Apnea and local sleep: Mechanism and intervention in preclinical Alzheimers

https://neurodegenerationresearch.eu/survey/apnea-and-local-sleep-mechanism-and-intervention-in-preclinical-alzheimers/

Principal Investigators

BENDLIN, BARBARA BRIGITTA

Institution

UNIVERSITY OF WISCONSIN-MADISON

Contact information of lead PI
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USA

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Apnea and local sleep: Mechanism and intervention in preclinical Alzheimers

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NIH (NIA)

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1

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)... Brain Disorders... Clinical Research... Clinical Research - Extramural... Dementia... Lung... Neurodegenerative... Neurosciences... Prevention... Sleep Research

Research Abstract

? DESCRIPTION (provided by applicant): Alzheimer’s disease (AD) is reaching epidemic proportions, and in the absence of effective treatments, prevention strategies are needed. Accumulating evidence suggests that sleep plays an important role in regulating amyloid deposition, a hallmark of AD pathology. Both sleep disturbance and obstructive sleep apnea (OSA), a disorder characterized by frequent pauses in breathing during sleep and leading to hypoxemia and sleep fragmentation, are highly prevalent in AD and are associated with progression of AD pathology. Work from our group and others has shown that sleep disruption is associated with increased amyloid deposition in preclinical AD. Our group has pioneered the use of high density EEG (hdEEG, 256 channels) to demonstrate that sleep is not uniform throughout the brain, but is locally regulated and related to plastic changes during waking; different parts of the brain “”fall asleep”” at different times, such that certain brain regions may experience chronic deficits in local sleep. Further, this phenomenon has been shown by our group to occur in a variety of neuropsychiatric disorders. Importantly, we have recently shown that OSA is associated with a local deficit in sleeping brain activity in the posterior cingulate region, in precisely the same area where peak amyloid deposition occurs in AD, suggesting a mechanism by which OSA exacerbates AD pathology. Our overarching research objective is to identify AD risk factors and mechanisms that can be modified in midlife to prevent or delay progression to AD. Sleep provides such a target. The 3 Specific Aims of this study are to determine over a 2 year period (1) the association of OSA with amyloid deposition and neural damage; (2) whether OSA treatment decreases progression of AD pathology and memory loss; and (3) the effect of local sleep deficits in the cingulate cortex on AD pathology and memory loss. The proposed study will clarify which aspects of OSA-apnea/hypopnea index, hypoxemia or sleep fragmentation-contribute to AD pathology and tests the novel hypothesis that OSA-related local sleep deprivation mediates AD progression. This study will add comprehensive imaging, sleep and activity recordings including hdEEG and amyloid-PET collection to the extensive battery of data already being collected in participants enrolled in the Wisconsin Alzheimer’s Disease Research Center, comprising a cohort of asymptomatic, middle-aged subjects (50-65 yrs) at risk for AD based on parental family history. The proposed study provides an unprecedented opportunity to assess the effects of OSA, sleep features, and treatment in a well characterized and longitudinally followed group of participants at increased risk for AD. Results will also provide valuable preliminary data for a large-scale pragmatic clinical trial to test the value of OSA screening and treatment to prevent progression of AD pathology in at-risk individuals.

Lay Summary

PUBLIC HEALTH RELEVANCE: The goal of this research is to elucidate mechanisms by which obstructive sleep apnea leads to progression of Alzheimer’s disease (AD) pathology, and determine whether treatment of apnea can slow the progression of amyloid deposition, neural damage and memory loss during the preclinical phase of AD in at-risk adults. The results of this work are expected to provide insight into mechanisms involved in AD development and are critical to informing the design of a larger scale trial of apnea treatment as a preventative measure for AD.

Further information available at:

Types:

Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias

Years:
2016

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