Early macrostructural and microstructural cortical changes in Alzheimer’s disease: longitudinal and cross-sectional studies of early change

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United Kingdom

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Early macrostructural and microstructural cortical changes in Alzheimer's disease: longitudinal and cross-sectional studies of early change

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Research Abstract
Evidence suggests that Alzheimer’s disease (AD) is associated with a long period of progressive accumulation of molecular pathology, followed by increasing neuronal damage, before symptoms appear. The best chance of successful treatment may therefore come from offering therapies as early as possible. In order to do so we need to be able to identify those at risk, to stage their disease, and to track progression with robust and precise methods. Although rare, familial AD (FAD) provides a unique opportunity for prospective study of individuals who are cognitively normal but are destined to develop the disease. Whilst rates of brain atrophy increase prior to symptom onset, detecting subtle changes in cortical grey matter may be a more sensitive and earlier marker of neurodegeneration. Recent advances in imaging have led to the development of techniques for high quality macroscopic (cortical thickness) and microscopic (diffusion) measures of cortical change. Whilst by definition asymptomatic, those who have prodromal AD may have subtle cognitive deficits. Novel neuropsychological tests have been able to detect subtle abnormalities in memory, including binding of short-term memory and accelerated long-term forgetting, in other conditions involving mesial temporal cortex. These tests may also be useful in early AD. The aims of this study are: 1. To use serial MRI to investigate cross-sectional and longitudinal markers of early cortical and juxtacortical change using sensitive metrics (cortical thickness and diffusion) in those at-risk of developing FAD, those mildly affected by FAD and sporadic AD, and controls; 2. To evaluate the sensitivity of novel neuropsychological tests of mesial temporal dysfunction at detecting differences in these groups; 3. To evaluate how these markers of early degenerative change compare temporally to one another, and to more established cognitive and imaging outcomes; and how these correlate with molecular markers of AD pathology.

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