Quantitative MR Microscopy of Ex Vivo Normal and Diseased Human Cortex

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Introduction

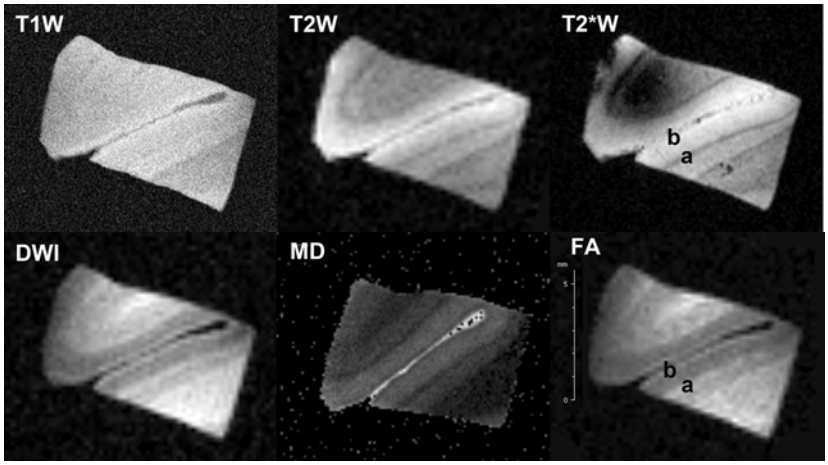
Human cortex is functionally organized into 6 distinct lamina on histology. In normal healthy brains, these layers vary in thickness, neuronal features (cytoarchitecture) and myelination (myeloarchitecture) for different functional regions of the brain [1]. Further, certain neurologic diseases demonstrate sequential layer-specific accumulation of neuropathology (e.g. preclinical and early Alzheimer's disease [2]). Our previous experiments demonstrated that diffusion MR microscopy can detect the functional organization of hippocampal layers in human samples [3]. The initial hypothesis of this project was that MR microscopy can also detect layers of the human cortex.

Experimental

Donor brains from the UCSF Neurodegenerative Disease Bank were initially immersed in 10% formalin for 48 hrs, then sliced in the anatomic coronal plane and replaced into a phosphate buffered solution (PBS) containing sodium azide. Cylindrical tissue samples (4-mm diameter, 6-7 mm height, long axis orthogonal to the tissue surface) were dissected from the calcarine cortex in 3 healthy tissue donors (PMI< 20 hrs, mean age 72). These samples were imaged in a 5-mm NMR tube using the 600-MHz vertical 52-mm bore magnet at the NHMFL AMRIS facility (Gainesville, FL). 50-micron isotropic resolution images were obtained using T1, T2, T2* and 3D diffusion sequences. Quantitative analysis of layer MRI properties were obtained using Paravision (Bruker) and manually-drawn regions of interest with gradient echo sequences.

Results & Discussion

Human calcarine cortex demonstrates layer specific visual and quantitative differences in multiple MRI properties (Fig. 1). These MRI property differences can be attributed to differences in the density of neurons, neuropil and myelin. The line of Gennari in layer IV of the calcarine cortex (a) is evident as a dark band in T2 and mean diffusivity (MD) images, while demonstrating bright signal in the fractional anisotropy images due to its dense myelination and coherent orientations within the cortex. In contrast, the molecular layer of the cortex (b) demonstrates high anisotropy in the FA image, but bright signal on other contrast due its coherent orientation parallel to the surface, but lack of myelination.



Conclusions

Layer-specific MRI contrasts are consistent across multiple calcarine cortex samples and preliminary results are statistical significant ($P < 0.001$ for T1, T2, proton density, mean diffusivity & fractional anisotropy). Accurate diffusion measurements have required substantial experiment time, but we now plan to apply these validated MRI protocols to compare layer properties 1) between different brain regions and 2) between samples with and without hallmarks of Alzheimer's disease pathology.

References

1. Vogt & Vogt. J Psychol Neurol 1942;50:162-154., 2. Braak & Braak. Acta Neuopath 1991:82:239-259., 3. Shepherd et al. AJNR 2007;28:958-964.