Functional MRI in white matter: Experimental evidence at 4-T

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Introduction The idea that fMRI activity can be detected in white matter (WM) is controversial. At least two factors suggest that measurable signal changes are expected to occur only in gray matter (GM). First, cerebral blood flow/volume is reduced in WM relative to GM (e.g., [1, 2]). Second, the primary source of the fMRI signal has been linked to neuronal input via post-synaptic potentials (e.g., [3]). In spite of this, fMRI activity patterns are not neatly restricted to GM - a fact that cannot be explained entirely as an artifact (e.g., intravascular signals, movement, partial volume effects, etc). Indeed, an increasing number of studies report WM activation, confirming this observation (e.g., [4-8]). These studies show that, despite the expected reduction in signal strength, the WM activation clusters survive the same artifact corrections as performed for GM clusters. One key aspect of this work involves the utilization of paradigms that require information transfer via known WM tracts. This, in turn, allows for specific anatomical hypotheses to be formulated *a priori* and evaluated against the null hypothesis that the activity is simply an artifact.

In the current study, we investigated whether interhemispheric transfer across the corpus callosum (the largest white matter commissure in the brain) can be detected in fMRI. The experiment used an established model of lateralized cognitive processing ([4, 5]), in which the importance of interhemispheric transfer via the corpus callosum has been demonstrated in split brain patients (e.g., [9]). High field fMRI was used to improve the sensitivity to WM fMRI and the time course data were compared to that from active regions in nearby GM (anterior cingulate).

Methods Stimuli: All visual stimuli were presented to the visual hemifields in order to initially stimulate a single hemisphere (150ms duration to avoid saccades). Stimuli consisted of words (i.e., left hemisphere stimuli) and faces (i.e., right hemisphere stimuli) presented in real or scrambled format. Experimental design: A mixed block/fast event-related design was used. Visual hemifield and response hand were varied to examine difference between crossed and uncrossed conditions in the corpus callosum. Words and faces were presented to either the hemisphere of specialization, or the reverse, to elicit a visual interhemispheric crossing effect. Left and right response hand requirements were also varied (to involve either the ipsilateral or contralateral hemisphere) in order to elicit a motor interhemispheric crossing effect. Data acquisition and analysis: Data were acquired using an Oxford 4T MRI system equipped with a Varian INOVA console. Functional MRI was carried out using a two shot spiral-out sequence (TR/TE=1000/30ms, flip 60°, 20 slices, 6mm thick, 0.6mm gap, 240mm FOV, 64x64 matrix). A T1-weighted anatomical image was also acquired using MPFLASH (TR/TI/TE=10/650/5ms, flip 11°, 240x240x192mm FOV, 256x256x64 matrix, 4 segments, 200ms segment delay). Images were interpolated using the input spiral waveforms (no measured trajectories) as well as a field map and navigator correction. All data were then corrected for motion, co-registered, normalized and spatially smoothed. Statistical analyses were performed using both model-based (General Linear Model) and model-free (independent component analysis) approaches. Analyses included examination of whole brain and region-of-interest activity, group and individual activity, and block and event-related activity.

Results and Discussion WM activation was elicited in the corpus callosum, including clusters in both the posterior and anterior regions (Figure 1). Examination of the time course data revealed that, as expected, the amplitude of the response was reduced relative to GM activity in nearby anterior cingulate regions (Figure 2). Nonetheless, WM activity was observed regardless of the type of analysis (i.e., whole brain versus ROI and block versus event-related). Also, the WM activity was not eliminated by modeling physiological or residual motion related noise using independent components analysis. Individual variance was a significant factor, with WM activity being detected in only 15/25 subjects (60%).

The current results may be specific to the corpus callosum. In fact, the majority of studies to date have focused on the corpus callosum ([4-8], so the feasibility of detecting fMRI activation in other WM regions has not been established. The corpus callosum is organized such that fibres connecting adjacent cortical regions are grouped together, which could result in a high density of action potentials and a corresponding summation of metabolic demand. This architecture may make the corpus callosum particularly amenable to detecting fMRI activation. It will be important to evaluate whether the phenomenon is restricted to the corpus callosum, or whether the scope of detectable signal changes generalizes to other WM tracts in the brain.

The findings suggest that it is possible to elicit task related activation in the corpus callosum, but it requires a paradigm specifically designed to elicit information transfer along WM tracts and enhanced methods for detection because the activity is typically reduced relative to GM. The results highlight the need for more work examining the idea of fMRI activity in WM. 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).

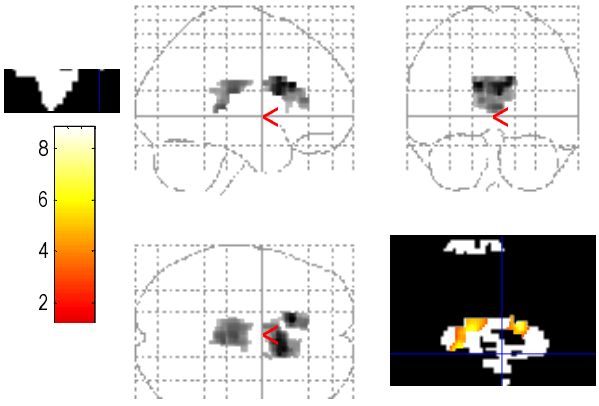

Figure 1. Representative WM activation for visual and motor crossing in the corpus callosum. T-contrast maps were derived from an ROI analysis (p<0.001 uncorrected, extent=6).

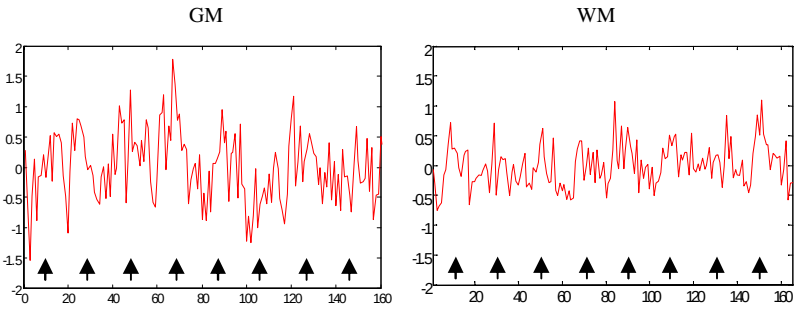

Figure 2. Raw time course data from the anterior cingulate (GM) and corpus callosum (WM) (AU). Note that the data were derived from a mixed block/event related design (with the block timing indicated by arrows). WM activity is clearly identifiable despite the fact that the responses are reduced relative to those in GM.

References

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