The Impact of Sleep on Cognitive and Mental Health Outcomes in Older Adults: A Longitudinal Study of Circadian Rhythms and Early Cognitive and Emotional Change

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Thesis Portfolio Abstract

Sleep disturbances are common in later life and have been linked to poor psychological health and cognition. However, findings remain unclear regarding which sleep characteristics and cognitive domains are most affected, and how these relationships change over time. Genetic vulnerability from apolipoprotein E ε4 (APOE ε4) carrier status, a well-established genetic risk factor for Alzheimer's disease, may further influence these associations.

A systematic review explored associations between sleep characteristics and visuospatial memory and spatial navigation in adults over 50 years. An empirical longitudinal study then examined associations between subjective and objective actigraphy-derived sleep measures, cognitive outcomes, and psychological wellbeing over time, and whether relationships differed according to APOE ε4 status.

The systematic review revealed predominantly null findings, with substantial heterogeneity across measures and study designs. However, some evidence suggests that sleep continuity and aspects of sleep architecture are related to visuospatial and navigational performance. The empirical study found no consistent longitudinal associations between changes in sleep parameters and cognitive performance, and no evidence that APOE ε4 status moderated sleep-cognition relationships. In contrast, poorer subjective sleep quality was significantly associated with increased depressive symptoms, and poorer objective sleep efficiency was associated with increased depressive and anxiety symptoms over time.

Overall, findings suggest that sleep characteristics may be more closely related to psychological wellbeing than cognitive changes in cognitively healthy older adults, highlighting sleep as a potentially modifiable factor for supporting mental health in aging populations. Findings should be interpreted in the context of measures and methodological limitations discussed in this thesis.

Keywords: sleep, psychological wellbeing, cognition, ageing, APOE ε4, longitudinal

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Chapter One: Introduction to the Thesis Portfolio

Sleep disturbances are highly prevalent in later life, with an estimated 20-40% of older adults reporting significant sleep difficulties (Schubert et al., 2002). Age-related changes in sleep are well established, including reductions in sleep efficiency, increased sleep fragmentation, and decreased sleep duration (Mander et al., 2017). While some degree of sleep changes may be considered normative in older adulthood, growing evidence suggests that sleep difficulties may have important implications for psychological wellbeing (Baglioni et al., 2016; Scott et al., 2021) and cognitive health, particularly memory performance and markers of dementia risk (Musiek et al., 2022; Wu et al., 2017).

A substantial body of research has demonstrated associations between poorer sleep and greater mental health difficulties, namely increased symptoms of depression and anxiety (Taylor et al., 2005). Evidence further suggests that the relationship between sleep and mental health is bidirectional, meaning that sleep problems can contribute to the development or worsening of affective symptoms, and in turn, psychological difficulties can disrupt sleep (Koffel & Watson, 2009; Komada et al., 2009). This is clinically relevant for aging populations, as both sleep disturbance and affective symptoms are common and are independently associated with a reduced quality of life (Tsaras et al., 2022) and increased risk of cognitive impairment (Correa-Muñoz et al., 2023; Guan et al., 2020). Taken together, these findings suggest that sleep may play an important role within the broader relationship between psychological wellbeing and cognitive health in later life.

The increasing interest in cognitive ageing and dementia risk further highlights the clinical importance of understanding these relationships, especially as prevalence rates of dementia are projected to triple by 2050 (Nichols et al., 2022), with Alzheimer's disease (AD) representing the most common form of dementia and the leading neurodegenerative disorder worldwide (Scheltens et al., 2021). These projections raise important questions regarding the accurate and early detection of AD, particularly during preclinical stages when interventions may be most effective.

Both cognitive changes, especially in memory and spatial processing (Liguori et al., 2020; Veitch et al., 2021), as well as affective symptoms of mental health (Da Silva et al., 2013), are increasingly recognised as early features of AD and often emerge years before a formal diagnosis.

Genetic vulnerability also seems to play a critical role within this context. The apolipoprotein E ε4 (APOE ε4) allele is the strongest common genetic risk factor for late-onset AD (Corder et al., 1993; Farrer et al., 1997). Consequently, findings suggest that APOE ε4 carriers both may experience more sleep disruptions (Drogos et al., 2016), as well as higher levels of anxiety and depression (Holmes et al., 2016) compared to non-carriers. This highlights the importance of examining how genetic risk may interact with potentially modifiable factors, such as sleep and mental health in ageing populations.

