A Correlational Analysis of Cognitive fMRI, DTI, and Clinical Assessment of Multiple Sclerosis

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Introduction

Magnetic resonance imaging (MRI) holds great potential as a reliable measure of the progression of relapsing-remitting Multiple Sclerosis (RRMS), as it can measure changes in brain pathologies that are potentially persistent and changing with disease. Diffusion tensor MR imaging (DTI) has demonstrated a decrease in water diffusion along white matter fibre bundles in the presence of MS lesions, especially within the corpus callosum (CC)[1,2], and there is also increasing interest in using functional MRI (fMRI) to investigate cortical activity in response to cognitive or sensory tasks as a possible indicator of MS severity.[3-5] To date, studies have not investigated the inter-relationship of cognitive fMRI and regional white matter integrity as measured by DTI, as well as their correlation with current clinical assessments of MS severity. Understanding these inter-relationships may provide a more complete description of the progression or severity of MS in individual patients, and could lead to an imaging protocol that, in combination with behavioral assessment, is a comprehensive and accurate clinical evaluation. The objective of this study, then, was to identify correlations between existing clinical measures of MS severity with brain activity evoked by a cognitive task as measured using fMRI and with region-of-interest (ROI) based measurements of fractional anisotropy (FA) using DTI.

Methods

Subjects were 5 MS patients (4 RRMS and 1 SPMS) aged 35 to 50 years, with EDSS ranging from 3 to 6. Six healthy volunteers also participated. All scans were completed using a quadrature birdcage RF head coil in a 3 Tesla Signa EXCITE MR scanner (GE Healthcare, Waukesha, WI). The protocol consisted of a 3-plane localiser to prescribe slices, a 3D T_1-weighted volume for anatomical registration, two fMRI datasets (interleaved 2-shot GRE-EPI, TR/TE=1500/30 ms, 96x96 matrix, 24-cm FOV, 26 slices, 5mm thick), and three DTI datasets (dual spin echo EPI: 11 directions, b=850, TR/TE=10000/77.8 ms, 128x128 matrix, 24-cm FOV, 32 slices, 4mm thick). During the collection of fMRI datasets, participants performed a 2-back task where numbers were presented serially (3 seconds per digit) and the volunteer was required to respond on a keypad to any digit same as one presented 2 digits previously (8 alternating blocks of 30 sec task, 30 sec rest; a visual cue during rest also required a keypad press). Analysis was performed using FSL (www.fmrib.ox.ac.uk/fsl) with spatial smoothing using a Gaussian kernel of 8mm FWHM. Z-statistic images were thresholded using clusters determined by Z>3.7 and a (corrected) cluster significance threshold of p=0.01. Registration to high-resolution images was carried out using FLIRT. Using scanner software (Functool2; GE Healthcare, Waukesha, WI), DTI images were co-registered and FA maps were calculated. Regions of interest were drawn on each participant's FA map using *Fslview*, part of FSL, to segment the anterior CC and posterior CC, and the average FA within each ROI (FA-ACC and FA-PCC) was recorded. FSL was used to perform correlation analyses of mean fMRI activity, EDSS, disease duration, FA-ACC, and FA-PCC.

Results and Discussion

Activity location and magnitude were typical for this task, incorporating activity within prefrontal, frontal, and parietal cortices as well as strong activation in anterior cingulate, bilateral posterior cerebellum, and midbrain structures such as the thalamus and caudate. The only regions exhibiting greater activity for patients compared to controls were small regions within the left superior frontal gyrus. Many regions exhibited greater activity in controls compared to patients, including posterior cerebellum, bilateral hippocampal gyri, right middle temporal gyrus, right inferior frontal and middle frontal gyri, inferior parietal lobule, and medial superior frontal gyrus.

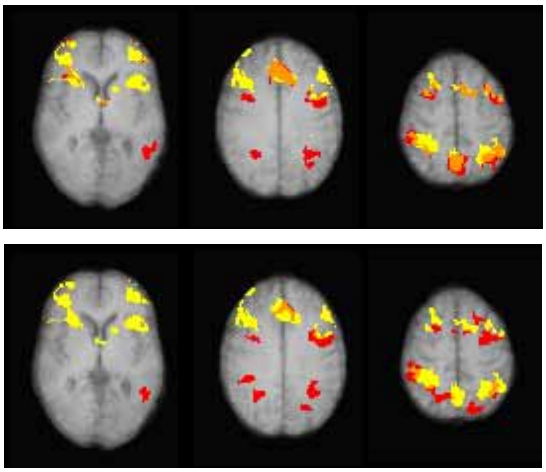

Figure: Regions showing significant correlation between 2-back activity and EDSS (yellow), FA-ACC (top, in red), FA-PCC (bottom, in red). Orange indicates regions of overlap.

EDSS correlated with FA-ACC (r = -0.69), whereas disease duration correlated with FA-PCC (r = -0.88). This was reflected in the correlative analysis with fMRI data, as there was significant overlap in anatomical regions showing significant correlation between fMRI activity and EDSS and regions showing a significant correlation between fMRI activity and FA-ACC. Little overlap was seen in regions showing significant correlation between fMRI activity and EDSS and regions showing a significant correlation between fMRI activity and FA-PCC. These preliminary results suggest that integrity of the anterior CC may be linked to disease severity and integrity of the posterior CC may be linked to disease duration.

References

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