White matter fMRI: Exploring functional differentiation in the corpus callosum

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Introduction White matter fMRI is a controversial idea. To date, the majority of fMRI studies have focused on gray matter, largely for two reasons: 1) cerebral blood flow/volume is reduced in white matter relative to gray matter (e.g., [1, 2]); and 2) post-synaptic potentials are thought to be the primary source of the signal measured in fMRI (e.g., [3]). Despite this, a growing number of studies have observed white matter activation (e.g., [4-9]). Indeed, we have recently reported the first two prospective white matter 4T fMRI studies using interhemispheric transfer tasks [8,9]. The initial study examined interhemispheric transfer during a visual word/face task, which elicited activation in the isthmus of the corpus callosum (Figure 1) [8]. White matter activation was present in 20% of individuals and detected at the group level using a liberal threshold ($p<0.005$, uncorrected). A subsequent study examined interhemispheric transfer using a visual-motor checkerboard task, which elicited activation in the anterior corpus callosum (Figure 2) [9]. White matter activation was observed in 100% of subjects as well as in the group averaged data ($p<0.05$, corrected). This study used a specialized asymmetric spin echo (ASE) spiral sequence [10], which collected three images (per slice/per volume) of equal BOLD contrast weighing and increasing T_2 weighting. The results showed increased sensitivity to white matter activation with increased T_2 weighting. It is noteworthy that these two studies elicited activation in different regions of the corpus callosum, suggesting that task type may be useful for mapping functional differentiation in white matter. To test this, the current study examined whether varying task type differentially activates white matter within the same subjects.

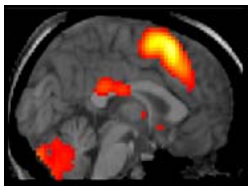

Figure 1. Word/Face (t-score: 5-20)

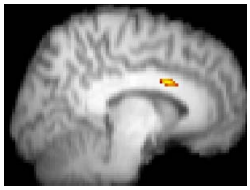

Figure 2. Checkerboard (z-score: 2.5-6)

Methods Experimental design: All stimuli were presented to the visual hemifields to initially stimulate a single hemisphere (using a block design format). Stimuli were presented rapidly to avoid saccades (words/faces: 150ms and checkerboards: 100ms). To avoid stimulating the vertical meridian, all stimuli were presented laterally >2.3 degrees from fixation. For the word/face task, interhemispheric transfer was elicited by varying the visual field of presentation for both words (i.e., left hemisphere stimuli) and faces (i.e., right hemisphere stimuli). In addition, response hand was crossed for all participants (i.e., left hand for words and right hand for faces). For the checkerboard task, checkerboard stimuli were presented randomly to the left and right visual fields and response hand was varied to create crossed and uncrossed conditions.

Data acquisition and analysis: All data were acquired using a 4T Varian INOVA whole body MRI system. Gradients were provided by a body coil (Tesla Engineering, UK) driven by 950 V amplifiers (PCI) at a maximum of 35.5 mT/m at 120 T/m/s. The RF coil was a quadrature driven TEM head coil (Bioengineering Inc) driven by a 7kW RF amp (AMT). Functional MRI was carried out using a two shot ASE spiral sequence (TR/TE*/TE=1000/27/68ms, flip 60°, 9 slices, 4mm thick, 0.4mm gap, 240mm FOV, 64x64 matrix). Images were interpolated using the input spiral waveforms (no measured trajectories) as well as field map and navigator corrected. The axial slices were prescribed to cover the corpus callosum. For structural registration, a high-resolution spiral out image was collected, with 22 axial slices (128 x 128 matrix, 240 x 240 mm) and 4 interleaved shots. High-resolution structural MRI data were acquired using a 3D MP FLASH with TR/TI/TE=10/500/5ms, 256x256 matrix, 3mm thick, and 192 phase encodes. Functional MRI data were corrected for motion, co-registered, normalized and spatially smoothed. Statistical analyses were performed using a model-based approach (General Linear Model in FMRIB Software Library). Analyses included examination of imaging slab and region-of-interest activity at both the individual and group levels.

Results and Discussion Corpus callosum activation was elicited using both task types, replicating the previous findings. Importantly, task type elicited different activation patterns in the corpus callosum using a within subjects design. The word/face task showed activation in the body of the corpus callosum (Figure 3). The checkerboard task showed activation in the genu of the corpus callosum (Figure 4). The pattern of results was consistent with that observed previously, suggesting that it is possible to map functional specialization within the corpus callosum.

Also, the current study provided additional data discounting alternative explanations related to partial volume and motion artifacts. Partial volume of nearby gray matter signals was unlikely given that slice thickness was further reduced (by 1/3). Again, the clusters were localized within white matter, rather than spanning into white matter from nearby gray matter tissue. Motion artifact was similarly addressed by including motion parameters as a covariate (in addition standard motion correction). As with previous results [8], including motion parameters as a covariate increased (rather than decreased) sensitivity to white matter activation.

While the findings provide additional support for white matter fMRI, it remains unclear as to whether the current results were specific to the corpus callosum. The corpus callosum is organized such that fibres connecting adjacent cortical regions are grouped together (which makes an ideal candidate for evaluating white matter fMRI). From a physiological perspective, this could result in a high density of action potentials and a corresponding summation of metabolic demand (along with associated differences in vasculature). Also, the ability to detect white matter activation appears to be particularly augmented by the use of specifically designed tasks (e.g., interhemispheric tasks) and pulse sequences (e.g., ASE spiral) [9].

These recent findings highlight the need for more work examining white matter fMRI. Potential applications include studies of brain connectivity that allow for the characterization of functional dynamics in relation to tracts identified using diffusion tensor imaging. In addition, this approach may create new avenues of clinical research where the ability to assess the function of WM is critical (e.g., multiple sclerosis).

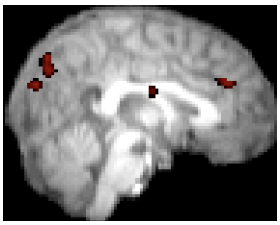

Figure 3. Word/Face (z-score: 2-5)

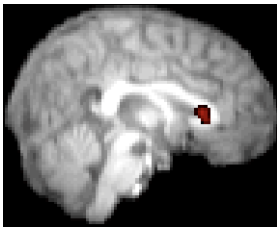

Figure 4. Checkerboard (z-score: 2-5)

References

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