Despite findings indicating a high prevalence of sleep disturbances, cognitive change, and poorer mental health in later life, the nature and clinical significance of their interrelationships remain under-researched, particularly from a longitudinal perspective. Although research has examined sleep in relation to cognitive or psychological wellbeing outcomes in later life, these domains are rarely investigated together, particularly alongside genetic risk, limiting our understanding of how these factors interact over time. Longitudinal studies integrating sleep, psychological wellbeing, cognitive outcomes, and genetic risk are therefore needed to improve understanding of how cognitive decline and dementia risk develop over time.

This thesis aims to address these gaps in research by examining the associations between sleep characteristics, mental health, and cognitive functioning in older adults, while keeping a particular focus on the moderating role of the APOE ε4 genotype. By using a longitudinal design and focusing on cognitive domains that are sensitive to early neurodegenerative change, this thesis seeks to clarify whether sleep disturbances represent a meaningful marker of risk or potentially modifiable factor in later life. The hope is that this will contribute to a clearer understanding of pathways to cognitive decline and poorer mental health and inform future research on the early identification and intervention approaches within the field of clinical psychology.

Chapter Two: Systematic Review

Prepared for submission to The Journal of Sleep Research

Author Guidelines can be found in Appendix A

Systematic Review of Sleep Characteristics and their Association with Spatial Memory or Navigation Performance in Older Adults

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Abstract

Understanding whether sleep relates to visuospatial memory and spatial navigation, abilities central to independence and vulnerable in early cognitive decline, has implications for the early identification and intervention of ageing populations. However, this area remains relatively under-researched, and existing findings are mixed. This review aimed to synthesise evidence on associations between sleep characteristics and visuospatial and spatial navigation performance in adults aged ≥50 years.

Studies were screened using PRISMA guidelines and quality was appraised using the Mixed Methods Appraisal Tool (MMAT). Findings were synthesised using a narrative approach due to heterogeneity in study design, sleep measures, and cognitive outcomes.

Seventeen studies met inclusion criteria. Most studies reported null findings, however, a small number of studies found associations between objective sleep characteristics, including sleep architecture and sleep regularity, and visuospatial and spatial navigation performance. Findings for spatial navigation were more variable, and no single sleep parameter consistently predicted outcomes across studies.

The evidence suggests that sleep is not a consistent predictor of visuospatial memory or spatial navigation in older adults. However, specific objective features of sleep, such as sleep continuity and sleep architecture, may be relevant for certain aspects of spatial cognition.

Variation in study methods makes it difficult to draw causal conclusions. Future high-quality research, using longitudinal designs and integrating both subjective and objective sleep measures, while also considering individual vulnerability factors, such as cognitive risk, is needed to better understand the clinical importance of sleep for visuospatial cognition in later life.

Keywords: sleep, visuospatial, spatial navigation, ageing, cognitive performance.

Introduction

Visuospatial memory and spatial navigation are key cognitive functions that support independence in later life, such as finding one's way in familiar and unfamiliar environments, remembering the location of objects, navigating shops or public transport, and moving safely around the home and community. These abilities are known to decline as part of normal ageing and are particularly affected in the early stages of cognitive impairment (Laczó et al., 2018; Wams et al., 2017). These difficulties in cognition are clinically relevant because they are linked to reduced quality of life, increased cost of care, as well as higher risks of accidents, and mortality for older adults (Klepac et al., 2008).

At the same time, sleep undergoes significant age-related changes, including reduced sleep efficiency, increased fragmentation, and alterations in sleep architecture (Dzierzewski et al., 2018; Klerman et al., 2013; Ohayon et al., 2004), as well as an overall reduction in sleep quality (Hoch et al., 1994), all of which in turn may have negative impacts on cognitive functioning (André et al., 2019; Blackwell et al., 2011, Dzierzewski et al., 2018; Kaneshwaran et al., 2019). In a meta-analysis of 35 samples (*n* = 97,264), Lo et al. (2016) found that reduced sleep quality significantly impaired cognitive performance across multiple domains in older adults, with short sleep linked to executive function and verbal memory deficits and long sleep linked to poorer overall cognitive performance.

