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

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Introduction

Cortical layers are not readily identified on *in vivo* MRI. In Diffusion Weighted Imaging (DWI), the prevailing assumption is that diffusion is isotropic in the cortex (no prefered direction). However, with the advent of high-resolution *in* and *ex vivo* DWI, this has recently been shown incorrect [1-5]. Gray matter voxels show anisotropy with orientation radial to the cortical surface, but in some areas the primary diffusion direction is tangential, e.g. M1 vs. S1 [1,2]. We investigated this newly discovered cortical anisotropy in more detail, because it could solve one of the great challenges in tractography: following fibers to their cortical termination.

Hypothesis:
Diffusion in the human cortex is layer-specific.

Methods

Samples: Human V1

Human brain tissue samples of primary visual cortex (V1) including underlying white matter.

MRI: DWI and MGE @ 11.7T

Diffusion Weighted Imaging (DWI): 0.3 mm

DW-SE with segmented EPI readout; TR=13.75 s; TE=26.6 ms; b-value=4000 s/mm2; FOV=28.8x28.8 mm; matrix=96x96;

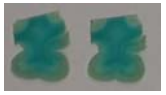
	Sample1	*Sample2*
directions/b=0	61/8	768/64
repetitions	14	1
slices	55	70
scan time (h)	14	14

Multi-echo Gradient Echo (MGE): 0.1 mm

3D FLASH; TR=40 ms; TE=3.36-38.36 ms; ΔTE=5 ms; flip angle=30°; matrix=256x256x256; FOV=28.8x28.8x28.8 mm; scan time 33 min

Histology: Luxol Fast Blue

Tissue sample samples were stained en bloc for myelinated nerve fibers with Luxol Fast Blue



Tensor metrics

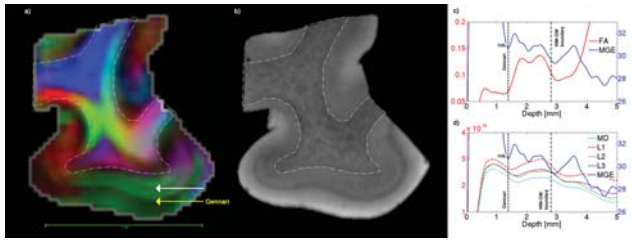


Figure 1. MR results Sample 1. a) color-coded FA image showing layer-specific FA (yellow arrows) b) MGE image averaged over echoes. The line of Gennari (layer IVb) is visible as a low intensity band. c) FA and d) MD/tensor eigenvalue cortical profiles from a small patch of V1 (Ø 2.25 mm). MGE profiles (blue traces) are included in each panel for anatomical reference.

Fractional Anisotropy is non-uniform over layers (Fig.1a).

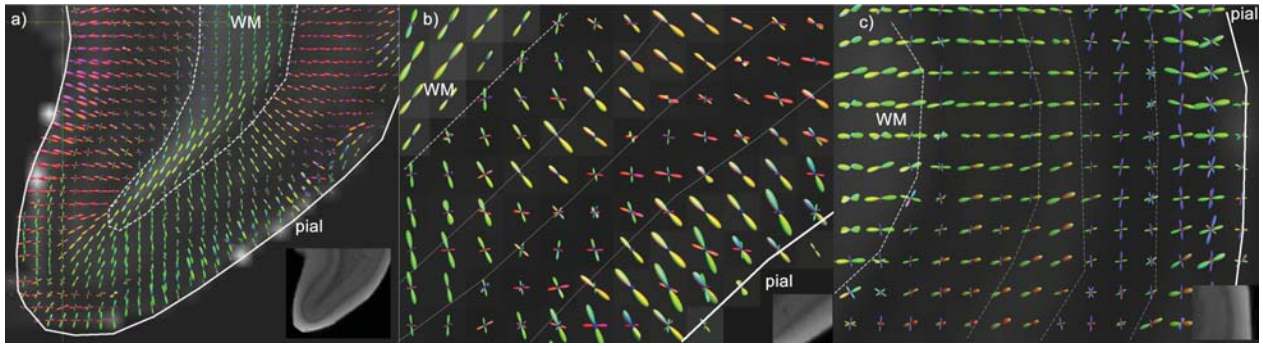
The stria of Gennari (tangential layer) shows reduced anisotropy and diffusivity (Fig.1cd). FA is also reduced in one of the deep layers.

Fiber Orientation Distribution

In the cortex fiber orientation is predominantly radial (Fig.2a), but many tangential components are observed.

The size and complexity of the tangential components are layer-specific (Fig.2c).

Figure 2. Fiber Orientation Distributions of Sample 2. A Pattern of various layers can be observed from white matter to pial, putatively: WM; u-fibers+VI+outer band of Baillarger; layer Va+IV; IVb (Gennari), III+II+I a+b) 'axial' and c) sagittal view.



Tractography and histology

Myelin-stained sections (Fig.3c) clearly show fibers fanning out radially into the cortex.

DT tractography (Fig.3b) results are in excellent correspondence with the fiber trajectories in the histological sections.

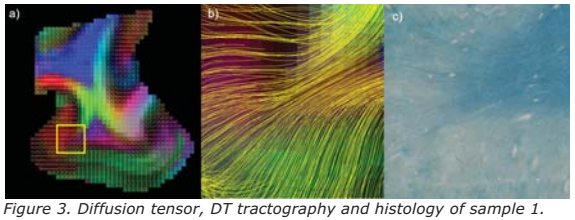


Figure 3. Diffusion tensor, DT tractography and histology of sample 1.

Discussion and Conclusion

The benifit for connectivity research has to be investigated, as tractography within the cortex might be challenged by an isotropic component within layers.

Cortical diffusion of particular pathologies can provide insight on the disease-related changes in the cortex

Layer-specific diffusion parameters have been demonstrated in human primary visual cortex *in vitro*.

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1] Anwander et al., ISMRM 2010
2] McNab et al., ISMRM 2011
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4] Leuze et al., ISMRM 2011
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6] Miller et al., NI 2011

Bruker BioSpec 11.7T Investment grants:
NWO middelgroot 40-00506-90-0602
NWO BIG (VISTA) to A.Heerschap

VIP Brain Networks MIRA