Application Of A Double Inversion-Recovery Sequence To Diffusion Tractography

S. J. P. Meara[1], D. M. Morris[1], K. V. Embleton[1], H. A. Haroon[1], and G. J. M. Parker[1]

[1]Imaging Science and Biomedical Engineering Research Group, University of Manchester, Manchester, United Kingdom

Introduction

Diffusion tractography algorithms typically require the definition of a region of interest (ROI), from which the pathways of anatomical connections are investigated. Recent studies have used areas of activation as detected by functional magnetic resonance imaging (fMRI) experiments to define seed regions for tractography[1, 2]. It is possible, however, that the locations of such activations may be subject to some uncertainty (for example, they may cross the boundary between grey matter and white matter), and it is not known what effect this has on the tractography results. A grey matter-selective double inversion-recovery (DIR) sequence[3] with an echo-planar imaging (EPI) readout has previously been used to improve the statistical analysis of fMRI data[4]. The present study has implemented a white matter-selective DIR-EPI sequence, and applied the resulting anatomical information to probabilistic tractography. In particular, a DIR-EPI image was used to restrict ROIs defined from a fMRI experiment to contain only grey matter; the tractography results from the restricted regions were then compared with those from the whole fMRI-derived ROIs.

Methods

Images of a normal volunteer were obtained with a Philips Achieva 3-T MR system (Philips Medical Systems, Best, The Netherlands). Two DIR-EPI images, with a spin-echo (SE) EPI readout, were acquired with the phase encoding set to be in opposite directions. The imaging parameters used were: repetition time (TR) = 6000 ms, echo time (TE) = 59 ms, inversion times of TI_1 = 2510 ms and TI_2 = 740 ms, in-plane resolution = 1.875 mm, slice thickness = 2.1 mm, 60 slices, SENSE factor = 2.5, scanning time = 2 × 18 min. Two SE EPI images (again with the phase encoding in opposite directions) were also obtained without the two inversion pulses, with TR = 1000 ms but with all other imaging parameters set to match the prescription for the DIR-EPI images; the scanning time was 24 s per data set. These images were used to calculate a distortion-corrected DIR-EPI image of the white matter, by implementing a procedure that has previously been described[5]. Diffusion imaging data were acquired of the same subject using a SE EPI sequence with the following imaging parameters: TR = 11 884 ms, TE = 54 ms, in-plane resolution = 1.875 mm, slice thickness = 2.1 mm, 60 slices, SENSE factor = 2.5, G = 62 mT m^{-1}, 61 diffusion sensitisation directions at b = 1200 s mm^{-2} (Δ = 28.5 ms, δ = 13.5 ms) and one b = 0 image, total scanning time = 2 × 14 min. The same individual also underwent a fMRI experiment (with SE EPI) on six separate occasions each a week apart, using a word-categorisation task[6] requiring semantic memory. Imaging parameters used were: TR = 4200 ms, TE = 70 ms, in-plane resolution = 1.875 mm, slice thickness = 3 mm, 42 slices, SENSE factor = 2.5, 225 time points, scanning time = 16 min per data set. The diffusion data and the fMRI data were both distortion corrected[7]; the DIR image and the fMRI data were registered to the diffusion data using FLIRT (FSL, FMRIB, Oxford, U.K.). A fixed-effects analysis of the fMRI data was performed using FEAT (FSL), with a probability threshold of P = 0.001 uncorrected for multiple comparisons. Three-dimensional (3D) clusters of activation thus identified were then used to define ROIs for initiating probabilistic fibre tracking using the PICo algorithm[8] with 1000 streamlines per voxel, incorporating q-ball analysis[9] to discern multiple fibre orientations per voxel and bootstrapping to generate the probability density functions[10]. Tractography experiments were carried out using the whole ROIs, as derived from the fMRI results, and also using the same ROIs but restricted to only those voxels that were within the grey matter. The latter process was carried out by reference to the DIR data, following a simple thresholding procedure to produce an image showing the distribution of the white matter.

Results

Figures 1 and 2 show output images from the tractography algorithm, for two different ROIs as defined from the fMRI results. Figure 1 is for a cluster located in the inferior frontal gyrus/insula, and Figure 2 is for a cluster located in the superior temporal gyrus/planum temporale. Figures 1(*a*) and 2(*a*) show the respective results when the whole ROIs were used to seed the tractography algorithm, and Figures 1(*b*) and 2(*b*) show the respective results when each ROI was restricted to contain only grey matter. In all cases, the results presented are maximum intensity projections of the tractography results displayed on a 3D rendered brain image. It can be seen in both Figures 1 and 2 that whereas the tractography results obtained with the restricted ROIs show a great deal of similarity with those obtained from the entire ROIs, there are certain loci where a higher probability of connection was detected when using the whole ROIs, as indicated by the yellow arrows. It is presumed that these tracts correspond to connections that emanated not from the grey matter, but from areas of white matter that were included in the whole ROIs. It should be noted that the differences between the results from the restricted ROIs and those from the whole ROIs were greater than the variability observed from repeated applications of the probabilistic tractography algorithm.

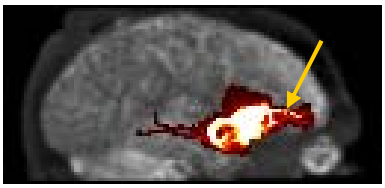

Figure 1(*a*)

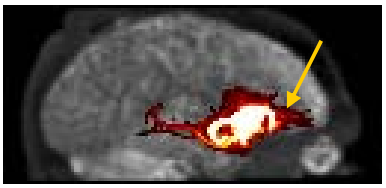

Figure 1(*b*)

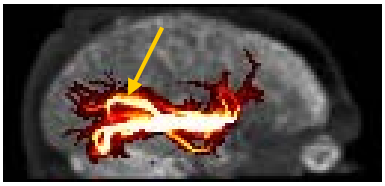

Figure 2(*a*)

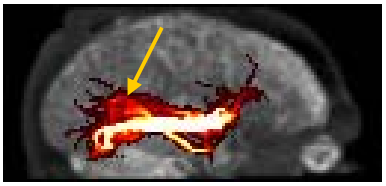

Figure 2(*b*)

Conclusions

The results show that subtly different tractography results will be obtained depending on how the ROI is defined, and this should be borne in mind for future studies that aim to use fMRI activations as seed regions. In cases where the intention is to investigate the anatomical connections from a region of grey matter that is activated in a given fMRI experiment, it must be ensured that the ROI used does not contain any of the surrounding white matter. It should be noted that the differences seen in Figures 1 and 2 are present even despite the fact that the clusters of activation identified here were located almost entirely within the grey matter, with only a few voxels in the white matter. If gradient-echo EPI were to be used for the fMRI data acquisition, for which the localisation of activation is not as precise as for SE EPI as used here, then it would probably be even more important to ensure that the ROIs were within the grey matter prior to their use as seed regions for diffusion tractography.

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