

Participation in cognitively-stimulating activities is associated with brain structure and cognitive function in preclinical Alzheimer's disease

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Background: Prior studies have shown that participation in cognitively-stimulating activities might delay the onset of Alzheimer's disease (AD). However, the mechanism underlying this effect is not well understood. In this study, we tested the hypothesis that frequent participation in cognitively-stimulating activities, specifically those related to playing games and puzzles, favorably alters brain structure and cognition in a sample of middle-aged adults at increased risk for AD. **Methods:** Three hundred twenty-nine cognitively normal, middle-aged adults (age=60.31±6.25 years, 69% women, 40% APOE4 positive, and 74% with family history of AD) enrolled in the Wisconsin Registry for Alzheimer's Prevention participated in this study. They reported their current engagement in cognitive activities using a modified version of the Cognitive Activity Scale (CAS), underwent a structural MRI scan, and completed a comprehensive cognitive battery. FreeSurfer was used to derive gray matter (GM) volumes from AD-related regions of interest (ROIs), and composite measures of episodic memory and executive function were obtained from the cognitive tests. Covariate-adjusted least squares analyses were used to examine the association between the Games item on the CAS (CAS-Games) and both GM volumes and cognitive composites. **Results:** Higher scores on CAS-Games were associated with greater GM volumes in several ROIs including the hippocampus, posterior cingulate, anterior cingulate, and middle frontal gyrus (p 's<.04). Similarly, CAS-Games scores were positively associated with scores on the Immediate Memory, Verbal Learning & Memory, and Speed & Flexibility domains (p 's<.02). These findings were not modified by known risk factors for AD, including age, APOE4, and family history of AD. In addition, the Total score on the CAS was not as sensitive as CAS-Games to the examined brain and cognitive measures. **Conclusions:** Engagement in cognitively-stimulating activities is associated with increased brain volume and higher cognitive test scores in middle-aged adults at risk for AD.