Perspective: Home-based Sleep Intervention for Dementia Prevention

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Abstract

Dementia poses a significant and escalating public health challenge, necessitating effective preventative strategies. Age-related sleep disturbances, particularly loss of slow-wave sleep (SWS), are linked to an increased risk of dementia. This study employs a two-stage approach to develop a biomarker of cognitive decline from sleep parameters using machine learning and investigate a non-pharmacological intervention in adults aged 50 and older. We evaluate the efficacy of home-based closed-loop auditory stimulation (CLAS), which enhances slow oscillations using synchronized auditory cues delivered using wearable EEG technology. We aim to assess the potential of CLAS, through improved sleep quality, to delay the onset of cognitive impairment, potentially offering a scalable intervention for dementia prevention.

Keywords: sleep; dementia; mild cognitive impairment (MCI); closed-loop auditory stimulation (CLAS); slow-wave sleep (SWS); polysomnography (PSG); machine-learning; EEG.

Introduction

Dementia represents a heterogeneous group of conditions marked by cognitive impairments, with Alzheimer's disease identified as the predominant etiological factor (Livingston et al., 2024). Around the world, it is estimated that 57 million people are living with dementia, a number projected to increase to 150 million by the year 2050 (World Health Organization (WHO), 2025; Nichols et al., 2022). Currently, there is no cure; however, there are ways to slow the progress of cognitive decline, and improve the quality of life of those living with dementia (World Health Organization (WHO), 2019; Herrup, 2021). The largest known risk factor is age. One of the key elements of a dementia diagnosis is impairment of daily functioning (Livingston et al., 2024). When a person experiences symptoms, such as memory loss, but the full diagnosis criteria are not met, one can be diagnosed with mild cognitive impairment (MCI) (Petersen & Negash, 2008). Five years after an MCI diagnosis, dementia is several times more likely to occur (Tuokko et al., 2003). This period is crucial for early identification to make the prevention of future decline possible. Previously, MCI was often detected using questionnaires such as the Montreal Cognitive Assessment (MoCA) by Nasreddine et al. (2005), but recently is more accurately predicted with ACE-III test by Hsieh, Schubert, Hoon, Mioshi, and Hodges (2013). It is also possible to use EEG to independently assess the severity of impairment (Rutkowski et al., 2023; Wijaya, Setiawan, Ahmad, Zakaria, & Othman, 2023). This study proposes a two-stage methodological framework. Initially, machine-learning algorithms will be employed to identify correlations between sleep stage pattern sequences extracted from four-channel overnight electroencephalography (EEG) recordings conducted within a controlled university sleep laboratory, and cognitive function evaluated by the ACE-III test (Hsieh et al., 2013). Cognitive function will first be directly measured (e.g., via neuropsychological tests), then inferred from sleep EEG features after machine-learning model development. Subsequently, these findings will be translated to a home-based setting utilizing wearable EEG devices. This approach will facilitate the application of closed-loop auditory stimulation for personalized sleep intervention.

Sleep and dementia: Optimal sleep duration is essential for cognitive function, with both insufficient and excessive sleep associated with adverse effects on brain health. Specifically, studies have demonstrated a bimodal relationship between sleep duration and dementia risk, wherein both sleep durations below six hours and exceeding ten hours are implicated as significant risk factors (Sabia et al., 2021; Xu, Tan, Zou, Cao, & Tan, 2020). Epidemiological studies have established an association between sleep disorders, such as insomnia and sleep-disordered breathing, and an increased risk of dementia (Shi et al., 2018). A critical component of restorative sleep, slow-wave sleep (SWS), defined by slow wave activity (SWA) below 4 Hz and corresponding to the $N3$ stage, has been identified as a key factor in this relationship. Specifically, the loss of SWS correlates with a heightened risk of dementia (Himali et al., 2023). Mechanistically, SWS is thought to facilitate the clearance of $\beta-$amyloid from the brain (Xie et al., 2013), and its disruption can lead to rapid $\beta-$amyloid accumulation (Ju et al., 2017). Moreover, genetic factors, such as the APOE $\varepsilon 4$ allele, which predisposes to Alzheimer's disease, have been shown to influence SWS levels, potentially explaining, at least in part, the observed link between SWS and dementia (Himali et al., 2023). Old age is associated with a deterioration in both quantity and quality of sleep, and this is reflected in an increased number of awakenings and a decrease in SWS and REM (Edwards et al., 2010). These findings suggest that EEG sleep data could serve as a biomarker of dementia severity, which has been previously demonstrated (Ye et al., 2023). SWS also plays a crucial role in memory consolidation through hippocampal reactivation, which leads to strengthening of neocortical representations (Walker, 2009).

To mitigate the risk of cognitive decline, it is important to address sleep disorders and get enough rest (Lam, Kong, & Naismith, 2024). With new methods, it is also now possible to increase the amount of SWS with a targeted intervention both in a healthy population (Diep et al., 2020) and in patients with Alzheimer's disease (Van den Bulcke et al., 2023).

