Extended Summary

1. Description of the Project

Project Overview

The project *Objective Sleep-Wake measures and COgnitive Function: associations and mediating mechanisms using Artificial Intelligence methods* (OSCOFAI) was designed to investigate the relationship between objectively measured sleep-wake patterns and cognitive function, as well as to identify the biological mechanisms that may explain this relationship. The project was implemented within the framework of the Greece 2.0 National Recovery and Resilience Plan under the Basic Research Financing Action (Sub-action II: Funding Projects in Leading-Edge Sectors). OSCOFAI was coordinated by the National and Kapodistrian University of Athens, Medical School, Aiginition Hospital, and conducted in collaboration with the Department of Informatics and Telecommunications, Biomedical Data Science – Bioinformatics group, embedded within the ongoing longitudinal ALBION cohort study.

By combining high-quality clinical assessments, neuropsychological testing, brain imaging, cerebrospinal fluid (CSF) analysis, and wearable activity monitoring (actigraphy), the project addressed critical gaps in our understanding of how sleep patterns and daily activity rhythms relate to cognitive aging and early dementia risk. A central innovation of OSCOFAI was the application of advanced signal processing, machine learning, and artificial intelligence (AI) methods to extract clinically meaningful information from continuous activity recordings, extending beyond the simple sleep summaries typically provided by commercial devices.

The project developed a comprehensive analytical framework designed to operate reliably with moderate sample sizes and unequal group distributions typical of clinical research—a common challenge in studies of specialized patient populations. Over the course of 22 months (March 2024–December 2025), more than 75,000 separate machine learning experiments were conducted to systematically identify the most informative patterns in activity data and the most reliable prediction methods. All scientific objectives, work packages, milestones, and deliverables were completed as planned.

Main Objectives

The main goal of OSCOFAI was to advance understanding of how objectively measured sleep-wake characteristics relate to cognitive function and cognitive decline, and to translate this knowledge into practical tools that clinicians can use and trust. The specific objectives were:

1. To examine associations between objective sleep-wake measures derived from wrist-worn activity monitors and cognitive performance, both at a single point in time and over a two-year follow-up period.

2. To develop and apply advanced signal processing and machine learning methods for extracting informative features from continuous activity recordings—capturing the full

richness of 24-hour rest-activity patterns rather than relying solely on conventional sleep statistics.

3. To investigate whether biological markers—including proteins in cerebrospinal fluid, brain imaging measures, and metabolic biomarkers—help explain the pathway from disrupted sleep to cognitive decline.

4. To design and implement an "explainable AI" (AI that reveals the reasoning behind its predictions rather than acting as an opaque "black box") clinical decision support tool capable of predicting cognitive impairment risk using activity data. Crucially, this tool was designed to be transparent: rather than providing predictions as uninterpretable outputs, it shows clinicians which features of a patient's sleep-wake pattern drive the risk assessment, enabling them to validate the AI's reasoning against their own clinical expertise.

5. To disseminate the project results to the scientific community and broader public through conferences, publications, and accessible online resources.

Key Activities

To achieve these objectives, OSCOFAI was structured into six interrelated work packages (WPs), each addressing a core component of the project.

WP1: Actigraphy-based sleep-wake data and cognitive function focused on standardizing activity-derived sleep measures and examining their associations with cognitive performance. An important emphasis was placed on sleep continuity, fragmentation, and night-to-night variability rather than solely on average sleep duration, recognizing that *how well* someone sleeps matters as much as how long.

WP2: Advanced AI analysis of actigraphy data involved developing a comprehensive computational pipeline that processes raw activity recordings and extracts meaningful patterns at multiple levels, from overall daily rhythms to minute-by-minute fluctuations. Multiple complementary approaches were used, including mathematical models of circadian rhythms and wavelet analysis (a technique that reveals patterns occurring at different time scales, from minutes to hours). A key innovation was developing methods that work robustly even when the number of participants is modest and when one group (such as cognitively impaired individuals) is smaller than another, challenges that often undermine machine learning in clinical settings.

WP3: Mediating biological mechanisms examined whether biological pathways help explain the connection between sleep-wake patterns and cognition. Both hypothesis-driven analyses (testing specific proteins known to be relevant to brain health) and data-driven approaches (discovering new patterns in hundreds of proteins simultaneously) were employed. This work package sought to answer the question: *why* does disrupted sleep relate to cognitive decline?

WP4: Development of an explainable AI Advisor tool translated the analytical findings into a practical clinical decision support system. This tool processes activity data from standard monitoring devices, predicts cognitive impairment risk, and, critically, provides transparent explanations of its predictions using interactive visualizations. Clinicians can see exactly which aspects of a patient's sleep-wake pattern (such as reduced daytime activity or fragmented rest periods) are contributing to the risk score, allowing them to validate the AI's reasoning and explain findings to patients with confidence.

WP5: Dissemination and communication included the development of a project website, preparation of informational materials, engagement with patient organizations, and presentation of results at international scientific conferences.

WP6: Project management ensured timely coordination, monitoring of progress, and successful completion of all deliverables through regular team meetings and continuous oversight.

No major deviations from the initial scientific objectives occurred. Minor methodological refinements, such as prioritizing cerebrospinal fluid protein analysis over blood-based markers, enhanced the scientific relevance and innovation of the project without compromising its goals.

