A probabilistic white matter atlas approach to assessing age related changes in the brain

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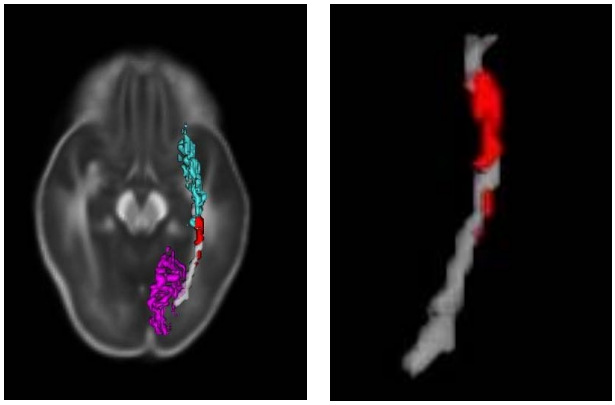
Introduction: Spatial normalisation of diffusion data allows diffusion properties to be compared across a population without any bias from macro-structural differences in tissue anatomy. Standard approaches perform spatial normalisation of diffusion tensors. However streamline tractography through lattices of tensors is mainly suited to reconstruction of major white matter fibres. In contrast probabilistic approaches allow tractography through areas of fibre crossing and low anisotropy. This study constructs a probabilistic white matter atlas by combining posterior distributions on the principal direction of diffusion (PDD) at each voxel for multiple subjects. Tracts are then propagated through the atlas using probabilistic tractography. These therefore represent a consensus for the population. We compare fractional anisotropy (FA) at all voxels along tracts between the insula and lingual gyrus across two populations: 20-30, and 60-90 years. This demonstrates age related changes in FA between frontal and posterior regions of the brain.

Method: The framework is based on the tractography approach proposed by Behrens et al [1]. This uses a partial volume model of diffusion, where the PDD, is represented by a vector (direction: θ,φ) whose size reflects the proportion of anisotropic diffusion in a voxel. Uncertainty distributions on (θ,φ) are found using Bayesian inference. For each subject 50 samples are taken from the distribution at each voxel using Markov Chain Monte Carlo (MCMC) sampling. Transformation of diffusion data is then performed by first non-rigidly [2] registering FA images for all subjects to the subject judged to be most similar to all others by comparing cross correlation in a common co-ordinate space. Registration is constrained from large deformations to prevent different white matter structures from deforming to match one another. The resulting spatial transformations are then applied to all samples from the distributions on (θ,φ), where re-orientation of the samples is performed according to the finite strain approach for spatial normalisation of diffusion tensors [3]. Here affine transformations (F) (obtained from the Jacobian of the non-rigid transformation at each point) are decomposed into pure rotational (R) and deformation (U) components according to $F=UR$ ($R=F(F^TF)^{-1/2}$). These rotation matrices are then used to re-orient each sample on the PDD. This ensures that the posterior distributions continue to align with the tissue microstructure but disallows stretches or shears which may change the representation of the uncertainty. Following re-orientation, all samples the PDD for all subjects are combined at each voxel in the common co-ordinate space to form a joint probability density function for the population. In this instance 1000 samples are drawn from the inverse of the joint cumulative distribution function to form the atlas. The tractography is performed by first defining probabilistic regions of interest (ROI) by propagating labels from all subjects in the atlas. Subjects are first segmented by propagation of labels from multiple manually delineated atlases. These segmentations are then transformed to a spatially normalised T1 atlas of the population, and probabilities are assigned at each voxel according to the proportion of subjects that agree: these are used to modulate the number of streamlines seeded. Next anatomical labels are merged with tissue segmentations to retain only grey matter regions. Probabilistic tractography is performed between ROIs and tracts are probabilistically thresholded so as to retain only the most likely path trajectories. Finally statistical comparison of FA along tracts is performed by transforming FA for every subject to the frame of the tract in the atlas co-ordinate space. FA at each voxel is then compared using permutation testing.

Results: The probabilistic white matter atlas was built from 169 (88 female, 81 male) subjects aged 20-86 years with single shot echo planar DTI, acquired in 15 non-collinear directions using the following parameters: TR 12000ms, TE 51ms, slice thickness 2mm, voxel size = 1.75 x 1.75 x 2mm^3, b- value 1000s/mm^2. Diffusion images were first co-registered to B_0 and eddy current corrected. Because of limited gradient directions a single fiber model of diffusion was fit at each voxel. However, the proposed approach can be easily extended to multiple fiber data by registering each fiber direction at each voxel separately.
A sub-section of 40 subjects aged 20-30 years and 50 subjects aged 60-86 was selected from the population in order to study the effects of healthy ageing dataset. The figure shows results of a permutation test on FA values for the tract (white) that runs from anterior-posterior between the insula (blue) and lingual gyrus (purple). These show that FA is significantly stronger ($p < 0.01$: shown in red) in the 20-30 year population for many anterior voxels close to the insula. This agrees with the current consensus on the causes of healthy ageing which suggest FA decreases in a gradient from anterior to posterior regions of the brain, and this is related to poor performance in executive tasks [4]



The results of a permutation test on FA for all voxels in the tract between the left insula (blue) and lingual gyrus (purple). The tract (white) is overlaid on an axial slice in the left figure and with significance results only on the right. Red voxels show where FA is significantly higher in the 20-30 year population.

Discussion: This paper has introduced a framework for studying FA variability within tracts throughout the brain in common co-ordinate space. The approach generates a probabilistic white matter atlas, which characterises uncertainty across the population. This allows tracts to be traced using probabilistic tractography. FA at each voxel along the tract can be compared for significant statistical differences using permutation testing. This demonstrates age related changes in the tract between the insula and lingual gyrus.

References

[1] Behrens et al. MRM (2003). [2] Rueckert et al IEEE Trans. Med. Imag. (1999). [3] Alexander et al IEEE Trans. Med. Imag. (2001) [4] O'Sullivan et al, Neurology (2001).