Sleep supports hippocampal functioning, which underpins spatial navigation and visuospatial memory, by consolidating newly learned spatial information and refining the brain's internal maps of the environment (Bódizs et al., 2008; Nguyen et al., 2013; Noack et al., 2017). As the hippocampus is particularly vulnerable in ageing and early Alzheimer's disease, disrupted sleep may contribute to spatial cognitive difficulties in later life (Braak et al., 1993; Gómez-Isla et al., 1996; Wang et al., 2003; Whitwell et al., 2007; Braak and Del Tredici, 2015, as cited in Michallat-Bragg et al., 2025).

Most existing sleep-cognition research and systematic reviews in older adults have typically examined global cognition or memory (Bubu et al., 2020; Crowley et al., 2024; Lo et al., 2016, Rana et al., 2017), with less

attention given to visuospatial memory and spatial navigation. This represents an important gap, as spatial cognition may be a sensitive marker of early functional decline and neurodegenerative change. To our knowledge, no systematic review has synthesised evidence linking both subjective and objective sleep characteristics with spatial memory and navigation outcomes in adults ≥50 years. This review therefore aims to address this gap by synthesising and critically evaluating the available evidence.

Methods

Protocol Registration

This review was developed according to the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) Statement (Moher et al., 2009) and was registered with the International Prospective Register of Systematic Reviews (PROSPERO ID: CRD420251136732).

Search strategy

A systematic search was conducted by the primary author (RT) to identify all studies evaluating the associations between sleep characteristics and spatial memory/navigation performance in adults aged ≥50 years. Electronic databases PsycINFO, PubMed, and SCI (Science Citation Index) were searched from inception to October 2025, using terms for sleep, visuospatial/spatial cognition, and older adulthood. The following terms search terms were used on the databases: (("sleep") AND ("Rey–Osterrieth complex figure" OR "spatial memory" OR "visuospatial memory" OR "spatial navigation" OR "place memory") AND ("older adults" OR elderly OR "aging population" OR "late life")). Manual searches also looked at reference lists of articles included, systemic reviews, or meta-analysis relevant to the review topic.

Eligibility Criteria

Studies were included if participants were aged ≥50 years, defined either by a minimum age threshold or a mean sample age of at least 50 years. This threshold aligns with research examining sleep–cognition associations that capture an early window of cognitive vulnerability when pre-clinical age-related changes begin to emerge and sleep disturbances become more common, potentially influencing later cognitive decline (Gildner

et al., 2014; Legault et al., 2023; Lo et al., 2016; Scarlet et al., 2020). Studies with mixed-age samples were included if results were reported separately for older participants or if the mean age met eligibility criteria. All searches were limited to peer reviewed articles that were published in English.

Studies were excluded if participants had a diagnosed neurodegenerative condition at baseline, including dementia or related disorders, in order to ensure that any observed associations between sleep and cognition were likely due to sleep-related processes rather than driven by underlying or comorbid diseases. Studies focusing exclusively on children, adolescents, or young adults were excluded.

Screening and Study Selection

Following the database search, all records were imported into reference management software Zotero and then imported into Rayyan for screening. The initial search yielded 230 records, of which 42 duplicates were identified and removed. A total of 188 titles and abstracts were then screened for eligibility by the primary author. A second reviewer (EH) independently screened 100% of titles and abstracts, blind to the primary author's decision, and disagreements were discussed and resolved through consensus (*n* = 8 conflicts).

Full-text screening was then conducted for 38 articles assessed as potentially eligible. The second reviewer independently screened 100% of full-text articles, blind to the primary author's decisions. Following discussion and resolution of discrepancies, 17 studies met inclusion criteria and were included in the review. Five articles remained classified as uncertain at full-text screening due to unextractable data. The study selection process is presented in a PRISMA flow diagram (see Figure 1).

Data Extraction

This systematic review employed the framework for data extraction and synthesis as outlined on the Guidance on the Conduct of Narrative Synthesis Reviews (Popay et al., 2006). Data was extracted by the primary researcher, and the characteristics of the study were recorded by author, year of publication, study design, sample size, mean age of participants, sleep exposure measures, cognitive outcome measures, type of effect tested and, if available, effect size and/or p-value. This method of synthesis was used given the heterogeneity of

sleep assessment methods, cognitive outcome measures, and study designs. Quality assessment was conducted prior to data synthesis, in accordance with the guidance.

