In vitro layer-specific Diffusion Weighted Imaging in human primary visual cortex

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Introduction:

The human neocortex is a six-layered structure of gray matter that has an intricate network of short-range and long-range connections between its constituent areas. The long-range connections through the white matter have been investigated using diffusion MRI for some years now. However, the fibers in the cortex itself (i.e. short range and input/output) pose a challenge for Diffusion Weighted Imaging (DWI) due to the low anisotropy observed in the cortex and the relatively large typical DWI voxel size with respect to the fiber bundles. Recently, with the advent of DWI at high field strength, cortical anisotropy has been shown in humans indicating a radial orientation (Heidemann et al., 2010). More complex configurations have been shown in the deeper cortical layers *ex vivo* in pigs (Dyrby et al., 2010). The variable fiber density and configurations over the layers of the human cortex (Nieuwenhuys et al., 2007) is also likely to be reflected in the diffusion properties. Primary visual cortex (V1) is an excellent candidate area to investigate this, because it features the line of Gennari: the prominent layer IVb consisting of horizontal myelinated fibers. In the present study we therefore image tissue samples of human V1 *in vitro* with diffusion MRI at ultra-high field strength, as this allows for the spatial resolution necessary and validation with histological techniques can be performed.

Methods:

Human brain tissue samples of primary visual cortex (V1) including underlying white matter were fixed in 10% buffered formalin and stored at 4°C at autopsy (15 h post-mortem). Before MRI, the samples were rehydrated in phosphate buffered saline (> 2weeks). MRI was performed on an 11.7T Bruker BioSpec system. Diffusion-weighted images were acquired in a DW-SE protocol using a segmented EPI readout (TR=17.5 s; TE=26 ms; 68 directions + 7 non-diffusion-weighted; 14 repetitions; b-value=4000 s/mm^2; FOV=28.8x28.8 mm; matrix=96x96; 70 slices of 0.3 mm thickness). Multi-echo gradient-echo images (MGE) were acquired for anatomical reference of cortical cytoarchitecture (3D FLASH; TR=40 ms; TE=3.36-38.36 ms; ΔTE=5 ms; flip angle=30°; matrix size 256x256x256; FOV 28.8x28.8x28.8 mm). DWI and MGE volumes were realigned and coregistered. Calculation of diffusion tensors, fractional anisotropy (FA) and mean diffusivity (MD) and tractography were performed with Camino. MGE images were averaged over echoes.

Results:

In the cortex FA and MD were non-uniform over layers. In particular, a layer decreased FA (Figure 1) and MD is evident throughout most of the sample that coincides well with the line of Gennari in the MGE image. Orientation density functions confirm the presence of a pronounced component of horizontal fibers in this layer. A second layer of reduced FA in the deeper layers of the cortex is less pronounced but clearly visible. The white matter shows an abundance of fiber crossings. Especially at the gray-white matter interface reduced FA was observed, where u-fibers cross with fibers penetrating the cortex. Tractography results (Figure 2) show predominant radial fiber tracts in the cortex and many u-fibers spanning most of the gray-white matter boundary.

Conclusions:

We have provided a clear demonstration of layer-specific diffusion parameters in the human neocortex. DT

Tractography results show anatomically plausible fiber reconstructions. The usefulness for connectivity research has to be investigated further, as tractography within cortical layers is challenged by a probably isotropic diffusion component within the layer (i.e. horizontal fibers are likely to be equally distributed over all within-layer directions). To elucidate this, reconstruction of the orientation density functions is a topic of active investigation, as is validation with histological methods.

