Human in vivo myeloarchitecture using whole-brain diffusion MRI

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Introduction: The spatial organization of myelinated fibres in the cortex makes it possible to parcellate areas based on their myeloarchitecture, due to differences in the properties of the fibre layers and radial fibres.[1] Non-invasive mapping of cortical myeloarchitecture has received increasing interest, with MRI methods based on T_1-, T_2- and T_2*-weighting shown to produce detailed maps of human cortical areas based on myelin content.[2-4] In particular, many of these studies have shown well-defined areas of high myelination, among others, in the sensory-motor strip in the central sulcus, visual cortex, and auditory areas in the Sylvian fissure, and low myelination in, for example, frontal areas.[2-4] Recent improvements in MRI hardware, acquisition methods, and higher-order models for the diffusion MRI signal have opened up the possibility of achieving a more robust characterisation of the microstructure properties of cortical grey matter (GM) using diffusion MRI, with very promising results.[5,6] However, this requires further detailed investigation in whole-brain in vivo human data. In this study, we exploit high-quality diffusion MRI data[7,8] and recent advances in diffusion fibre orientation modelling[9] to investigate cortical myeloarchitecture in the living human brain.

Methods: *Data acquisition:* Data from 8 healthy subjects were acquired on a customised Siemens Skyra 3T with a 32-channel head coil as part of the Human Connectome Project.[7,8] In brief, the relevant diffusion MRI parameters were: 18 b=0 images and b=1000, 2000 and 3000 s/mm^2 (90 diffusion directions each); TR/TE=5520/89.5 ms; 1.25mm isotropic resolution. In addition, all images were acquired with reversed phase encoding for distortion correction. Structural scans: high-resolution T_1-weighted images (0.7mm isotropic). See refs.[7,8] for further details regarding acquisition and pre-processing steps. *Data processing:* Fibre orientation distributions (FODs) were calculated using multi-shell multi-tissue (MSMT)[9] constrained spherical deconvolution (CSD),[10] which uses the multi-shell data to separate the diffusion contributions from white matter (WM), GM, and CSF.[9] For comparison, single-shell data (corresponding to the b=3000 s/mm^2 shell) were also analysed using CSD as implemented in ref.[9] To study myeloarchitecture, the l=0 term of the FOD spherical harmonic expansion (i.e. the orientational average of the FOD) was computed in each cortical voxel (Note: for the MSMT case, the l=0 term of the FOD is directly proportional to the estimated 'WM tissue' component, which can be non-zero in voxels within the cortex in order to fit the anisotropic component of the diffusion signal[9]). For consistency with the terminology used in the apparent fibre density (AFD)[11] method, this term is referred to as AFD_{total}, since it corresponds to the total AFD summed over all orientations. The cortical distribution of AFD_{total} values are displayed as inflated brain surface views using FreeSurfer.

Results: Figure 1 confirms that the recently proposed MSMT-CSD approach provides a much more reliable estimate of the fibre architecture in the cortex compared with CSD (cf. Figs. 1a and 1b):[9] the predominant radial fibre orientation is more clearly identified with MSMT-CSD. Importantly, the smaller FODs observed in certain cortical structures are not artefactual, but do correspond with known myeloarchitecture. For example, close inspection of Fig. 1 shows the known transition between the high myelin *area 4* and low myelin *area 3a* (arrow), consistent with previous T_1 and myelin histology studies (e.g. cf. Fig. 1 of Geyer et al[3]). The myeloarchitecture pattern is further demonstrated in Figs. 2a and 2b, where the population average results of AFD_{total} from MSMT-CSD are shown: the location of areas of high AFD_{total} show a striking similarity to well-characterised areas of high myelin (e.g. cf. Fig. 3 of Glasser et al[2]), including sensory-motor strip ('*sm*' in figure), visual cortex ('*vc*'), and auditory areas ('*aa*'), and areas of low myelin (e.g. frontal areas). Interestingly, Fig. 1c shows that areas with reduced AFD_{total} are not necessarily devoid of coherent fibre architecture, but that they are mostly reduced in their overall magnitude (cf. Figs. 1a and 1c). In contrast, due to partial volume with the isotropic components of GM and CSF, AFD_{total} from single-shell CSD does not reflect the myelin distribution (see Figs. 2c and 2d).