Quality Assessment

The Mixed Methods Appraisal Tool (MMAT; Hong et al., 2018) was used to assess the quality of both randomised controlled trials (RCT's) and non-randomised trials included in the analysis. This tool was selected as it allows quality appraisal across heterogeneous study designs within a single framework. This was particularly relevant in this review, which included randomised, observational, longitudinal and experimental studies, that would not have been comparably assessed using a single quantitative risk-of-bias tool. The MMAT evaluates study quality across five design-specific criteria following two screening questions assessing the clarity of research questions and the adequacy of data to address them (Hong et al., 2018). Consistent with MMAT guidance, studies were first required to meet both screening criteria before further appraisal was undertaken. All included studies met the initial MMAT screening criteria, and full ratings for each study are shown in *Table 1.*

In line with MMAT scoring instructions, each criterion was scored as a "Yes," "No," or "Can't tell". In accordance with MMAT guidance, no overall numerical quality score was calculated, nor were studies excluded on the basis of quality appraisal alone. Only one study employed a randomised controlled trial (RCT) design and was therefore appraised using the MMAT criteria for randomised studies (criteria 2.1–2.5). The remaining studies used quantitative non-randomised designs and were appraised using the corresponding MMAT criteria (criteria 3.1–3.5).

Results

Study Characteristics

This review includes 17 studies published between 2012 and 2025, comprising of community-dwelling and research cohort samples of adults aged 50 years and above, with sample sizes ranging from small experimental groups (*n*=13) to large observational samples (*n*= 267,889). All characteristics can be seen in *Table 2*.

Sleep Measures

Sleep was assessed using objective measures, subjective measures, or a combination of both (Li et al., 2024).

Objective sleep measures were used in laboratory-based polysomnography (PSG) or experimental sleep studies (n = 5; Champetier et al., 2023; Cherdieu et al., 2013; Hamel et al., 2025; Pasula et al., 2018; Varga et al., 2016), as well as in home-based or community-based settings (n = 2; Mullins et al., 2025; Seelye et al., 2015). Objective sleep measures included PSG, actigraphy, and experimentally manipulated sleep. PSG-derived outcomes included sleep stage distributions (sleep architecture), sleep spindles, slow-wave activity (SWA), arousal indices, and obstructive sleep apnea (OSA) severity. Actigraphy-derived outcomes included sleep duration, sleep fragmentation, and circadian variability. One study experimentally manipulated sleep, looking at total sleep deprivation interactions.

Subjective sleep was typically assessed using self-report questionnaires or single-item reports in community cohort studies or at-home participants (n = 6; Coutrot et al., 2022; Cox et al., 2019; Guan et al., 2020; Qiu et al., 2018; Richards et al., 2019), as well as lab-based observational studies, intervention, or controlled-clinical trial groups (n = 5; Filipczyk et al., 2021; Iglesias et al., 2012; Li et al., 2024; Maybrier et al., 2024; Siddarth et al., 2021). Subjective measures included instruments such as the Pittsburgh Sleep Quality Index (PSQI), the Insomnia Severity Scale and single-item sleep duration reports, measuring sleep duration, sleep quality, insomnia symptoms, sleep latency, and daytime sleepiness.

Cognitive Outcomes

Cognitive outcomes differed across studies and included spatial navigation or visuospatial performance.

Spatial navigation outcomes were assessed using a range of tasks, including one large online video-game–based navigation task (Coutrot et al., 2022), and laboratory-based virtual navigation tasks (n = 3; Maybrier et al., 2024; Mullins et al., 2025; Varga et al., 2016).

Visuospatial outcomes were assessed using laboratory-based memory tasks (n = 3; Champetier et al., 2023; Li et al., 2024; Pasula et al., 2018), one internet memory matrix training game (Richards et al., 2019), experimental object-location tasks (n = 2; Cherdieu et al., 2013; Hamel et al., 2025), or standardised neuropsychological tests (n = 4; Filipczyk et al., 2021; Guan et al., 2020; Iglesias et al., 2012; Siddarth et al., 2021). Several studies also measured visuospatial performance using broader standardised test batteries (n =3; Cox et al., 2019; Qiu et al., 2018; Seelye et al., 2015).

