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Cross-sectional and longitudinal association of sleep and Alzheimer biomarkers in cognitively unimpaired adults

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Sleep abnormalities are prevalent in Alzheimer's disease, with sleep quality already impaired at its preclinical stage. Epidemiological and experimental data point to sleep abnormalities contributing to the risk of Alzheimer's disease. However, previous studies are limited by either a lack of Alzheimer's disease biomarkers, reduced sample size or cross-sectional design. Understanding if, when, and how poor sleep contributes to Alzheimer's disease progression is important so that therapies can be targeted to the right phase of the disease. Using the largest cohort to date, the European Prevention of Alzheimer's Dementia Longitudinal Cohort Study, we test the hypotheses that poor sleep is associated with core Alzheimer's disease CSF biomarkers cross-sectionally and predicts future increments of Alzheimer's disease pathology in people without identifiable symptoms of Alzheimer's disease at baseline. This study included 1168 adults aged over 50 years with CSF core Alzheimer's disease biomarkers (total tau, phosphorylated tau and amyloid-beta), cognitive performance, and sleep quality (Pittsburgh sleep quality index questionnaire) data. We used multivariate linear regressions to analyse associations between core Alzheimer's disease biomarkers and the following Pittsburgh sleep quality index measures: total score of sleep quality, binarized score (poor sleep categorized as Pittsburgh sleep quality index > 5), sleep latency, duration, efficiency and disturbance. On a subsample of 332 participants with CSF taken at baseline and after an average period of 1.5 years, we assessed the effect of baseline sleep quality on change in Alzheimer's disease biomarkers over time. Cross-sectional analyses revealed that poor sleep quality (Pittsburgh sleep quality index total > 5) was significantly associated with higher CSF t-tau; shorter sleep duration (<7 h) was associated with higher CSF p-tau and t-tau; and a higher degree of sleep disturbance (1–9 versus 0 and >9 versus 0) was associated with lower CSF amyloid-beta. Longitudinal analyses showed that greater sleep disturbances (1–9 versus 0 and >9 versus 0) were associated with a decrease in CSF Aβ42 over time. This study demonstrates that self-reported poor sleep quality is associated with greater Alzheimer's disease-related pathology in cognitively unimpaired individuals, with longitudinal results further strengthening the hypothesis that disrupted sleep may represent a risk factor for Alzheimer's disease. This highlights the need for future work to test the efficacy of preventive practices, designed to improve sleep at pre-symptomatic stages of disease, on reducing Alzheimer's disease pathology.

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