Abstract Title: Sleep Disruption and Risk of Preclinical Alzheimer Disease

Press Release Title: Trouble Sleeping? It May Affect Your Memory Later On

Objective: Determine if abnormal sleep in cognitively normal individuals is associated with markers of amyloid pathology.

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Background: Alzheimer Disease (AD), the most common cause of dementia, begins years before the onset of symptoms. Accumulation of amyloid-beta (Aβ) into amyloid plaques is one of the earliest steps in pathogenesis. Biomarkers of amyloid plaques are present in asymptomatic individuals with "preclinical AD." Recent evidence demonstrates a close relationship between sleep and soluble Aβ dynamics, and mouse models indicate sleep disruption causes increased amyloid plaque burden. We measured sleep with actigraphy in cognitively normal individuals to assess for any relationship between sleep disruption and preclinical AD in humans.

Design/Methods: Participants (n=100) aged 45-80 were recruited from the Adult Children Study, a cohort of which half has family history of AD. Standardized assessments at the Washington University Knight Alzheimer Disease Research Center determined participants were cognitively normal (clinical dementia rating 0). Participants wore an actigraph for 14 days to objectively measure sleep. Sleep diaries and questionnaires provided subjective sleep measures. Preclinical AD was diagnosed in 25% of participants by abnormal levels of cerebrospinal fluid Aβ-42 and/or increased retention of Pittsburgh compound B during amyloid imaging.

Results: Mean time in bed was ~8h, similar to subjective report, however mean sleep time was significantly shorter at ~6.5h, due to brief awakenings through the night. Individuals with frequent awakenings (>5/hour) were more likely to have abnormal biomarkers indicating amyloid pathology. A greater proportion of individuals with low sleep efficiency ([sleep time/time in bed] <85%) had preclinical AD, compared to those with high sleep efficiency.

Conclusions: Disrupted sleep, as measured by frequency of awakenings or sleep efficiency, is associated with amyloid pathology in a cognitively normal population. Further investigation will be required to determine the mechanisms underlying this association and whether sleep changes predict cognitive decline.

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