Age-Dependent Differences in Brain Tissue Microstructure Assessed with Neurite Orientation Dispersion and Density Imaging

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BACKGROUND

Normal human aging is accompanied by alterations in brain structure in both white and gray matter, and these changes can be visualized with modern imaging techniques (Pannese, 2011).

Neurite Orientation Dispersion and Density Imaging (NODDI) is a technique that uses magnetic resonance imaging (MRI) to assess the density of axons and dendrites (neurites), the amount they disperse away from each other, and overall water diffusion (Zhang et al., 2012).

In conjunction with tests of memory and executive function, NODDI may be able to resolve early brain changes and their relation to cognitive functioning with more specificity than traditional brain imaging techniques.

OBJECTIVES

To determine how age affects the density of neurites and isotropic water diffusion in a group of cognitively healthy older adults.

To determine if NODDI measures relate to cognitive function.

METHODS

Participants:

N=117 cognitively healthy adults (mean age 61.7 years, SD 6.1) enriched for parental family history of Alzheimer’s disease (AD) and APOE e4 genotype from the Wisconsin Registry for Alzheimer’s Prevention (WARP) and Alzheimer’s Disease Research Center (ADRC) cohorts, both designed to identify biological and lifestyle risk factors associated with development of subsequent AD.

Brain Imaging:

Participants underwent a 15-minute Hybrid Diffusion Imaging (HYDI) protocol, which acquires 126 diffusion-weighted measurements including those at substantially higher b-values than traditional diffusion tensor imaging, up to 7,500 mm²/s. Modeling was accomplished with NODDI to produce maps of neurite density, orientation dispersion, and the volume fraction of isotropic water diffusion.

Cognitive Data Collection:

Subjects completed a comprehensive neuropsychological battery, including tests of episodic memory and executive function; the Rey Auditory Verbal Learning Test (RAVLT), Trail Making Test Part B, and the Mini Mental State Exam (MMSE). Across participants, the average time between brain imaging and neuropsychological testing was 110 days, SD=128 days.

Statistical Analyses:

NODDI Parameters: Separate voxel-wise regressions were performed in Statistical Parametric Mapping (SPM) 12 for each of the NODDI parameters as dependent variables and age as the independent variable of interest, controlling for the covariates of sex, APOE e4 status, and family history of AD. Significance was inferred at p<0.05 with FWE correction with cluster extent > 25 voxels.

Cognitive Measures: We performed partial correlations between NODDI measures in the statistically significant regions with scores on each cognitive test (controlling for age, sex, PHQ, and APOE e4) in SPSS 22.

RESULTS

COGNITIVE SCORES

• Neurite density decreases with age.

• Isotropic water diffusion increases with age.

DISCUSSION

• Widespread increases in water diffusion were observed throughout the brain with increasing age, as well as decreases in neurite density in frontal white matter regions.

• These results suggest that NODDI is capable of measuring age-related brain changes and cognitive functioning, findings that are in agreement with historical studies as well as other diffusion-weighted imaging techniques (Dickstein et al., 2013; Anderson and Rutledge, 1996)

• This study sheds light on the processes underlying normal brain development, knowledge that is crucial for differentiating healthy aging from pathology associated with Alzheimer’s disease and other dementias.

WORKS CITED


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