Anatomical Connectivity Mapping

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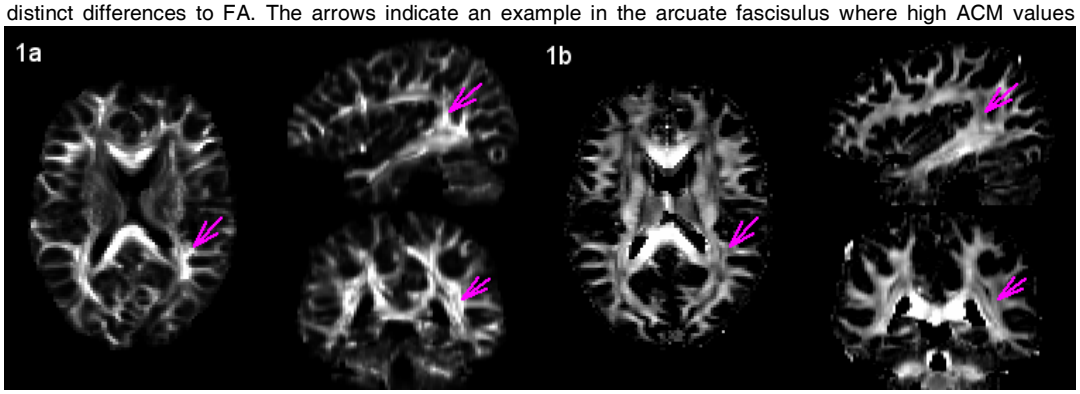
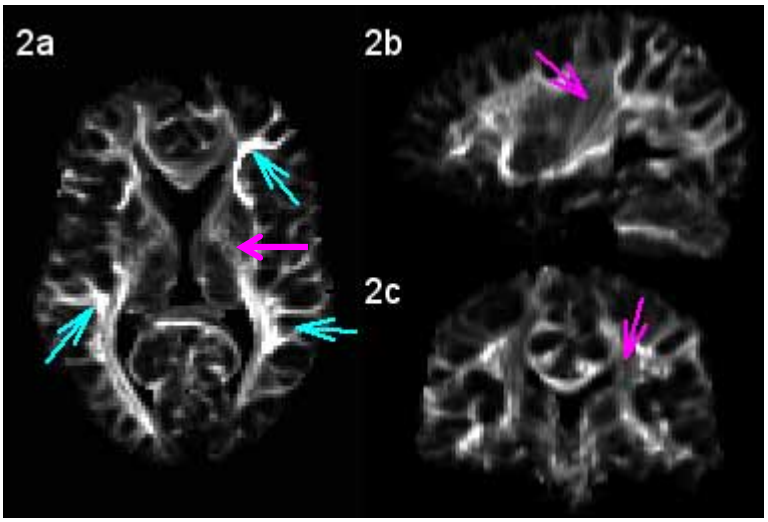
Introduction Diffusion weighted imaging of the brain is used to extract surrogate markers of white matter condition in many studies of disease and developmental processes. However, measures of diffusion anisotropy provide at best an approximation to tissue integrity - an approximation that fails in areas of complex fibre geometry (e.g. crossings), Also, anisotropy measurements tell us nothing about the degree of anatomical connectivity associated with any given point in the brain. Tractography methods have been developed to provide this information, with probabilistic methods providing quantitative measures of the evidence for inter-voxel or inter-regional connection. Here we introduce the concept of **a**natomical **c**onnectivity **m**apping (ACM), which combines the connection information available from probabilistic tractography with the scalar parameter map utility of anisotropy indices. This provides an indication of relative anatomical connectivity of each voxel for the whole brain for both white and grey matter. When complex fibre parameterisations (such as q ball[1]) are used, ACM is not subject to failure in, for example, areas containing crossing fibres. ACM provides a quantitative measure of anatomical connection that will be of use in group mapping to define connection variation and abnormalities.

Methods We performed high angular resolution diffusion weighted imaging on subjects using a previously-described reversed k-space distortion corrected protocol[2]. Acquisition: 3 T Philips Achieva scanner; 8 element SENSE head coil; SENSE factor 2.5; phase-encoding in L-R orientation; SE-EPI with TE = 54 ms, TR = 11884 ms, G = 62 mTm^{-1}, 112 × 112 matrix, reconstructed resolution 1.875 mm, slice thickness 2.1 mm, 60 slices, 61 diffusion sensitisation directions at b = 1200 smm^{-2} (Δ, δ = 28.5, 13.5 ms), and 1 b = 0 image.

The *PICo* probabilistic tractography method[3,4,5] was performed incorporating q ball[1] to discern multiple fibre orientations per voxel. To generate the anatomical connectivity map n Monte Carlo streamlines are initiated for every voxel in the brain (excluding CSF spaces) and for each voxel the number of streamlines passing through it is summed over all seed voxels and Monte Carlo runs. This map is then divided by the maximum possible count (total no. voxels tracked from x n) to normalise for brain volume and Monte Carlo duration, resulting in a map of voxel-wise anatomical connectivity. For this work we chose n = 10.

Results Fig. 1a shows a slice from an anatomical connectivity map with a corresponding fractional anisotropy (FA) map (1b) for comparison. ACM highlights white matter tracts but has distinct differences to FA. The arrows indicate an example in the arcuate fascisulus where high ACM values correspond to relatively low FA due to crossing fibres. Fig. 2 demonstrates the range of anatomical connectivity information available in ACM. Very high ACM values can be seen in tracts connecting regions involved with language processing such as Wernicke's areas and left Broca's area (blue arrows), while much lower ACM scores are found in the corticospinal tracts (CST) (2b & c, magenta arrows). This is consistent with the extensive inter-regional connections within the language system and the relatively small number of connections from the motor system to regions other than the brainstem and thalamus (2b & c, magenta arrows).





Discussion & Conclusions As every voxel in the brain volume is used to seed the tractography stage in ACM there are no difficulties with precisely locating regions of interest, as is required for most tractography studies. This also means that connectivity differences in brain regions that might not have been predicted could be detected using methods such as voxel-based morphometry. Importantly, ACM provides maps of anatomical connectivity not only in white matter, but also for all grey matter voxels, allowing the possibility of examining comparative grey and white matter connectivity across groups.

ACM uniquely provides information concerning the degree of cerebral interconnection to/from a given voxel position. The relatively low ACM values in the CST illustrate this point – while high values of diffusion anisotropy are to be expected here due to the coherent structure of the corona radiata, anisotropy tells you nothing about how 'well-connected' these voxels are. Conversely, the high, and lateralised, ACM values in regions connecting language areas indicate the specificity of the method in distinguishing different degrees of 'connectedness'. We therefore anticipate that the method will be sensitive to pathologies such as semantic dementia, MS, stroke, and schizophrenia that affect the degree of connection between brain regions.

References 1. Tuch, *Magn. Reson. Med.* 52, 1358, 2004. 2. Embleton *et al*, *ISMRM*, 1070, 2006. 3. Parker & Alexander. *Lect. Notes Comput. Sci.* 2732, 684, 2003. 4. Parker & Alexander. *Phil. Trans. Roy. Soc. Series B* 360, 893, 2005, 5. Parker & Alexander, ISMRM Workshop on Diffusion, Lake Louise, Alberta, Canada 2005:74

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