Poor Sleep Altered Circadian Rhythms and Alzheimers Disease

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Poor Sleep Altered Circadian Rhythms and Alzheimers Disease

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NIH (NIA)

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2

The project/programme is most relevant to:

Alzheimer's disease & other dementias

Keywords

Acquired Cognitive Impairment... Aging... Alzheimer's Disease... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Behavioral and Social Science... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Diagnostic Radiology... Neurodegenerative... Neurosciences... Prevention... Sleep Research

Research Abstract

? DESCRIPTION (provided by applicant): Numerous studies have identified associations between poor sleep (i.e., abnormal sleep duration, sleep fragmentation, or delayed sleep onset) and cognitive impairment and decline, and sleep is significantly disrupted among those with Alzheimer's disease (AD), the leading cause of dementia. Altered (i.e., weak, phase-delayed) circadian rest/activity rhythms also have been linked to cognitive decline, and are common among older adults with AD. Recent research in an AD mouse model demonstrated that sleep disruption promotes ß-amyloid (Aß) deposition, but little is known about the extent to which, in living humans, poor sleep and altered rest/activity rhythms may promote Aß burden and neurodegeneration, two of the core features of AD. Given effective treatments are available for poor sleep and altered rest/activity rhythms in older adults, a causal link between sleep/wake variables and AD pathology would suggest that interventions aimed at improving sleep and rest/activity rhythms might be leveraged to prevent or slow AD. In the proposed research, we will study the extent to which poor sleep and altered circadian rest/activity rhythms are prospectively associated with Aß deposition, measured in vivo by [11C]-Pittsburgh compound B (PiB) positron emission tomography (PET), neurodegeneration, measured by atrophy on structural magnetic resonance imaging (MRI), and cognitive decline in adults aged ≥ 60 years enrolled in the Baltimore Longitudinal Study of Aging (BLSA). We will also study potential mechanisms linking sleep/wake variables to these outcomes, including reduced slow-wave sleep, sleep-disordered breathing, and apolipoprotein E genotype. The BLSA is a continuous enrollment cohort study of aging that already contains repeated measures of cognition and adjudication of cognitive status, and in which a subset completes repeated MRI and PiB PET scans. Importantly, our preliminary cross-sectional data from BLSA indicate that self-reported indices of poor sleep are associated with greater ß-amyloid burden. We propose to measure poor sleep and altered rest/activity rhythms objectively in approximately 440 BLSA participants at ≥ 2 BLSA study visits using wrist actigraphy. We will also conduct in- home polysomnography (PSG) among subjects who are cognitively normal at baseline and complete PiB PET and MRI. In addition to standard methods for actigraphic data analysis, which involve averaging across intervals to obtain estimates of sleep/wake variables, we will employ novel approaches that capitalize on the variability in raw actigraphy and PSG data to identify data-driven signatures of poor sleep and altered rest/activity patterns. The availability of repeated neuroimaging measures of ß-amyloid and atrophy, and cognitive assessment make the BLSA an excellent, cost-effective resource for this research. Results could significantly advance our understanding of the role of poor sleep and altered rest/activity rhythms in the development of AD, and could have critical implications for interventions aimed at preventing or slowing AD.

Lay Summary

PUBLIC HEALTH RELEVANCE: Poor sleep (i.e., abnormal sleep duration, sleep fragmentation, or delayed sleep onset) and altered circadian rest/activity rhythms have been linked to cognitive impairment and decline, but it is unclear whether these sleep/wake variables promote Alzheimer's disease (AD). In the proposed research, we will collect wrist actigraphy data and perform polysomnography among participants in the Baltimore Longitudinal Study of Aging, a continuous enrollment cohort study of aging that already contains repeated measures of cognition with adjudication of cognitive status, and repeated neuroimaging measures of ß-amyloid and atrophy. This research will advance our knowledge of the role of sleep/wake variables in the course of AD and evaluate whether poor sleep and altered rest/activity rhythms may be modifiable risk factors that might be targeted by interventions to prevent or slow AD progression.

Further information available at:

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Investments > €500k

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United States of America

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Alzheimer's disease & other dementias

Years:
2016

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