Closed-loop auditory stimulation: Closed-loop auditory stimulation (CLAS) facilitates the modulation of neural oscillations by delivering auditory stimuli synchronized with specific phases of brain waves. This technique enables the targeted enhancement of slow oscillations (SOs) during sleep through the real-time detection of SO peaks and the subsequent presentation of temporally coupled auditory stimuli (Ngo, Martinetz, Born, & Mölle, 2013). The efficacy of SO entrainment via CLAS is critically dependent on the precise temporal alignment of auditory stimuli with the detected SO peaks (Navarrete et al., 2020). Jourde, Merlo, Brooks, Rowe, and Coffey (2024) employed magnetoencephalography (MEG) to localize the origin of slow oscillations (SOs) elicited by closed-loop acoustic stimulation (CLAS), identifying the orbitofrontal cortex as the primary source. The propagation of SOs from this region, and the predictive power of its phase state for CLAS efficacy, validate the use of frontal electrode synchronization. Nevertheless, the reported discrepancy between EEG-derived phase and local up states underscores the need for improved stimulation timing. This may require either more precise localization of relevant neural activity or the development of alternative neurophysiological markers.

Machine learning (ML) techniques offer the potential to identify individualized signatures within brain signals. This capability has been applied to phase estimation in CLAS systems (Lu et al., 2023) and, more recently, to dementia onset prediction through the implementation of signature path and Riemannian geometry classification (Rutkowski, 2025). Optimal stimulation efficacy requires accurate real-time sleep stage classification to specifically target the $N3$ stage. This can be accomplished using automated real-time algorithms (Patanaik, Ong, Gooley, Ancoli-Israel, & Chee, 2018), or by employing advanced techniques such as signature path analysis, which we propose to implement, drawing inspiration from the work of Rutkowski (2025). The second stage of this study aims to evaluate the feasibility and efficacy of home-based CLAS for sleep intervention, utilizing wearable EEG, and to develop an application and machine learning algorithm for individualized stimulation.

The subsequent methods section outlines the study design, participant selection, intervention protocol, and data analysis procedures employed to assess the impact of this intervention on sleep and cognitive function.

Methods

This study targets individuals aged 50 years and older. This age range was selected to capture the heterogeneity in SWS quantity, which is known to decline with age (Li, Vitiello, & Gooneratne, 2022), thereby facilitating robust comparative analysis. This demographic supports the development of an EEG sleep-based biomarker for the progression from healthy aging to MCI and dementia. Cognitive function will be assessed using the ACE-III (Hsieh et al., 2013) before enrollment. Following informed consent, obtained under a protocol approved by the [masked for review] Institutional Ethical Committee, eligible participants will undergo an initial overnight polysomnography (PSG) study in a sleep laboratory (Rundo & Downey III, 2019). This study incorporates closed-loop auditory stimulation (CLAS), as detailed below. This PSG session will diagnose potential sleep disorders, predict cognitive decline or mild cognitive impairment (MCI) using a machine learning (ML) model, and establish a baseline for comparison with home-based electroencephalography (EEG) recordings, all of which may influence dementia risk. Following the PSG, participants receive a wearable EEG headband and instructions on its use at home, along with a corresponding application, for two consecutive nights. Daily morning questionnaires are administered to assess subjective sleep quality. One of the two nights is randomly assigned as a control condition, employing sham stimulation.

ML models will be employed to predict ACE-III scores based on measured sleep characteristics, including sleep stage distribution, sleep and REM latencies, wake after sleep onset, and slow-wave sleep (SWS) quantity. These predicted ACE-III scores, correlated with sleep parameters, will inform the individualized planning of CLAS delivery. We hypothesize that EEG sleep data can serve as a predictive biomarker for dementia, as reflected in estimated ACE-III scores, and subsequently guide personalized CLAS intervention protocols. We plan to leverage pretrained models (e.g., those from iEEG) to learn robust representations, offering a computationally lightweight alternative to end-to-end methods while potentially achieving comparable or superior decoding performance (Chau et al., 2024).

CLAS will deliver 50 ms pink noise bursts (55 dB) synchronized with the up-phase of slow waves ($0.5 \sim 4$ Hz, $> 40\mu$V), detected online from the FPz electrode during $N3$ sleep. To avoid awakening, stimulation is withheld when arousal is detected. Real-time slow wave estimation, employing a $30-$second window with a minimum of five slow waves, adjusts stimulation frequency to match endogenous activity, with a hardware delay compensation. Sham stimulation, used during the control night, will be delivered out-of-phase and at 1.5 times the endogenous frequency. Individual hearing thresholds will be accounted for in sound level calibration.

Conclusions

This study proposes home-based Closed-Loop Acoustic Stimulation (CLAS) to improve sleep in at-risk older adults, aiming to optimize personalized sleep interventions and advance EEG biomarkers for dementia progression. We hypothesize this tailored approach offers a scalable mitigation strategy for the global dementia burden, with long-term impacts to be assessed longitudinally.

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