Deliverables

The main deliverables of OSCOFAI included:

- A standardized dataset of sleep–wake measures derived from wrist-worn activity monitors (actigraphs).
- Analytical reports documenting associations between objective sleep–wake measures and cognitive function, both at a single time point and over a two-year follow-up period.
- A comprehensive computational pipeline for analyzing activity recordings, including modules for extracting meaningful patterns, selecting the most informative features, and evaluating prediction models.
- AI predictive models linking activity features to mild cognitive impairment (MCI), cognitive decline trajectories, and biological markers.
- An explainable AI-based clinical decision support tool ("AI Advisor") for assessing cognitive decline risk.
- Dissemination materials and four abstracts presented at major international conferences (the Alzheimer's Association International Conference and the International Conference on Alzheimer's and Parkinson's Diseases), including three oral presentations and one poster.

All deliverables directly contributed to the achievement of the project objectives by enabling robust analysis, mechanistic insight, and translation of findings into clinically relevant tools. The project website (https://oscofai-project.github.io/) serves as a central access point for information on project goals and outcomes.

2. Conclusions

Results

OSCOFAI generated a comprehensive set of scientific results that substantially advance current understanding of sleep, daily activity rhythms, and cognitive aging.

Traditional statistical analyses demonstrated that objectively measured sleep continuity and regularity, particularly nocturnal awakenings, time to fall asleep, and night-to-night variability, are more strongly associated with cognitive function than simple average sleep duration. Following participants over time showed that greater sleep fragmentation and irregularity predict faster cognitive decline, especially in memory and language domains. These findings reinforce that sleep *quality* matters as much as sleep *quantity* for brain health.

Machine learning analyses confirmed that continuous activity recordings contain rich and clinically meaningful information beyond what conventional sleep summaries capture. The best-performing models correctly identified approximately 70% of individuals with mild cognitive impairment (avoiding missed cases) while also correctly classifying about 80% of cognitively healthy individuals (avoiding false alarms), a level of performance achieved using only a week of wrist-worn activity data, without any invasive tests. This balance between catching true cases and avoiding unnecessary concern is particularly important for a potential screening tool. Remarkably, simple interpretable models using few carefully selected features (e.g. age, the contrast between day and night activity levels, and peak daytime activity intensity) performed nearly as well as complex algorithms analyzing hundreds of features. This finding is important because simpler models are easier for clinicians to understand and trust. The analyses also revealed that activity patterns occurring at very short time scales (3–12 minutes), essentially, micro-fragmentation of activity, were particularly informative for both current diagnosis and prediction of future decline.

Mediation analyses provided novel insights into the biological mechanisms linking disrupted sleep-wake patterns to cognitive decline. A key finding was that total tau protein in cerebrospinal fluid, a marker of general neuronal injury, consistently helped explain the connection between disrupted daily rhythms and subsequent mild cognitive impairment, accounting for approximately 27–36% of this relationship. This suggests that poor circadian rhythm consolidation may impair the brain's natural waste-clearance system (the "glymphatic system," which operates primarily during sleep), leading to accumulation of harmful proteins. Importantly, this effect required temporal proximity between measurements: when we included biological samples collected more than one year from the activity recording, the effect disappeared, suggesting a true biological relationship rather than a statistical artifact. Other biomarkers, including those specific to Alzheimer's disease pathology, did not show consistent mediating effects, indicating that the relevant pathway operates through general neuronal health rather than disease-specific mechanisms.

The AI Advisor tool demonstrated the feasibility of translating research findings into a practical clinical support system. The tool employs a “dual archetype” approach: clinicians can choose between highly accurate complex models when maximum discrimination is needed, or simpler transparent models when understanding the reasoning is paramount. The system generates interactive visualizations, including decision plots showing how each feature pushes the risk score up or down, and circadian rhythm diagrams showing how a patient’s daily pattern compares to healthy norms, enabling clinicians to see exactly why the AI reached its conclusion. This transparency addresses a critical barrier to AI adoption in healthcare: the reluctance to trust “black box” systems that cannot explain their recommendations.

Overall, the project met all its planned objectives. Where initial hypotheses were not confirmed, such as the expectation that certain protein signatures associated with sleep would also explain cognitive effects, these null findings provided valuable clarification, distinguishing between biomarkers that *correlate with* sleep problems versus those that actually *transmit* their effects on cognition.

Impacts and Added Value

The scientific impact of OSCOFAI lies in its integration of objective sleep measurement, longitudinal cognitive assessment, biological marker profiling, and advanced AI methodologies within a single coherent framework. The project contributes robust evidence that sleep fragmentation and circadian disruption are early and potentially modifiable markers of cognitive decline, detectable before clinical symptoms become apparent.

From a societal and public health perspective, OSCOFAI underscores sleep as a modifiable lifestyle factor with potential for early intervention. Unlike genetic risk factors or age, sleep habits can be improved through behavioral changes, environmental modifications, or treatment of underlying sleep disorders. The findings support the development of preventive strategies aimed at improving sleep regularity and quality to help maintain cognitive health during aging, a message with direct relevance to millions of older adults and their families.

Technologically, the project delivers methods that can be applied to other wearable sensor data and clinical domains. The computational pipeline’s ability to extract reliable insights from moderate-sized studies with unequal groups addresses a common bottleneck in clinical research, where large, balanced datasets are often unavailable. The explainable AI framework enhances trust, interpretability, and clinical usability, addressing a key barrier to AI adoption in healthcare settings where understanding “why” matters as much as knowing “what.”

Looking forward, the expected long-term impacts include improved early identification of individuals at risk for cognitive decline, support for personalized preventive approaches, and the potential for at-home monitoring solutions using consumer wearable devices or smartphones. The biological findings suggesting a pathway through impaired brain waste clearance point toward specific intervention targets that could be tested in future clinical trials.

Collectively, OSCOFAI provides significant added value by bridging fundamental research, advanced analytics, and clinical application. The project demonstrates that objective, non-invasive, and cost-effective monitoring of daily activity patterns can provide meaningful information about brain health, laying the groundwork for future large-scale studies and real-world implementation in clinical practice and public health programs.

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