Title: Relating structural and chemical changes in Alzheimer's disease using MRS and DTI at 7 Tesla

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Structured Abstract:

Introduction: Alzheimer's disease (AD) is a type of dementia that causes problems with memory, thinking, and behaviour. Diagnosis and prognosis in AD remains a challenge, but MRI biomarkers could meet this need. Using magnetic resonance spectroscopy (MRS) at 4T, we previously reported a decrease in hippocampal glutamate (Glu) and a trend for hippocampal myo-inositol (mlns) increase in AD. These changes may be potential biomarkers for AD. In the present study, we aimed to replicate these metabolic changes at 7T and extend the work by relating these changes to neurodegeneration.

Methods: We recruited normal elderly controls (NECs, n=12, 71.4 +/- 9.6 yrs), individuals with mild cognitive impairment (n=5, 69.5 +/- 6.9 yrs), and with prodromal AD (n=5, 82.4 +/- 4.7 yrs). Recruitment will continue until there are 15 participants in each group. MRS data was acquired using the semi-LASER sequence (TE=60 ms, TR=7500 ms, 64 avgs) from single voxels in the left hippocampus (23x12x12 mm3) and posterior cingulate cortex (PCC, 16x20x18 mm3) and was analysed with in-house software. Diffusion weighted imaging was performed using a multi-shot diffusion-weighted spin-echo EPI sequence (b=1000, TR=5100 ms, TE=50.2, 64 directions, 2 mm iso). Using Camino (UCL), whole-brain mean diffusivity (MD) and fractional anisotropy (FA) maps were obtained. Bayesian probabilistic streamline tractography was performed on the FA maps to find fibres passing through both spectroscopy voxels. Fibres were grouped by geometric similarity, allowing for the removal of outliers, identification of the white matter tract connecting the two spectroscopy voxels, and tract-based measurements of fibre count, MD, and FA.

Results: In the left hippocampus, a trend towards decreased Glu in ADs compared to MCIs (p=0.09) and NECs (p=0.07) was observed. mlns was higher in ADs compared to MCIs (p<0.05) and there was a trend towards increased mlns in ADs compared to NECs (p=0.07). We observed no significant differences in metabolite levels in the PCC. In the hippocampal-PCC tract identified by tractography, ADs had lower tract FA values compared to MCIs or NECs. ADs also had higher tract MD values when NECs. We saw no significant differences in fibre count between groups. However, we did observe a negative correlation (r=-0.55, p=0.02) between hippocampal mlns level and fibre count. Hippocampal mlns was also negatively correlated (r=-0.63, p=0.006) with the average FA value and positively correlated (r=0.50, p=0.04) with the average MD value of the hippocampal-PCC tract.

Discussion: MRS results from this preliminary dataset agreed with our previous findings at 4T. Higher MD and lower FA in the hippocampal-PCC tract of AD participants indicates less restricted diffusion, which may reflect a loss of neuronal density. MD and FA were correlated to mlns levels, suggesting a link between mlns and neurodegeneration. Thus, hippocampal mlns has the potential to be a biomarker for neuronal cell death in AD.