Study Quality

Across the included studies, several consistent strengths and limitations were identified using MMAT. All studies demonstrated clear research questions, appropriate outcome measures, and adequate alignment between study aims and analytic approaches. In contrast, two domains were identified as frequently unclear; namely sample representativeness (MMAT 3.1) and control of confounding variables (MMAT 3.4). These items were commonly rated as *Can't tell*, which indicates insufficient reporting to judge whether a criterion is met (rather than evidence that it was not met, which would be rated *No*).

Only one study (Filipczyk et al. 2021) was found to have risk of bias across four of the five MMAT domains, and was the only study to score a *No* rating (for confounder control; MMAT 3.4). Among the remaining studies, six had concerns in only one MMAT domain, seven had concerns in two domains, and three had concerns in three domains.

Overall, while the included studies offered sufficient methodological quality to address the review question, the predominance of *Can't tell* ratings, particularly around sample representativeness and confounding variables, limit confidence in the generalisability of findings and increase uncertainty around whether associations may be partly explained by uncontrolled factors.

Relationship between Sleep and Outcome Measures of Cognition

Across all 17 studies, four reported a positive association between sleep parameters and visuospatial and navigational outcomes (Champetier et al., 2023; Cox et al., 2019; Hamel et al., 2025; Seelye et al., 2015),

one reported a negative association (Maybrier et al., 2024), two reported mixed or non-linear findings (Coutrot et al., 2022; Mullins et al., 2025), and ten reported null findings (Cherdieu et al., 2013; Filipczyk et al., 2021; Guan et al., 2020; Iglesias et al., 2012; Li et al., 2024; Pasula et al., 2018; Richards et al., 2019; Qiu et al., 2018; Siddarth et al., 2021; Varga et al., 2016). Summary of findings can be found in *Table 2.*

Subjective Sleep and Visuospatial Performance

Five studies in this category reported null associations between subjective sleep measures and visuospatial memory tasks, and only one reported a positive association.

No relationship between insomnia severity and visuospatial performance was found in a clinical rehabilitation sample (Filipczyk et al., 2021). This study assessed the impact of a 3-month intervention on 29 older adults with insomnia and mild cognitive disorders, combining physical, social, and cognitive rehabilitation. However, several methodological limitations were identified, relating to unclear sample representativeness, limited reporting of outcome data and intervention adherence, and lack of cofounder control strategies. The study design further limits interpretation, as it uses a small single-group pre-post intervention design with several components (cognitive, physical and social rehabilitation), making it difficult to isolate specific contributions of sleep on visuospatial outcomes.

Similarly, Siddarth et al. (2021) reported no association between subjective sleep quality and visuospatial memory in a population of older adults with mild subjective memory complaints. This study was more methodologically sound in several domains, aside from one MMAT domain (representativeness of samples), where it described the target population and inclusion/exclusion criteria well, but lacked information around recruitment flow, reasons for non-participation, and information to determine representativeness.

In two very large sample populations, Qiu et al. (2018) and Richards et al. (2019) also found no association between self-reported sleep duration and visuospatial memory. These large datasets provide greater statistical power which strengthen the evidence base.

Guan et al.,2020, which investigated the mediation effects of sleep quality and depression on cognitive functions, reported no associations between subjective sleep measures and visuospatial ability. Qiu et al. (2018) and Guan et al., (2020) were two of the stronger designs among the studies, with clearly defined criteria and appropriate analyses, with only one MMAT limitation identified for both and related to lack of reporting on non-participation, supporting confidence in the null finding. Richards et al. (2019)'s limitations primarily related to representativeness, confounder reporting, and some outcome measurement not fully documented, making it one of the least methodologically robust studies.

In contrast, one longitudinal cohort study reported a positive association between shorter sleep latency and less daytime sleepiness and better visuospatial performance (Cox et al., 2019). This study had two MMAT limitations, reporting incomplete outcome data and attrition, as well as reporting restricted generalisability. However, this study was particularly informative for the review, as it modelled longitudinal change across three waves and demonstrated clearly that some sleep–cognition associations persisted (daytime sleepiness) after adjusting for health covariates and multiple comparisons, whereas sleep latency weakened once confounding was accounted for.

