In vivo Ultra-High Resolution Diffusion Tensor Imaging of the Microscopic Pathways of the Medial Temporal Lobe

Michael Zeineh[1], Samantha Holdsworth[1], Stefan Skare[2], Anh Van[1], Scott Atlas[1], and Roland Bammer[1]
[1]*Radiology, Stanford, Stanford, CA, United States,* [2]*Dept of Neuroradiology, R3:00, Karolinska Hospital, Stockholm, Sweden*

Introduction: Alterations in microcircuitry of the medial temporal lobe (MTL) are thought to be important components of several neurologic disorders such as Alzheimer's disease and medial temporal epilepsy. The purpose of this study is to identify *all* of the microscopic connections within the medial temporal lobe using high-resolution diffusion tensor imaging, which to our knowledge has not been accomplished previously *in vivo* or *ex vivo*. We couple a near-mm isotropic voxel size and advanced eddy/motion correction with a detailed segmentation of the MTL to identify tracks in all subjects that may represent the major pathways of the MTL, including the perforant pathway.

Methods: *Acquisition:* Six right-handed subjects provided consent and were imaged on a GE 750HDx 3.0T magnet using an 8-channel receive head coil and body transmit using a 2nd order high-order shim. Structural sequences included a thin-section coronal T2FSE. DTI utilized the axial plane, GRAPPA R 2, two shots, b=1500 s/mm^2, TR 3150 ms, TE 69 ms with a partial Fourier acquisition, single-refocused, 70 directions, 10 T2s, phase encoding A/P, fat saturation, 128 x 128, 18cm FOV, 1.4mm thick contiguous, 27 slices, 1.4mm isotropic, 8.5 min per repetition, 7 repetitions.

Image Processing: To preserve SNR, a single-refocused acquisition was chosen, but this results in significant eddy currents. These were corrected with a novel eddy-current correction algorithm that registered each 2-D reconstructed image to 2nd order with an isotropic diffusion weighted image (isoDWI). The diffusion-weighted and T2-weighted volumes were aligned using FSL's FLIRT and sinc-interpolating to a final isotropic resolution of 0.7mm. The b-matrix was corrected to account for motion. Diffusion tensor processing was performed using Camino with a non-linear least squares model. Quiver plots were made with FSLView.

Segmentation and Tractography: On the isoDWI, a detailed segmentation was performed of all hippocampal subregions according to anatomic atlases, facilitated by the extremely high resolution used in this study. FA/MD were computed for each subregion. These subregions served as seeds and targets for bidirectional tractography that was performed with Camino to identify seven key MTL pathways.

Results: *ROI Analysis:* Comparing the left and right sides (n=6 subjects x 10 subregions = 60), FA was higher and MD lower on the left (p=0.0034 and 0.0007, respectively). Examining each subregion separately, FA was higher in the left ERC and fornix (p=0.033, n=6).

Tractography: All of the seven medial temporal pathways were present in each subject. Comparing the left and right side (n=7 pathways x 6 subjects = 42), the number of tracks was higher on the left (p=0.018). Examining pathway separately, more ERC-PRC/PHC fibers (#6) were present on the left (p=0.033). Tract-based measurements demonstrated a slightly lower MD on the left side (p=0.021).

Conclusions: Ultra-high resolution DTI can resolve the substructures in the medial temporal lobe and provided a quantitative analysis that may reflect connectivity. In this cohort of right-handers, the language-dominant MTL demonstrated a slightly higher FA, a slightly lower MD, and more fiber tracks. This high-resolution analysis may have clinical applications.

