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

Michiel Kleinnijenhuis1,2, Markus Barth3, Valerio Zerbi1,4, Kees-Jan Sikma1,5, Benno Küsters6, Keess Slump7, David Norris2,3, Dirk Ruiter1,2, Anne-Marie van Cappellen van Walsum1,7

1,4,6Departments of Anatomy, Radiology, Pathology, Radboud University Nijmegen Medical Centre, Netherlands; 2Donders Institute for Brain, Cognition and Behaviour, Nijmegen, Netherlands; 3Erwin L. Hahn Institute for Magnetic Resonance Imaging, Essen, Germany; 
4University of Twente, Signals and Systems, Electrical Engineering, Mathematics and Computer Science, Enschede, Netherlands; 1University of Twente, MIRA Institute for Biomedical Technology and Technical Medicine, Enschede, Netherlands

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 preferred 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
DWI-SE with segmented EPI readout; TR=13.76 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

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).

Discussion and Conclusion

The benefit 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.