White Matter Integrity in Mild Cognitive Impairment and Alzheimer's Disease: A Diffusion-Tensor Imaging Study

C. E. Sexton[1], C. E. Mackay[1], M. E. Bastin[2], J. Lonie[3], and K. P. Ebmeier[1,3]

[1]Psychiatry, University of Oxford, Oxford, United Kingdom, [2]MRC Centre for Cognitive Ageing and Cognitive Epidemiology, University of Edinburgh, Edinburgh, United Kingdom, [3]Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, United Kingdom

Introduction

Mild Cognitive Impairment (MCI) is a descriptive category that identifies patients referred with memory and other cognitive problems, who do not qualify for a diagnosis of dementia [1, 2]. Per annum, approximately 10-15% of individuals with MCI progress to dementia [3]. Thus, there is great interest in finding biomarkers that could be used to diagnose MCI, predict the later emergence of Alzheimer's Disease (AD) and track deterioration or progress of treatment.

Diffusion-Tensor Imaging (DTI) is an MRI technique that can uniquely study the orientation and integrity of white matter tracts, with Fractional Anisotropy (FA) providing a measure of the degree of anisotropy within neural tissue.

Tract-Based Spatial Statistics (TBSS) is a fully automated whole brain analysis technique that projects all subjects' FA data onto a mean FA tract skeleton, before applying voxelwise cross-subject statistics. TBSS minimises the effects of misalignment and provides more consistent results across subjects and sessions than after VBM-preprocessing or manual placement of ROIs [3].

Here we will use TBSS to compare patients with AD and MCI with healthy controls in order to investigate the effect of MCI on white matter integrity.

Methods

Subjects: 9 subjects with MCI (age = 75.89 ± 4.31, 4 male), 6 subjects with Alzheimer's Disease (AD) (age = 73 ± 4.31,4 male), 6 healthy control subjects (74.17 ± 7.44, 2 male).

Image Acquisition and Pre-Processing: Subjects underwent a 60 direction diffusion-weighted sequence on a 1.5 T scanner

Image Analysis: Voxelwise statistical analysis of the data was carried out using TBSS [3], part of FSL [4].

Statistics: Differences in global FA integrity were calculated by comparing mean FA values within the skeleton mask between groups using nonparametric two-sample Mann-Whitney U-tests. Voxelwise statistics were performed using a permutation-based inference tool for nonparametric statistical thresholding ("randomise", part of FSL) [3]. The significance threshold for between-group differences was set at $P < 0.05$, using the threshold-free cluster-enhancement option in the "randomise" permutation-testing tool in FSL.

Results

Global FA Integrity

The global FA values per group are shown in figure 1. A significant decrease in global FA integrity was detected in AD subjects compared with controls ($P = 0.047$, one-tailed) and for MCI compared to controls ($P = 0.018$, one-tailed).

Spatial Distribution

The spatial distribution of significant differences between the groups in FA is summarised in table 1 and illustrated in figure 2. In AD, significant differences in FA were concentrated in the corpus callosum, forceps minor, cingulum (cingulate gyrus), inferior longitudinal fasciculus and inferior fronto-occipital fasciculus. In MCI, significant differences paralleled those in AD, and were concentrated in the corpus callosum, forceps minor, right cingulum (cingulate gyrus), right inferior longitudinal fasciculus and right inferior fronto-occipital fasiculus.

Discussion

This is the first study to detect significant differences between subjects with MCI and control subjects using TBSS. Due to the similarities in the significant reductions in FA in both MCI and AD, DTI may become a useful clinical tool for the early diagnosis and monitoring of MCI. Future work will examine the association between white matter integrity and performance on neuropsychological tests.

Figure 1: Box plots depicting mean global FA values per group

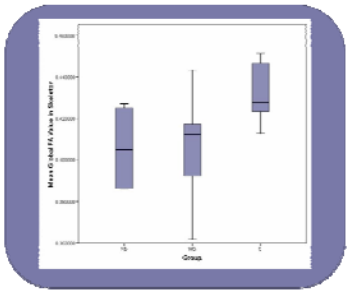

Figure 2: Significant reductions in FA that are detected in both MCI and AD groups are displayed in red, significant reductions in FA that are detected only in AD are displayed in blue, on a green skeleton of mean FA. Images (coronal, axial and sagittal) are t-statistics, $P < 0.05$.

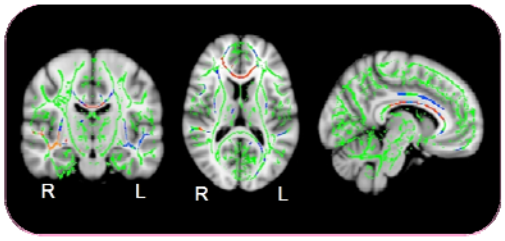

Table 1: Summary of the spatial distribution of significant abnormalities in FA

	AD		MCI	
	L	R	L	R
Corpus Callosum	✓		✓	
Forceps Minor	✓		✓	
Cingulum (cingulate)	✓	✓	×	✓
Inferior Longitudinal Fasciculus	✓	✓	×	✓
Inferior Fronto-Occipital Fasciculus	✓	✓	×	✓

References

[1] Petersen et al, (1999) Arch Neurol, 56: 303-308

[2] Petersen et al, (2001) Arch Neurol, 58: 1958-1992

[3] Smith et al (2006) Neuroimage 31: 1487-1505

[4] Smith et al (2004) Neuroimage 23: S208-S219