Cortisol Levels in Alzheimer’s Patients are Related to Premorbid Functioning and Rate of Progression

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Introduction

• Prolonged stress and therefore chronic activation of the HPA axis and the resultant high cortisol levels can lead to damage to the hippocampus and perhaps other brain regions; and to memory and cognitive dysfunction.
• Since AD strongly impacts the hippocampus and other medial temporal regions early in the disease, the effects of prolonged stress/cortisol could interact with the AD changes.
• Relationships between cortisol levels and other AD patient characteristics (current cognitive functioning, premorbid ability, rate of progression of cognitive deficits) have not been clearly established, and will be investigated in the current study.

Methods

• Serum cortisol was measured (in nmol/L) using multiplexed immunoassay human Multi-Analyte Profile by Rules-Based Medicine (Austin, TX) and APOE genotype was determined.
• Neuropsychological measures included WMS Logical Memory and Visual Reproduction (I and II), FAS, the Boston Naming Test, Digit Span, and the Geriatric Depression Scale (GDS).
• Estimated level of premorbid verbal intellectual functioning was assessed using the AMNART formula.
• Physicians gathered information to estimate duration of patients' symptoms, and estimated rate of MMSE decline prior to the initial visit was calculated: (30 – MMSE score) / duration.

Results

• Serum cortisol was significantly higher in AD patients (M=140.9) than in controls (M=126.4). Values were positively skewed, and the group difference persisted when log-transformed values were analyzed.
• In AD patients, cortisol values were not significantly correlated with any neuropsychological test scores, but were negatively associated with AMNART estimated IQ (r = -0.20, p < .01).
• Cortisol was also associated with estimated rate of MMSE decline, r = 0.20, p < .01.

• The relationship between cortisol and MMSE decline was moderated by APOE status: In patients with no ε4 alleles, the correlation was 0.37 (p < .001), and in patients with 1 or 2 ε4 alleles, it was 0.09 (p > .35).

Conclusions

• In AD patients, cortisol levels were not significantly related to current neuropsychological functioning, but were associated with AMNART IQ—patients with lower estimated premorbid IQ had higher cortisol values. These patients may have had poorer cognitive resources for coping with stress.
• Non-ε4 carriers with higher cortisol levels exhibited a faster estimated rate of cognitive decline (prior to the initial visit) than those with lower cortisol levels. This suggests that cortisol levels may partly contribute to progression in these patients, at least early in the disease. Alternatively, patients who are declining more rapidly may experience greater stress, and therefore exhibit higher cortisol levels.