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Risk Factors for Alzheimer’s Disease and Longitudinal Memory Performance

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**Conclusions:** Our results demonstrate APOE genotype differentially impacts cerebrovascular function across the lifespan as well as the relationship between CBF and cognition. Findings may partially support suggestions that the gene exerts antagonistic pleiotropic effects.

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**Objective:** Greater risk for Alzheimer’s disease (AD) is associated with carrying the apolipoprotein E (ApoE) ε4 allele and a family history (FH) of AD. Little research has examined the long-term cognitive effects of these risk factors. We examined longitudinal memory performance over five years in elders with a combination of risk factors.

**Participants and Methods:** Sixty cognitively intact elders underwent neuropsychological assessment at baseline, 1.5 years, and five years. Among ApoE ε4 non-carriers, 16 participants had a FH of AD, while 20 participants had no FH of AD. Twenty-four ApoE ε4 carriers comprised a third group of participants, either with (n=17) or without (n=7) a FH of AD. We used univariate repeated measures ANOVAs to identify possible group differences in memory performance and to examine potential time-by-group interactions.

**Results:** Longitudinally, there were significant interaction effects for time and group on the Rey Auditory Verbal Learning Test Immediate Learning, Delayed Recall, and Percent Retention variables, with ApoE ε4 carriers declining from baseline differently than the other groups. Follow-up analyses revealed that differences in memory across groups were not apparent until the five-year follow-up assessment, when the ApoE ε4 carriers performed worse than those without the ApoE ε4 allele.

**Conclusions:** Results suggest that the ε4 allele is associated to a greater degree than FH for AD with reduced memory performance over time. Longitudinal studies of cognitively intact individuals may require long follow-up periods, perhaps 5 years or more, to detect the influence of AD risk factors between groups.

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T. FUJITA, M. NOTOYA, N. SUNAHARA, K. KATO, T. NAGAI & Y. HATTORI. Differences in behavioral disorders in Alzheimer’s disease patients with regard to dementia severity measured using the at-the-desk instrumental activities of daily living (IADL) test.

**Objective:** We developed a test for the desk evaluation of instrumental activities of daily living (IADL) in Alzheimer’s disease (AD) patients, and examined its credibility and adequacy. In this study, we examined whether differences in behavioral disorders can be mapped using the at-the-desk IADL (ATD-IADL) test in AD patients classified using the clinical dementia rating (CDR) scale.

**Participants and Methods:** The study included 24 normal control (NC) patients (CDR0), 24 mild AD patients (CDR1), and 11 moderate AD patients (CDR2). The ATD-IADL test comprised 8 tasks (4 tasks with 2 patterns) that included 2 object and classification tasks, a parallel task, and a prospective memory task. The subjects were instructed to determine the sequence of the 8 tasks. We recorded the number of people performing a task and the task sequence being performed, and thus calculated the score.

**Results:** A significant difference was observed between the NC and the 2 AD groups in the number of subjects who performed all the tasks (x² test, p < 0.05); however, not much difference was noted in the number of people who performed the classification and 2 object tasks. The 2 AD groups had significantly lower implementation sequence scores than the NC group (Kruskal-Wallis test, p < 0.05)

**Conclusions:** This results indicated that AD patients faced a high degree of difficulty while performing prospective memory or parallel tasks. We suppose that the AD patients’ ability of efficiently assessing the task sequence starts deteriorating during the mild AD stage.

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**Objective:** The presence of HPA axis dysregulation, and concomitant cortisol elevation, is well established in Alzheimer’s disease. Disagreement exists on what role this increased cortisol plays in the progression of the disease. It was hypothesized that higher levels of serum cortisol would predict greater rate of decline in functioning in future years.

**Participants and Methods:** Archival data was obtained from the Baylor College of Medicine Alzheimer’s Disease and Memory Disorders Center in Houston, Texas and the Texas Alzheimer’s Research Consortium. Subjects were 40 patients with a diagnosis of probable AD. Serum cortisol was measured using immunoassay human Multi-Analyte Profile. APOE genotype was also determined. Patients were then administered a full neuropsychological battery which included measures of memory (WMS-R LM and VR), language (Boston Naming Test, FAS), attention (VSAF), visuospatial functioning (Block Design), and dementia severity (MMSE, CDR-Sum of Boxes). This battery was repeated yearly for 2 to 4 years.

**Results:** Growth curve analyses within a multilevel fixed effects model framework were used to predict the decline in performance on neuropsychological tests and disease progression. Serum cortisol levels did not significantly predict the decline in functioning in any of the neuropsychological measures or the increase in disease severity. Inclusion of APOE ε4 status as a predictor moved results closer to, but did not reach, significance for increase in CDR–Sum of Boxes.

**Conclusions:** Higher cortisol levels did not predict an increased rate of decline in AD patients’ neuropsychological test scores or dementia severity, implying there is not a substantial relationship between the physiological stress response and disease progression. Analyses did suggest that APOE ε4 carriers with high cortisol levels may exhibit more rapid increase in dementia severity, but this possible effect needs to be demonstrated in future, more statistically powerful studies.

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V.A. GUZMAN, O.T. CARMICHAEL, C. SCHWARZ, M.E. ZIMMERMAN & A. BRICKMAN. White matter hyperintensities and amyloid are independently associated with entorhinal cortex volume in the Alzheimer’s Disease Neuroimaging Initiative.

**Objective:** Current hypothetical models of Alzheimer’s disease (AD) pathogenesis emphasize the role of beta amyloid, tau deposition, and neurodegenerative changes in the mesial temporal lobe (particularly entorhinal cortex). However, many individuals with clinical AD who come to autopsy also exhibit cerebrovascular disease. The relationship between AD and vascular pathology is unclear, especially whether they represent additive or independent effects on neuronal injury. We used data from the Alzheimer’s Disease Neuroimaging Initiative (ADNI) to 1) confirm whether entorhinal cortex volume (ECV) is associated with cognitive functioning among individuals with mild cognitive impairment (MCI) who are at risk for AD; and 2) determine whether regional white matter hyperintensity (WMH) volume, a radiological marker for small vessel cerebrovascular disease, is associated with ECV above-and-beyond putative AD biomarkers.

**Participants and Methods:** Data from 397 subjects with MCI (mean age=74.09±7.47) were utilized, including ECV, intracranial volume, total tau, Aβ1–42, and cognitive test scores. Lobar WMH volumes were