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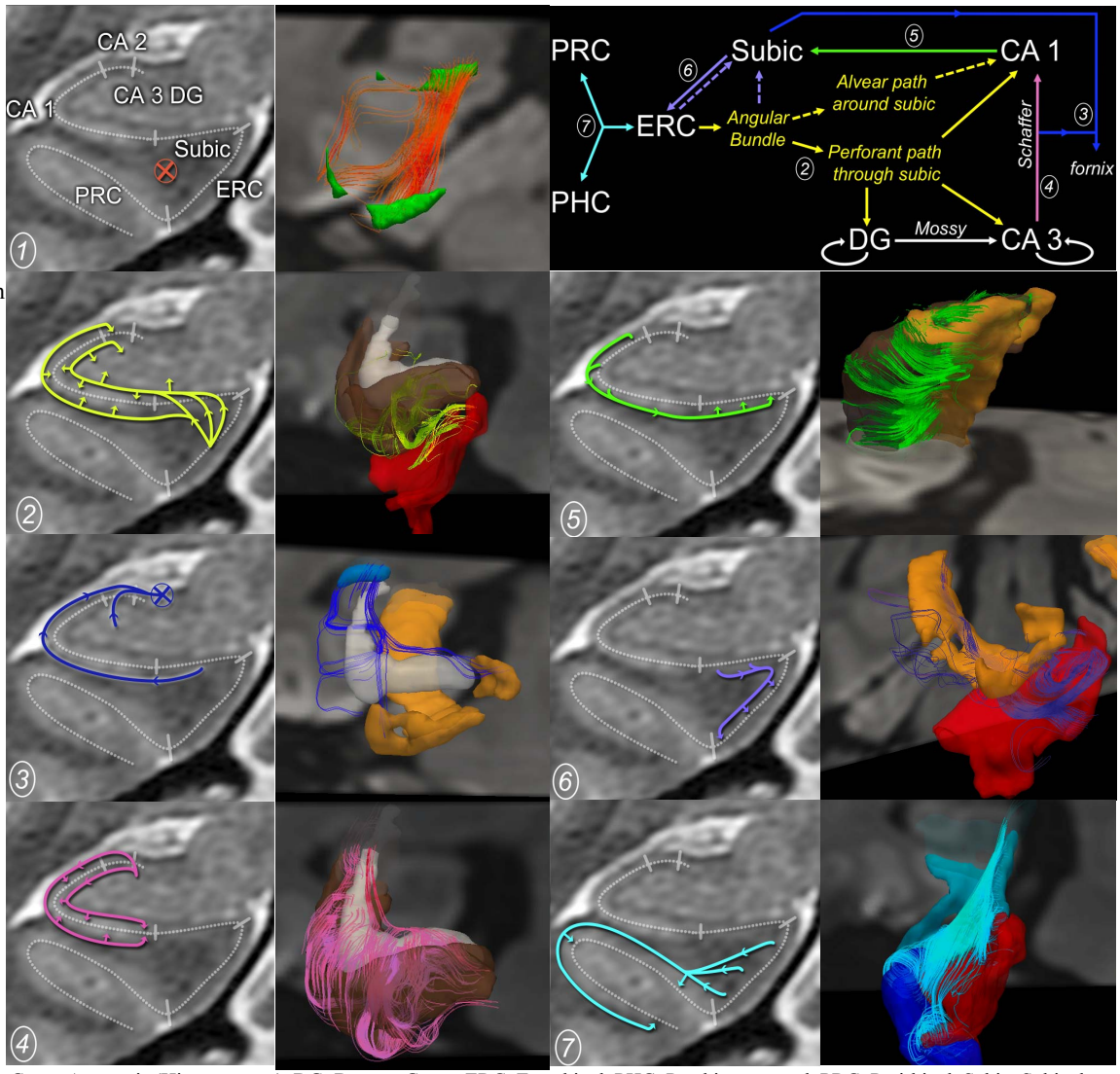

CA: Cornu Ammonis (Hippocampus), DG: Dentate Gyrus, ERC: Entorhinal, PHC: Parahippocampal, PRC: Perirhinal, Subic: Subiculum.
1: Cingulum Bundle, 2: Perforant Pathway, 3: Fornix; 4: CA 3 ⇒ CA 1, 5: CA 1 ⇒ Subic, 6: Subic ⇔ ERC, 7: ERC ⇔ PRC/PHC