Combining fMRI and Probabilistic Tractography in the Temporal Lobe

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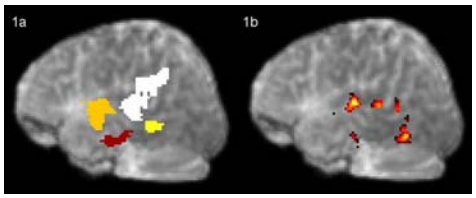
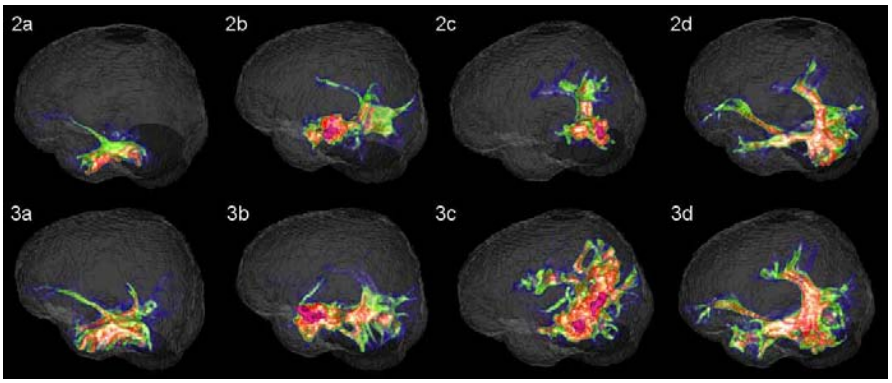
Introduction There has recently been substantial interest in using the results of fMRI tasks as seed regions for initiating diffusion based tractography (e.g. (1)). Here we describe our methodology for using a semantic memory fMRI task to identify activating regions of the temporal lobe and then use the activating regions to directly seed probabilistic tractography. The temporal lobes present particular challenges due to substantial susceptibility artefacts affecting the echo planar images (EPI) used for both fMRI and diffusion weighted imaging. We previously described our sequences and post-processing algorithms for correcting susceptibility related distortions in both spin echo (SE) EPI fMRI and diffusion weighted imaging (DWI) (2) and we concentrate here on the practicalities of using the fMRI results for seeding the tractography. We use SE EPI fMRI rather than the more common gradient echo (GE) as it does not suffer from signal loss in regions prone to magnetic susceptibility. However, SE EPI is considerably less sensitive to heamodynamic activation than GE EPI. Group analysis of fMRI data is therefore particularly important to establish whether activations can be generalised over individuals. However differences in brain morphology and size between individuals result in poorer localisation of group fMRI results when compared with results obtained from a single individual only. Diffusion tractography is generally applied to datasets at the individual level and is very sensitive to localisation and extent of seed points. In theory therefore, improved tractography could be obtained by seeding from an individual's activations. However, with a task involving reading and semantic understanding there is the possibility that some of the activation in a single fMRI acquisition of an individual may be unrepresentative of the task in general for that individual and for the group as a whole. To achieve high quality, reliable subject-specific activations we first performed fMRI on 12 Subjects to achieve group results and then used these coarse, large regions to identify more precise clusters from repeated fMRI acquisitions within individuals.

Methods A word categorisation task (3) requiring semantic memory was performed on 12 individuals and the resulting image sets corrected for susceptibility distortion as described previously (2). A fixed effects group analysis of these results was performed (FSL, Oxford, UK) and 4 major activations in the left temporal lobe were identified using a probability threshold of 0.01 uncorrected for multiple comparisons (activations outside the temporal lobe are not considered in this work). Three of the individuals then underwent the fMRI task on 6 separate occasions each a week apart and each with unique instances of the presentation material, to identify with high confidence the activations specific to each individual. Parameters included SE EPI with voxel size 1.875 x 1.875 x 3 mm, TR 4.2 s TE 70 ms, SENSE 2.5, 42 slices, 225 timepoints. Each acquisition consisted of 16 minutes of data collection resulting in a total fMRI imaging time of 96 minutes per individual. These later acquisitions were analysed within subject using fixed effects analysis in FSL and a smoothing of 5 mm FWMH Gaussian kernel. The results were thresholded at 0.01 uncorrected with a minimum of 16 contiguous voxels required. The large clusters from the group analysis were used to mask the individual's analysis, resulting in 5 smaller activations in the individual analysis shown (2 activating areas within the group cluster representing Wernicke's area). The individual's clusters were then used to seed probabilistic tractography using the *PICo* probabilistic tractography method (4,5,6) incorporating q ball (7) to discern multiple fibre orientations per voxel. The diffusion acquisition and distortion correction procedure was as described in (2).





Results Fig.1a shows the four clusters in the left temporal lobe resulting from the group fMRI analysis. Fig. 1b shows clusters from within these regions from the fixed effects analysis of 6 acquisitions from a single individual (min. significance 0.01, uncorrected, min 16 contiguous voxels). The cluster in white in the group activation (Wernicke's area) has a much greater spatial extent than the corresponding 2 clusters in the individual. Wernicke's area is involved with language processing and is known to exhibit considerable heterogeneity and variation in anatomical position between individuals.

Fig. 2 shows the results of probabilistic tractography in a single individual seeded from the clusters indicated in Fig. 1b. These seed clusters are located in a) inferior temporal gyrus, b) superior temporal gyrus, c) mid/superior temporal gyrus (Wernicke's area) d) posterior fusiform gyrus. For comparison the larger, less anatomically precise clusters from the group analysis were used to seed tractography in Fig. 3a-d, after registering the clusters to the diffusion data. The clusters from the group fMRI result in a loss of tractography precision in all cases, with the most extreme difference occurring between 2c and 3c where a posterior portion of the arcuate fasciculus is revealed using the individuals activation. This major language related tract is almost lost in a substantial mass of other, likely unrelated, fibre tracts when the group seed point is used in this individual.

Conclusions We have demonstrated how fMRI can be used to accurately seed tractography in the temporal lobes. The procedure requires distortion correction for both the fMRI and DWI. SE EPI is required for the fMRI due to signal loss occurring with GE EPI. SE EPI also gives better localisation of activation to the capillary beds with less signal occurring from draining veins. This is advantageous as it does not make sense to seed tractography from draining veins remote from the site of activation. The use of SENSE with a factor of 2.5 also helps localise the signal to the site of activation by reducing the echo train length, which is therefore better centred on the spin echo, reducing T2* weighting and signal from draining veins[8]. The reduced signal and the variable nature of the response to the task require the acquisition of a substantial quantity of repeat fMRI data to ensure quality reproducible results with the semantic memory task used.

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