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Investigating Early Markers of Alzheimer's Disease Using a Combination of Cognitive Tests and MRI to Probe Changes in Hippocampal Anatomy and Functionality

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Abstract : Background: Effective treatment of dementia will require early diagnosis, before significant brain damage has accumulated. Memory loss is an early symptom of Alzheimer's disease (AD). The hippocampus, a brain area critical for memory, degenerates early in the course of AD. The hippocampus comprises several subfields. In contrast to healthy aging where CA3 and dentate gyrus are the hippocampal subfields with most prominent atrophy, in AD the CA1 and subiculum are thought to be affected early. Conventional clinical structural neuroimaging is not sufficiently sensitive to identify preferential atrophy in individual subfields. Here, we will explore the sensitivity of new magnetic resonance imaging (MRI) sequences designed to interrogate medial temporal regions as an early marker of Alzheimer's. As it is likely a combination of tests may predict early Alzheimer's disease (AD) better than any single test, we look at the potential efficacy of such imaging alone and in combination with standard and novel cognitive tasks of hippocampal dependent memory. Methods: 20 patients with mild cognitive impairment (MCI), 20 with mild-moderate AD and 20 age-matched healthy elderly controls (HC) are being recruited to undergo 3T MRI (with sequences designed to allow volumetric analysis of hippocampal subfields) and a battery of cognitive tasks (including Paired Associative Learning from CANTAB, Hopkins Verbal Learning Test and a novel hippocampal-dependent abstract word memory task). AD participants and healthy controls are being tested just once whereas patients with MCI will be tested twice a year apart. We will compare subfield size between groups and correlate subfield size with cognitive performance on our tasks. In the MCI group, we will explore the relationship between subfield volume, cognitive test performance and deterioration in clinical condition over a year. Results: Preliminary data (currently on 16 participants: 2 AD; 4 MCI; 9 HC) have revealed subfield size differences between subject groups. Patients with AD perform with less accuracy on tasks of hippocampal-dependent memory, and MCI patient performance and reaction times also differ from healthy controls. With further testing, we hope to delineate how subfield-specific atrophy corresponds with changes in cognitive function, and characterise how this progresses over the time course of the disease. Conclusion: Novel sequences on a MRI scanner such as those in route in clinical use can be used to delineate hippocampal subfields in patients with and without dementia. Preliminary data suggest that such subfield analysis, perhaps in combination with cognitive tasks, may be an early marker of AD.

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