR may be compromised in MS populations.

Methods: Ten MS patients (mean age 44.4 ± 10.1, 2 males) and 10 age- and sex-matched controls (mean age 45.1 ± 9.8, 2 males) were scanned in an IRB-approved protocol at 3T in a 12-ch receive head coil. Scans included T1-MPRAGE and a rs-fMRI scan at 2×2×4mm^3 voxels, 1954 Hz/pix BW, 31 axial slices, TR/TE/FA=2800ms/29ms/80°. Bilateral complex finger tapping was performed in a block paradigm in 4.5 blocks of 32 volumes of rest/tapping using the same prescription as the rs-fMRI scan. BOLD activation was determined by taking the mean percent signal change during tapping versus rest in the 9-voxel region around the area in M1 with peak amplitude change. Mean RSFA was determined from the same voxels in the rs-fMRI scan.

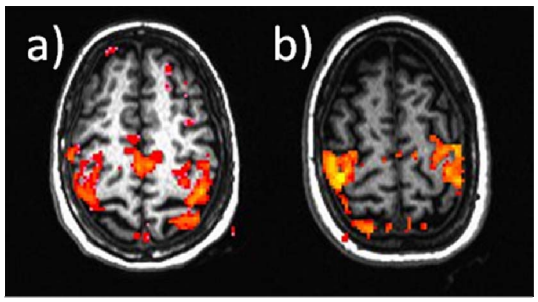

Figure 1: Bilateral finger tapping activation in a) healthy control and b) MS patient

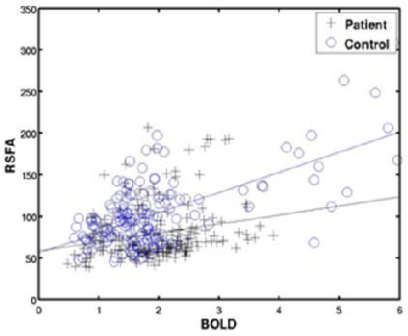

Figure 2: RSFA as a function of BOLD signal amplitude for a cohort of MS patients and healthy control subjects

Results: Figure 1 shows a typical activation map for an MS patient and a matched healthy control. Figure 2 shows a scatter plot of mean RSFA versus mean BOLD signal change for controls and patients. Control subjects had a very high correlation between RSFA and BOLD signal change ($r=0.7$, $p<10^{-19}$), similar to previous reports in the literature(3). MS patients, however, had a much lower correlation ($r=0.2$, $p<0.002$). Although still significant, the much lower coupling is dramatic.

Discussion: Differences in levels of neuronal activation in MS have been widely reported for many years(4, 5). Despite the well-known fact that CMRO2 and CBF are impaired in MS, there has been no investigation of the impact of cerebrovascular reactivity on fMRI in MS. This study indicates that CR appears to be impaired in MS, making comparisons of the underlying neuronal activation between healthy controls and MS patients difficult.

Conclusion: We present data that supports the notion that cerebrovascular coupling between hemodynamic response and neuronal activation in MS patients is impaired compared to matched healthy control subjects. This has important implications on the widespread literature that BOLD activation levels in MS are altered with respect to healthy control subjects. Methods have been proposed to account for CR differences in fMRI studies in patient populations, and it may be necessary to adopt these in future fMRI studies of MS.

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