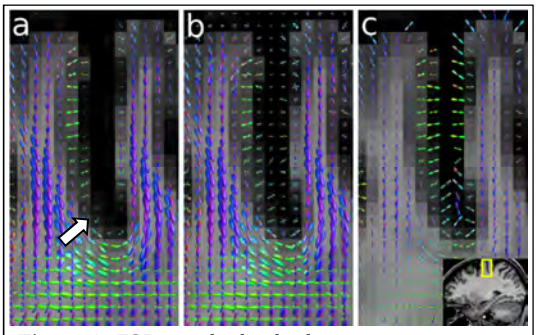

Figure 1. FODs in the border between primary motor (*area 4*) and somatosensory (*area 3a*) cortex in a single subject (see inset in (c) for location); calculated using MSMT-CSD (a) or standard CSD (b). (c) Same FODs as in (a), but normalised to unit AFD_{total}. Arrow: transition between *area 4* and *area 3a*.

Discussion: We have shown that diffusion MRI data can be used to study myeloarchitecture in human whole-brain in vivo data, providing cortical patterns similar to those previously shown with other MRI methods and to those shown by ex vivo histology,[1-4] and complementing previous work in the field.[5,6,12] This was made possible by combining high-quality MRI data with advanced diffusion MRI models. The observed patterns were not due to residual T_1 and T_2-weighting in the diffusion MRI data, given that they were not present in the single-shell results. These myeloarchitecture patterns also cannot be explained by a cortical thickness 'partial-volume' effect.[4] Furthermore, while AFD_{total} from MSMT-CSD provided useful myeloarchitectural information, it should be noted that this does not imply that the observed diffusion contrast was primarily due to the presence of myelin; the contrast is more likely related to the increased microstructural organisation often seen in those cortical areas.[1] These observations may also have implications for those interested in the extension of streamlines tractography to cortical structures.

In conclusion, this study demonstrates that in vivo human diffusion MRI data should provide a useful complementary non-invasive approach to study whole-brain cortical myeloarchitecture based on contrast related to tissue microstructure organisation.

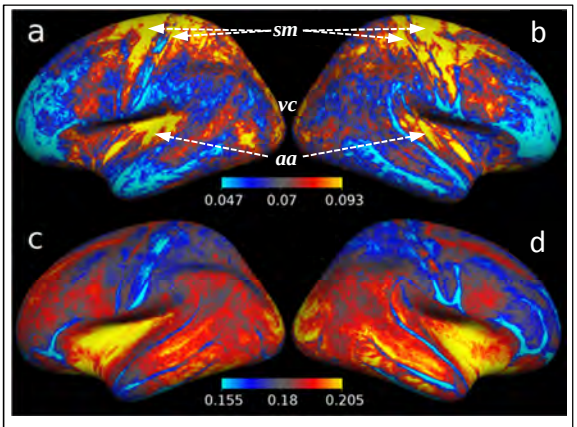

Figure 2. Population average AFD_{total} maps displayed on an inflated surface, from MSMT-CSD (a: left, b: right hemispheres), and from single-shell CSD (c: left, d: right). See Results for acronym definitions.

References: [1] Nieuwenhuys R. *Brain Struct Funct.* 218:303-352 (2013). [2] Glasser MF et al. *J Neurosci.* 31:11597-11616 (2011). [3] Geyer S et al. *Front Hum Neurosci.* 5:19 (2011). [4] Cohen-Adad J et al. *NeuroImage* 60:1006-1014 (2012). [5] McNab JA et al. *NeuroImage* 69 : 87-100 (2013). [6] Nagy Z et al. *PLoS ONE* 8 : e63842 (2013). [7] Van Essen DC et al. *NeuroImage* 80:62-79 (2013). [8] Sotiropoulos SN et al. *NeuroImage* 80:125-143 (2013). [9] Jeurissen B et al. *NeuroImage* 103: 411-426 (2014). [10] Tournier JD et al. *NeuroImage* 35:1459-1472 (2007). [11] Raffelt D et al. *NeuroImage* 59: 3976-3994 (2012). [12] Aggarwal M et al. *NeuroImage* (Epub).