Quantification of Fornix Tracts in MCI and AD

D. H. Hwang[1], S. Tsao[1], and M. Singh[1]

[1]Biomedical Engineering and Radiology, University of Southern California, Los Angeles, CA, United States

Introduction

Numerous studies have shown a pattern of progressive hippocampal shrinkage as a result of mild cognitively impairment (MCI) and Alzheimer Disease (AD). One of the major pathways affected by the hippocampus is the fornix, and it has been recently shown that fractional anisotropy (FA) is reduced in normal controls verses AD [DeCarli et al., Alzheimer's Imaging Consortium IC-P1,July 2008]. The purpose of this study was to (a) objectively define hippocampal ROIs as most previous studies rely on subjectively delineated ROIs to perform DTI analysis, (b) correct for varying subject head sizes using intracranial volume(ICV) of subjects in a novel way to equalize the number of seed points and their anatomical distribution so that total number of tracts becomes independent of the subject's head size, and (c) examine the differences in the equalized streamline fornix tracts.

Method

Data were acquired on a 3T GE scanner from three groups (10 normal control, 8 MCI, and 7 AD probable) as classified by neuropsychological testing. Multi-slice (2.04 x 2.04 x 4 mm^3 voxel size, 4 mm thick slices no gap) DTI data were acquired using 25 encoding gradient directions at b-values of 0 and 1000 sec/mm^2 with an acquisition matrix of 128x128. Anatomical data were acquired using a 256 x 256 acquisition matrix employing a SPGR sequence (1 x 1 x 1 mm^3 voxel size, 1 mm thick slices no gap) with TE=3.128ms, TR=7.832ms and TI=450ms.

The hippocampi were identified using high resolution SPGR images via the Freesurfer software package (Harvard/MGH). The automatically segmented hippocampal ROIs were then co-registered back to the DTI subject space using SPM. Seed points where normalized by adjusting spacing according to subject intracranial volume (ICV). ICVs were calculated based on a weighted combination of grey and white matter, and CSF segmented volumes generated by SPM. By using a control average ICV of $1.5x10^6$ mm^3, all seed spacing was adjusted to compensate for ICV in individuals. Streamline tractography was performed using tensor interpolation with a 0.2 mm step-size utilizing in-house DTI software.

Whole-brain tractography data were processed by several stages of filtering to obtain the fornix tracts. The steps are based on two known facts (1) fornix tracts connect the hippocampus and hypothalamus and (2) these tracts do not cross right/left hemispheres. First, only the tracts which intersect the hippocampal ROIs are considered. Next, all tracts originating from seed points outside of the fornix region are eliminated. Tracts originating from the fornix regions that progress out of the fornix region are kept for tract counting. However, the aforementioned tracts are cut back to where they deviate from the fornix for display purposes (**fig. 1**).

Figure 1: Normalized Fornix Tracts

Figure 2: ICV Normalized Freesurfer-based Hippocampus Volumes in Normal, MCI and Probable AD

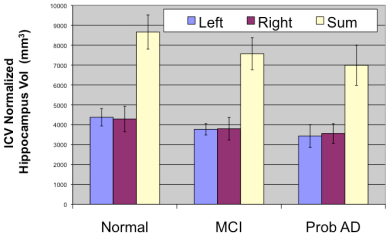


Figure 3: ICV-Normalized Tract Counts in Normal, MCI and Probable AD

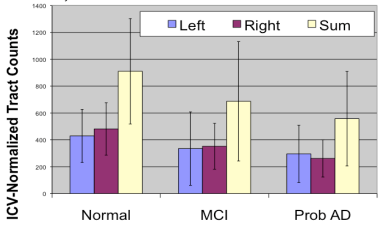
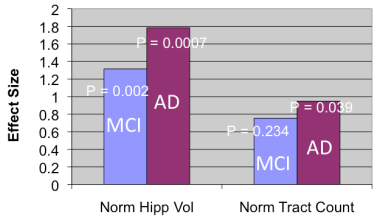


Figure 4: Hippocampus Volume and Tract Count Effect Sizes



Results and Conclusions

Results of hippocampal volume (**fig. 2**) confirm the progressive degenerative effects of MCI and AD and validate the usability of Freesurfer defined hippocampal ROIs without any subjective input. ICV-Normalized tract counts for the fornix (**fig.3**) show a similar progressive reduction. Although there is a measurable decrease in connectivity based on normalized tract count (Prob AD p=0.039,eff size = 0.9), the effect seems to be less than what is measured using normalized hippocampal volumes (Prob AD p=0.0007, eff size= 1.8) (**table 1**).

Table 1: Effect Sizes and t-test of Normalized Hippocampus Vol and Normalized Tract Count against Normal Population

		Normalized Hippocampus Volume	Normalized Tract Count
MCI			
Effect Size		1.315	0.754
t-score		3.553	1.246
df		24.822	13.435
Sig (P-value)		0.002	0.234
Mean Difference		1093.255	223.625
Std Error Difference		307.678	179.485
95% Confidence Interval	Lower	459.349	-162.857
	Upper	1727.161	610.107
Prob			
Effect Size		1.784	0.948
t-score		4.838	2.265
df		23.332	14.784
Sig (P-value)		0.001	0.039
Mean Difference		1650.224	353.167
Std Error Difference		345.224	155.870
95% Confidence Interval	Lower	956.635	20.513
	Upper	2383.812	685.820

Although the effect of Alzheimer Disease on hippocampal volume is known, its effects on the afferent and efferent connections between the hippocampus and other structures via the crucial fornix tract is relatively unknown. Relatively large voxel sizes were used in this study ($2x2x4mm^3$) creating partial volume confounds. We expect that as higher resolution DTI data are acquired, the effects of partial volume will be reduced leading to better tract quantitation and improvements in effect sizes corresponding to fornix and other affected tracts.