Subjective Sleep and Spatial Navigation Performance

Spatial navigation was measured using a virtual wayfinding task, which required participants to navigate through a computer-based environment and locate targets, providing indices of navigational accuracy and efficiency (Coutrot et al., 2022). Using subjective sleep duration, this study reported a non-linear association, with optimal navigation performance at approximately seven hours of sleep followed by poorer performance at both shorter and longer sleep durations. This study benefited from a very large sample and robust analytic methods, with only one MMAT domain identified relating to representativeness, namely reporting participant self-selection and non-participation.

Objective Sleep and Visuospatial Performance

Findings in this category were mixed.

One home-based objective sleep study reported a positive association between objective sleep and visuospatial memory. Seelye et al. (2015) found that greater sleep variability was modestly associated with poorer visuospatial ability at both one week and one month prior to testing. This study benefitted from an unobtrusive at-home sleep assessment, strengthening its ecological validity, though one MMAT limitation relating to no non-participation reporting remained.

Two PSG studies reported positive associations between sleep architecture and visuospatial memory consolidation, namely around greater spindle clustering being associated with better overnight memory performance (Champetier et al., 2023; Hamel et al., 2025). These studies were strengthened by using PSG-derived metrics and adopting a pre-post overnight design, although MMAT appraisal highlighted limited information to judge two domains, namely representativeness (limited reporting of non-participation) and confounder control, as analyses adjusted for only a restricted set of covariates.

In contrast, two laboratory-based studies using experimental manipulation reported null effects. Pasula et al. (2018) reported no visuospatial working memory impairment following 36 hours of total sleep deprivation compared with normal sleep in older adults. The MMAT appraisal for this study identified limitations in incomplete justification of sample representativeness and confounder reporting, however was strengthened by its experimental and within-subjects design, controlling sleep manipulation. Similarly, Cherdieu et al. (2013), examined whether normal sleep versus prolonged wakefulness improved consolidation of a newly learned visuospatial object-location task, and found no difference in visuospatial memory between sleep and wake conditions in older adults. This study was limited by only two MMAT conditions where it lacked enough reporting on non-participation and adjustments of potential confounders, but was strengthened in its design to compare sleep-versus-wake directly with PSG measures.

Interventional studies looking at sleep-related treatments also reported null findings (Iglesias et al., 2012; Li et al., 2024). Iglesias et al. (2012) reported no significant improvement in visuospatial memory following six months of Continuous Positive Airway Pressure (CPAP) treatment for OSA. This study was appraised to have

three MMAT limitations, relating to limited reporting on recruitment and non-participation information, incomplete reporting of outcome data and insufficiently reported adjustments for confounding variables. In addition, the sample size was very small (*n = 13*), which may have limited power to detect changes in visuospatial memory. Li et al. (2024) is reported below as this study incorporated both subjective and objective measures of sleep.

Objective Sleep and Spatial Navigation Performance

Spatial navigation outcomes were measured using virtual navigation paradigms, including allocentric and egocentric navigation tasks, virtual maze learning, and three-dimensional navigation tasks assessing learning and overnight improvement. This category reported mixed findings.

Mullins et al. (2025) found that participants without Obstructive Sleep Apnea (OSA) demonstrated improvements in virtual navigation performance overnight, whereas participants with OSA progressively worsened across trials. It also found that higher frontal SWA was positively associated with overnight improvements in the OSA group only. This study was appraised to have two MMAT limitations relating to limited reporting on non-participation and confounding variables.

Maybrier et al., (2024) found a negative association in their actigraphy study, with more sleep fragmentation linked to worse allocentric and egocentric navigation performance in a virtual cognitive-mapping task. However, interpretation is limited by incomplete reporting around exclusions/outcome data and uncertainty regarding confounder adjustment and non-participation, suggesting caution in interpreting the strength of the observed interaction. Finally, sleep and wake times were manually entered from sleep diaries when the algorithm was unable to detect the sleep data, potentially introducing some measurement uncertainty.

Finally, Varga et al. (2016), which investigated how aging affects slow-wave sleep (SWS), found no evidence of overnight improvement in spatial navigation performance following PSG-measured sleep. The

limitations of this study related to missing information of sample representativeness, small sample size *(n* = 13*)* and limited reporting of controlling for covariates*.*

Subjective and Objective Sleep

One study looked at both objective and subjective measures of sleep (Li et al., 2024) and found no association between changes in sleep parameters and visuospatial memory following a Tai Chi intervention. This study showed the lowest bias rating and strongest methodological quality, with no MMAT limitations, strengthening the results of these findings.

