Selective Degradation of White Matter Ultrastructure in Parahippocampal and Posterior Cingulate in Mild Cognitive Impairment and Alzheimer's Disease by Diffusion Tensor Imaging

Topic: None selected

Presentation Time: Sunday, 12:00 noon - 2:30 p.m.

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Background: Hippocampal atrophy has been considered the most sensitive MRI marker for Alzheimer's disease (AD). However, hippocampal atrophy generally failed to completely separate mild cognitive impairment (MCI) and AD from normal aging, in part because aging also impacts hippocampus. Based on the theory that AD evolves along strategic neuronal connections that are poorly myelinated, we investigated whether limbic fibers connecting hippocampus and posterior cingulate cortex show degradation in MCI and early AD, using diffusion tensor imaging (DTI). Objective: To test if AD pathology is associated with decreased water fractional anisotropy (FA) along limbic fibers, presumably indicating demyelination, while mean diffusivity (D), reflecting more diffuse fiber changes, is primarily related to aging. Methods: Thirteen AD patients (mean age 75.7±9.5 years), 15 MCI (73.1±7.8 yrs), and 12 cognitive normal (CN) subjects (70.4±8.2 yrs) were studied with volumetric T1-weighted MRI and DTI at 1.5Tesla. Hippocampal volumes were measured using semi-automated software. DTI was used to identify the limbic fibers and to measure FA and D values in parahippocampal and posterior cingulate regions along these fibers. In MCI, FA values were significantly ($p < 0.01$) reduced and D values slightly increased in posterior cingulate and in parahippocampal white matter compared to controls, as predicted. Furthermore, diagnosis generally explained the variation of FA in MCI and CN, while age primarily explained ($p < 0.05$) variations of D. In AD, a decrease of FA and an increase of D in the limbic fiber regions were further enhanced. Using FA of posterior cingulate alone correctly classified 81% ($p = 0.02$) of MCI and CN, in contrast to hippocampal volume, which - when used alone - made no significant contribution to the classification ($p > 0.05$), based on logistic regression. AD and CN subjects could completely separated by using FA of posterior cingulate and hippocampal volume together. Conclusions: Abnormal DTI measures of fibers connecting hippocampus and posterior cingulate may be a more sensitive indicator of early AD pathology than hippocampal volume. However, prospective studies are needed to determine if DTI is useful to predict conversion of MCI to AD.

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