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WHITE MATTER DEGRADATION IN NORMAL AGING AND APOE4 GENE CARRIERS AND ALZHEIMER DEMENTIA

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Abstract: **Background:** Age-related white matter alternations are a well-established finding. There is increasing evidence that white matter abnormalities play also a major role in AD in addition to cortical atrophy. So far, however, it is not clear if the pattern seen in AD extends to APOE 4 carriers even if there is no evidence of cognitive impairment.

Objectives: Using diffusion tensor imaging (DTI) to determine the regional patterns of: 1) age-related and AD-related white matter degradation in cognitive normal subjects and AD patients, respectively; 2) white matter changes in cognitive normal subjects carrying APOE ϵ 4 allele compared to subjects carrying ϵ 3. **Methods:** DTI was performed in 19 young adults (YNG, 41.6 ± 10.2 yo), 31 cognitive normal older adults (OLD, 68.2 ± 7.0 yo; 16 ϵ 3/3 and 15 ϵ 3/4 carriers), and 16 age-matched AD patients (68.6 ± 9.3 yo). Voxel-wised analysis of fractional anisotropy (FA) across groups and ROI analysis on the corpus callosum and cingulum fibers were performed. **Results:** Voxel-wise analysis found OLD subjects had significant FA reductions than YNG primarily in the frontal white matter, genu, superior temporal regions and posterior internal capsule. In contrast to aging, AD patients showed greater FA reduction than OLD primarily in the periventricle white matter, cingulum, posterior callosum, middle temporal, left precuneus, and frontal regions. ROI analysis yielded similar results with the voxel-wise analyses: notably, AD had greater FA reduction than OLD in all cingulum regions and posterior callosum. In OLD subjects, the ϵ 4 group showed significant lower FA than the ϵ 3 group in the middle temporal, right superior temporal, frontal, and thalamic regions. No region had higher FA in ϵ 4 than ϵ 3 group. **Conclusions:** This study confirms that aging is associated with characteristic pattern of ultrastructural alterations in frontal white matter. Furthermore, parietal and temporal white matter alternations seen in AD are distinctly different from normal aging. Interestingly, cognitively normal APOE4 carriers show a complex pattern of white matter abnormalities, which is different than the ones seen in aging or AD. However, whether white matter alternation in APOE4 is an early sign of AD needs to be determined in prospective studies.

Figure 1. Pattern of significant FA reduction in OLD than YNG

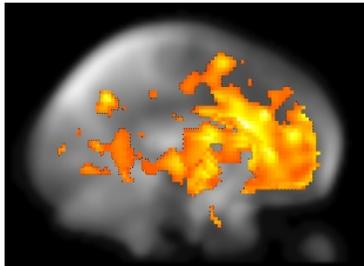
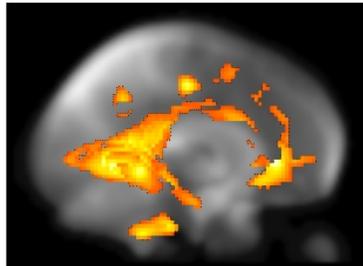


Figure 2. Pattern of significant FA reduction in AD than age-matched OLD



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Learning Objectives (Complete):

Verb: : predict

Learning Objective: : predict cognitive decline

Verb: : interpret

Learning Objective: : interpret pattern of aging and dementia by imaging

Verb: : develop

Learning Objective:: : develop new imaging method