Discussion

The aim of this review was to evaluate the associations between sleep characteristics measured objectively and/or subjectively, and visuospatial and spatial navigation performance in adults aged ≥50 years. Overall, the evidence base was predominantly characterised by null findings in each category, with only a small number of studies reporting positive, negative, or mixed associations between sleep and cognitive outcomes. Where associations were observed, they suggested that more specific sleep measures like sleep architecture, continuity or variability were associated with cognitive measures, rather than measures of sleep duration. Overall, findings suggest that sleep was not a consistent predictor of visuospatial and spatial navigation performance in ageing adults, with effects appearing task-specific and measure-specific.

Subjective Sleep

Across studies examining subjective sleep and visuospatial memory, null findings were consistently reported, including in studies with stronger methodology and larger sample sizes. This strengthens the findings and interpretation that subjective sleep parameters may not be reliably associated with visuospatial memory performance, and that the absence of an association is unlikely to be explained by methodological weakness. In contrast, Cox et al., 2019 reported a positive association, linking shorter sleep latency and less daytime sleepiness to better visuospatial performance. This study was methodologically robust and provided particularly stronger evidence for daytime sleepiness. By focusing on how easily participants fell asleep and daytime

sleepiness rather than overall sleep quality or duration, findings suggest that sleep latency and daytime alertness may be more relevant for visuospatial functioning in older adults.

Only one study examined subjective sleep in relation to spatial navigation, finding a non-linear relationship, with navigation performance being optimal at around seven hours of sleep and poorer at longer sleep durations (Coutrot et al., 2022). This study had a large sample size (*n* = 191,791) and strong methodological quality. The strength of this evidence suggests that sleep duration could be more relevant for spatial navigation than for visuospatial memory, potentially reflecting the different cognitive demands such as idiothetic cues of navigation tasks. Although this finding is based on a single study, findings are consistent with wider literature demonstrating that sleep-cognition associations may not be purely linear. Large cohort studies have reported inverted U-shaped patterns, with approximately 7–8 hours associated with better cognitive performance and both shorter and longer sleep linked to poorer cognitive outcomes (Kronholm et al., 2009; van Oostrom et al., 2018; Xu et al., 2011). Similarly, the evidence suggests that sleep–cognition associations may vary by age and individual factors rather than following a single linear pattern (Mohlenhoff et al., 2018). However, these findings should be interpreted cautiously, as self-reported sleep duration is limited to subjectivity and associations may be influenced by other factors such as health, lifestyle factors, mood, sociodemographic factors and other sleep-related problems (Kronholm et al., 2009).

Objective Sleep

In contrast, studies using objective sleep measures demonstrated more mixed patterns, particularly for visuospatial memory. Three studies reported positive associations between objectively-measured sleep and visuospatial memory, including two PSG studies focusing on sleep spindles in visuospatial memory consolidation and one home-based study monitoring night-to-night sleep variability. These studies met most MMAT criteria and showed on average robust methodology. This evidence offers meaningful theoretical support for the role that sleep architecture and sleep continuity play in visuospatial outcomes, and may be more informative than sleep duration alone when considering visuospatial performance in ageing populations.

However, these studies have to be considered alongside four studies that reported no associations between objective sleep and visuospatial memory. These studies varied in quality of methodology, and included both experimental sleep manipulation and intervention designs. The presence of null findings across several studies with reasonably robust designs suggest that the relationship between sleep and visuospatial memory could be task-specific or dependent on particular features of sleep physiology, rather than global sleep quality, duration or continuity.

Studies looking at spatial navigation were more varied in their direction and quality assessments. Overall, no clear sleep parameters consistently predicted navigation performance. While some findings suggested that navigation may be more sensitive to sleep disruption, fragmentation, or sleep disorders, the evidence base was not consistent or sufficient enough to report firm conclusions. One study reporting that greater sleep fragmentation was associated with poorer spatial navigation showed parallels with the negative association found in objective sleep and visuospatial navigation, though neither study found any significant effects whilst looking at sleep duration alone. This pattern aligns with wider literature findings that sleep continuity and disruption show more consistent associations with cognitive functioning in older adults than global sleep duration (Quin et al., 2023). Taken together, these findings support the possibility that spatial navigation performance may be more closely linked to sleep continuity and physiology than total sleep time.

