

# Biological Mechanisms of Stress Response and the Risk of Alzheimer's Disease

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Alzheimer's disease (AD), the most common form of senile dementia, is one of the leading causes of death in the U.S. A predisposition or expression of chronic stress-related symptoms has been considered a risk factor of AD. The goal of this project was to examine how the stress hormone cortisol relates to risk of AD biomarkers - abnormal aggregation of  $\beta$ -amyloid (AB) peptides, increased amount of tau proteins, and hippocampal atrophy - using in vivo human brain imaging, cerebrospinal fluid (CSF), and blood plasma samples across AD stages. It was hypothesized that increased plasma cortisol levels will relate to increased AD biomarkers and hippocampal atrophy via aberrant neuronal activity. Using the publicly available datasets of human neuroimaging, CSF, and blood plasma measures from Alzheimer's Disease Neuroimaging Initiative (ADNI), plasma cortisol levels, brain glucose metabolism, hippocampal volume, CSF AB and tau, and cortical amyloid plaque load were measured among cognitively normal older adults (CNs) and patients with Mild Cognitive Impairment (MCI) and AD. Multiple regression models were applied to assess the relationships between these measures across all groups as well as within-group analyses. The results showed that higher cortisol was associated with AD stages as well as smaller hippocampal volume across all groups. The relationships between plasma cortisol levels and brain glucose metabolism, however, varied across the disease stages. Furthermore, higher cortisol levels were associated with abnormal tau pathology especially among CNs. The results suggest a role of individuals' susceptibility to stress in an increased risk of neurodegeneration and the development of AD. Relaxation activities, such as meditation, may assist in lowering the risk of AD.