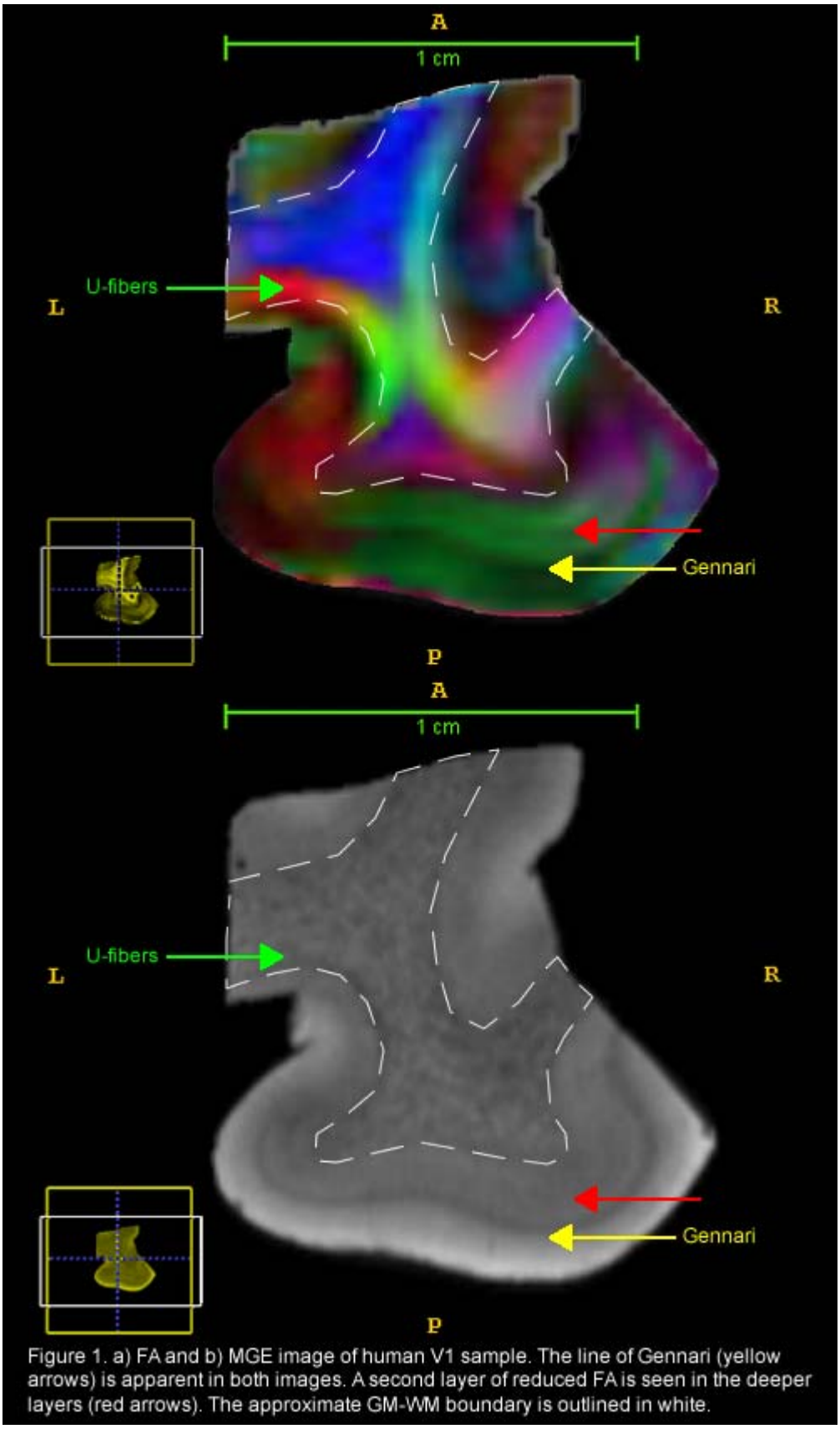

Figure 1. a) FA and b) MGE image of human V1 sample. The line of Gennari (yellow arrows) is apparent in both images. A second layer of reduced FA is seen in the deeper layers (red arrows). The approximate GM-WM boundary is outlined in white.

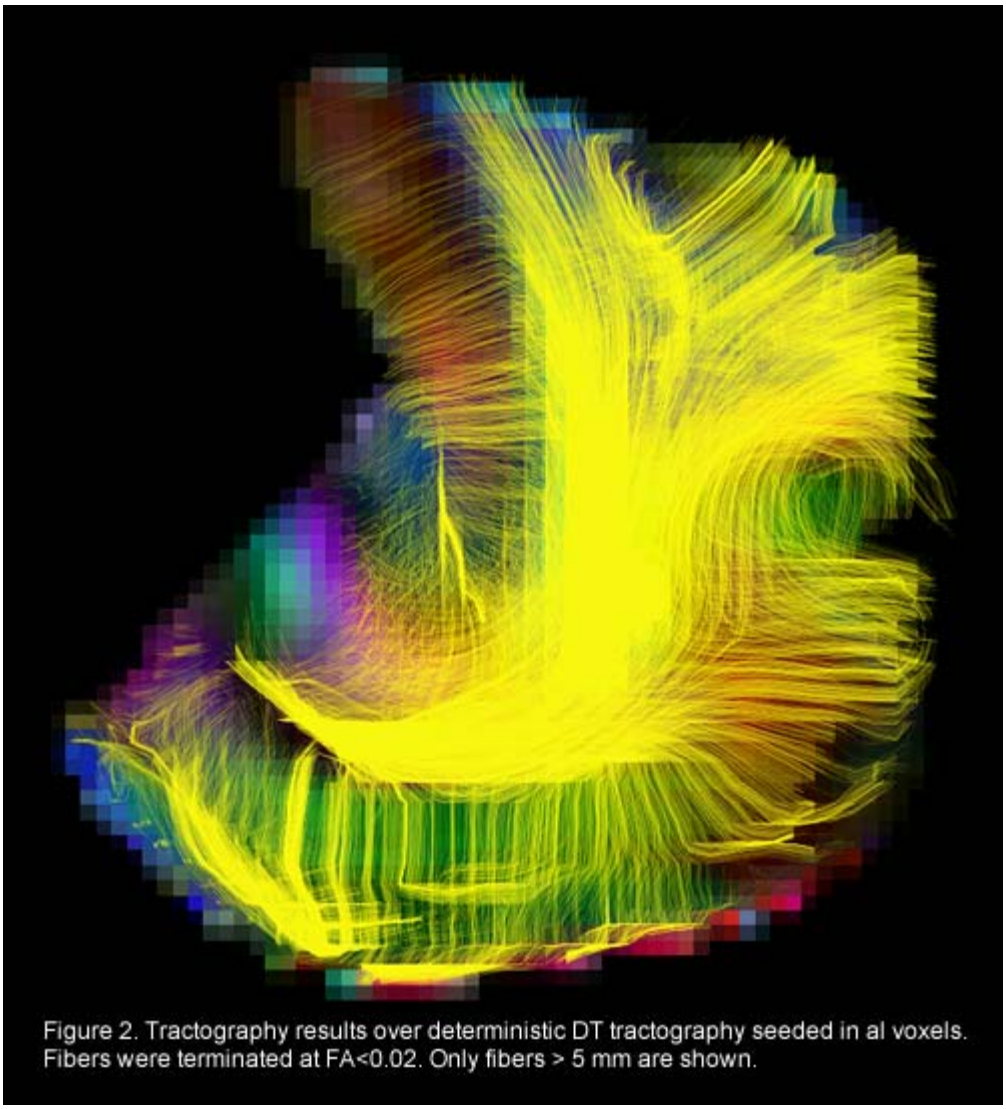

Figure 2. Tractography results over deterministic DT tractography seeded in al voxels. Fibers were terminated at FA<0.02. Only fibers > 5 mm are shown.

Neuroanatomy

Cortical Anatomy and Segregation

Abstract Information

References

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