MRI Predictors of Cognition in Early-Stage Alzheimer's Disease

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Objective: Examine magnetic resonance imaging (MRI) predictors of cognition in the earliest clinical stages of Alzheimer's disease (AD).

Background: Advancing age is associated with structural brain changes including brain atrophy, white matter lesions (WML), and "silent" cerebral infarcts (SCI) while hippocampal volume (HV) correlates with AD neuropathological burden. Few studies have examined the concomitant presence of these structural brain changes on cognition, particularly in the earliest clinical stages of AD.

Methods: Brain MRI and neuropsychological testing was performed in subjects enrolled in the Alzheimer Disease Research Center. Subjects were nondemented (Clinical Dementia Rating [CDR] 0, n = 86) or had very mild (CDR 0.5) or mild (CDR 1) AD (n = 62). MRI measures included WML burden, SCI, normalized whole brain volume (WBV) and HV. A composite measure of global cognition (factor score) was determined based on standard neuropsychological test performance. Group differences in demographic and neuroimaging variables were assessed using chi-square analysis and Student's t-test. Multivariate linear regression was used to assess the relation of the individual imaging variables to global and specific cognitive measures after controlling for age, education, and all other imaging variables.

Results: Individuals with early AD had reduced whole brain volume (0.72 (0.03 SD vs 0.75 (0.04 SD), $p < 0.001$), hippocampal volume (0.39 (0.08 SD) vs. 0.48 (0.07 SD), $p < 0.001$), and modestly more total WML burden (semiquantitative burden 22.7 (7.7 SD) vs. 19.9 (6.6 SD), $p < 0.05$) than nondemented individuals. There were no differences in the prevalence or number of infarctions. Global cognition (factor score) was independently predicted by measures of brain atrophy (WBV beta = 0.36, $p<0.001$), HV (beta = 0.30, $p < 0.001$), WML burden (beta = -0.26, $p < 0.001$), and SCI (beta = -0.20, $p < 0.01$). SCI were most strongly related to processing speed while WML, HV, and WBV were independently predictive of performance on nearly all specific neuropsychological tasks. In separate group analyses, all imaging variables were independently predictive of global cognition in early-stage AD while none were independently predictive of global cognition in nondemented aging.

Conclusion: Age-related structural brain changes of white matter lesions, "silent" cerebral infarctions, and brain atrophy additively influence cognitive performance in the early stages of AD.