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**Diffusion tensor MRI assessment of white-matter fibre changes in Alzheimer's disease and mild cognitive impairment**

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**Objective:** White matter (WM) changes have been reported by several histopathological studies in Alzheimer's disease (AD). These changes are heterogeneous, ranging from mild myelin attenuation to marked axonal loss and reactive gliosis. Diffusion tensor (DT) MRI, which is sensitive to WM tissue changes in vivo, may provide specific markers for regional changes in WM. Here we wished to assess the integrity of the normal appearing WM in the major fiber bundles in subjects with AD and mild cognitive impairment (MCI).

**Methods:** Twenty-one AD patients (age: 75+8SD, women: 9, MMSE: 19+6), eleven amnesic MCI (age: 69+8SD, women: 5, MMSE: 26+1) and fifteen healthy controls (age: 70+6SD, women: 9, MMSE: 29+2) underwent a clinical and neuropsychological evaluation, and brain conventional and DT-MRI on a 1.5T scanner. Subjects with major vascular damage were not included into the study. Mean diffusivity (MD), fractional anisotropy (FA), as well as parallel and radial diffusivities were measured in the normal-appearing WM of eight major fiber bundles (corpus callosum, cingulum, fornix, corona radiata, arcuate, uncinata, inferior longitudinal and inferior fronto-occipital fasciculi), using an atlas-based automated technique.

**Results:** Compared to controls, MCI and AD patients showed cognitive deficits in all the domains investigated ( $p < 0.02$ , ANOVA with Bonferroni correction). MD was significantly increased in AD patients compared to controls in the corpus callosum, cingulum, arcuate, inferior longitudinal fasciculus, and corona radiata ( $p < 0.05$ , ANOVA with Bonferroni correction). FA values did not differ between AD patients and controls ( $p > 0.17$ ); this pattern was likely due to an increased axial diffusivity ( $p < 0.007$ ) coupled with a non-significant increase in radial diffusivity ( $p > 0.08$ ). Diffusivity and FA values from MCI patients did not differ from those of AD patients and controls ( $p > 0.05$ ). However, a trend for progressively increasing MD from normal aging to AD was detected in all the tracts ( $p(\text{trend}) < 0.05$ ), except for the fornix ( $p = 0.43$ ).

**Conclusions:** The major brain WM fiber bundles show diffusivity alterations which followed the trajectory normal aging/MCI/AD. These changes are likely to be secondary to Wallerian degeneration of WM fiber tracts following neuronal injury.