Hippocampal subfield ICA multifiber tractography using 3T clinical diffusion data

Manbir Singh[1], and Bryce Wilkins[1]
[1]*Radiology and Biomedical Engineering, University of Southern California, Los Angeles, CA, United States*

Introduction

In several ongoing clinical studies including at our institute, DTI data have been acquired from clinical populations using a nominal number of gradient directions (25-30) at b-values around 1000 s/mm^2 in acquisition times of 5-10 min on a 3T MRI. A recently reported ICA approach (1) enables deterministic streamline tractography to be conducted in such clinical data incorporating ICA estimated multifiber orientations per voxel. As hippocampal connectivity is a key target of many clinical trials, particularly those involving elderly subjects (for example, studies of Alzheimer Disease) and recently it has become possible to demarcate hippocampal subfields with FreeSurfer v5.1 (2), the objective of this work was to perform hippocampal subfield tractography incorporating ICA based multiple fibers per voxel to gain a better understanding of hippocampal connectivity. Key hippocampal tracts such as the cingulum encounter several fiber-crossing regions along their path. Thus accurate recovery of hippocampal connections requires multifiber tractography since single-fiber DTI can only recover broken pieces of tracts and incomplete connections (3).

Method

Hippocampal subfield tracts were constructed from diffusion (DTI) data acquired at 3T from 50 elderly subjects (controls and cognitively impaired) in an ongoing clinical study. Twice re-focused single-shot EPI 128x128 data were acquired along 25 gradient directions with b=1000s/mm^2, one b=0 image, TR/TE=16000ms/86.1ms, Field of View 25.6cm, 2mm thick 60 contiguous axial slices with 2x2x2 mm^3 voxels in about 7 minutes. Orientations of up to 3 fibers per voxel were estimated by ICA from the 25-direction diffusion signals using a 3x3x3 cluster around each voxel (1). Assuming diffusion signals of individual fibers to be non-Gaussian, ICA unmixes signals from a mixture of fibers in a small neighborhood surrounding each voxel to yield orientations of individual fibers (1). Single seed per voxel whole-brain streamline tractography was conducted in 0.2mm steps using Euler's method along each fiber-orientation. Orientations within 6 neighboring voxels corresponding to the smallest deflection with respect to the incoming tract were used in the interpolation. Voxel DTI derived FA <0.05 and step-wise deflection or cumulative deflections in a voxel >45^0 were used as thresholds during tracking.

T1-weighted anatomical images acquired in 1x1x1 mm^3 voxels were segmented by FreeSurfer v5.1 to parcellate cortical/subcortical volumes and hippocampal subfields (2). The 0.5mm subfield probability map was transferred to the 1mm voxels native T1-space by FreeSurfer, and each voxel in this map was assigned to the subfield with the highest probability. Whole-brain ICA tracts were also mapped to the native T1-space using a 12-parameter affine EPI-T1 co-registration and filtered by TrackVis (4) using the FreeSurfer defined ROIs in T1-space.

Results and Discussion

The hippocampal subfields are color-coded as shown in Fig. 1 (top left). As an example, tracts assigned to each subfield for a subject are displayed in Fig 1, in the same color as their respective subfield. In addition to the subfields, the entorhinal cortex (shown as bright green), which is intrinsically linked to the hippocampus, was included in this work. Tracts from all subfields and the entorhinal cortex are shown in Fig 1 (top right) to present a comprehensive view of the hippocampal structural connectivity pattern. Also, as an example of subfield connectivity to other regions, the precunious-hippocampal tracts are shown in Fig. 1 (bottom right), illustrating the heterogeneity in precunious connections. Because of partial volume effects, it is understandable that there is some overlap in the subfield tracts, nonetheless differences are obvious, e.g., the fimbria and CA1 show strong connections to the fornix whereas CA2-3, CA4-Dentate gyrus, presubiculum and hippocampus proper show strong connections to the cingulum as well.

(1) Singh and Wong, *Magn Reson Med* 64, 1676 (2010)
(2) Van Leemput et al. *Hippocampus*, 19(6) 549-557 (2009)
(3) Concha et al. *Am J Neuroradiol* 26, 2267 (2005)
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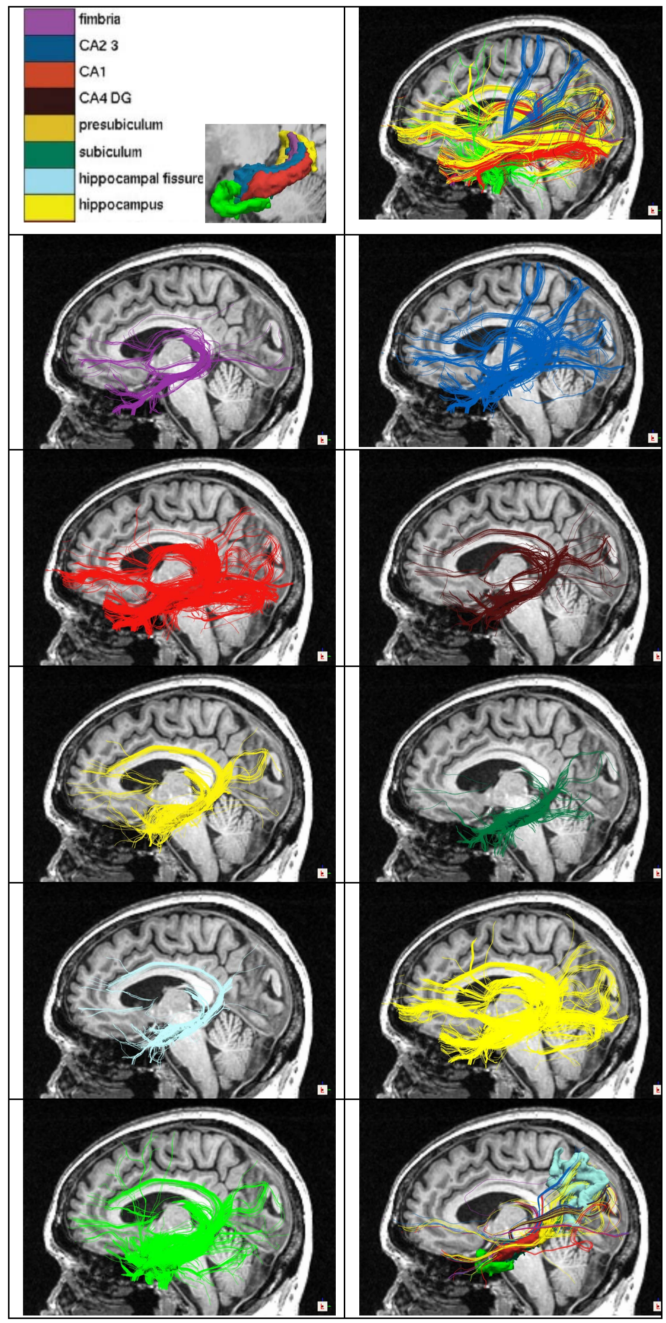

Fig. 1: (top left) Color-coded hippocampal subfields for a subject. The entorhinal cortex has been included in bright green. (Top right) All subfield and entorhinal color-coded tracts. (Rows 2-5) Individual subfield color-coded tracts. (Bottom left) entorhinal cortex tracts. (Bottom right) Precunious to subfield plus entorhinal cortex connections.