Subjective and Objective Studies

The strongest study overall, which incorporated both subjective and objective sleep measures and robust methodology, reported no association between changes in sleep parameters and visuospatial memory outcomes. The lack of findings across both types of sleep measures suggests that sleep–visuospatial relationships are not consistent and may only be present under specific conditions or for particular types of cognitive tasks.

Strengths and Limitations

Several limitations should be considered when interpreting the findings of this review. First, there was a high degree of variation across studies in terms of design, sleep measures, cognitive tasks and analytical approaches. As a result, findings were drawn using a narrative synthesis instead of being combined quantitively in a meta-analysis, limiting the strength of any causal conclusions. Second, many studies were cross-sectional, making it difficult to determine the direction of associations, such as whether sleep influences visuospatial cognition, whether cognitive abilities affect sleep, or whether both are influenced by other shared factors like age, physical health or mental health. Finally, as with all reviews, publication bias may have occurred and studies reporting significant findings may be underrepresented.

Despite these limitations, this review has several strengths. For instance, while the evidence-base largely contained cross-sectional and observational designs, five of these studies used longitudinal designs (Cox et al., 2019; Li et al., 2024; Filipczyk et al., 2021; Iglesias et al., 2012; Seelye et al., 2015). This represents a relative strength, as these studies allow for the examination of change over time. However, the longitudinal studies varied considerably in their designs, follow-up duration, and outcome measures, with several reporting null findings. As such, although the inclusion of longitudinal evidence strengthens this review, it remains insufficient to draw firm conclusions about directionality or causality, highlighting the need for further longitudinal research in this area.

Overall, the evidence base was characterised by clear study aims, generally sound methodology, and strong measurement practices, with most studies showing good methodology. The primary methodological limitations related to sample representativeness and control of confounding variables, and were considered in the narrative synthesis, with greater weight given to methodologically stronger studies. Uncertainty around representativeness was common, largely due to limited reporting of recruitment flow or non-participation, reflecting reporting limitations rather than clear sampling bias. Handling of confounders was more variable, with some studies adjusting for key demographic or clinical covariates, while others relied primarily on exclusion criteria or provided limited justification. In contrast, measurement of exposures and outcomes was a clear

strength, and was rated as *"Yes"* across all included studies, reflecting consistent use of validated sleep measures and experimentally established visuospatial and navigational tasks. Fidelity of exposure administration was also high, with only one study rated as *"Can't tell"*, indicating that sleep protocols were generally implemented as intended.

Consistent with the null findings from this review are several studies in the wider literature that also support the possibility that sleep may not be reliably associated with cognitive performance in older adults. For example, subjective sleep quality has been shown to be unrelated to cognitive performance in cognitively intact older adults (Westerberg et al., 2010) and several studies found largely null association between sleep duration and cognitive decline (Loerbroks et al., 2009; Martin et al., 2012). One explanation for these mixed results across the literature could be the different types of sleep assessment methods or differences in cognitive task designs, which vary widely among studies focused on sleep and cognition. Some sleep measures and cognitive tasks may lack the sensitivity required to detect subtle sleep-related effects, particularly in cognitively intact older populations. As such, null findings should be interpreted cautiously, as they may reflect limitations in measurement sensitivity or task selection, rather than the absence of any meaningful sleep-cognition relationships.

Conclusion

The evidence linking sleep and visuospatial memory and spatial navigation in older adults remains limited and under-researched, despite the clear clinical relevance of both sleep problems and cognitive change in later life. While most studies in this review reported null findings, some associations were observed for specific aspects of sleep, such as sleep architecture and sleep regularity, suggesting that not all sleep characteristics may be relevant for visuospatial functioning. The evidence in this review highlights the theory that sleep is not a consistent or universal predictor of visuospatial performance, with any effects likely to be small and task specific. Overall, this review provides a structured synthesis of emerging literature and highlights

the need for high-quality, theory-driven longitudinal research using standardised cognitive and sleep measures to clarify the role of sleep in visuospatial functioning in later life.

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Figure 1

PRISMA Flow Diagram of Selection of Studies

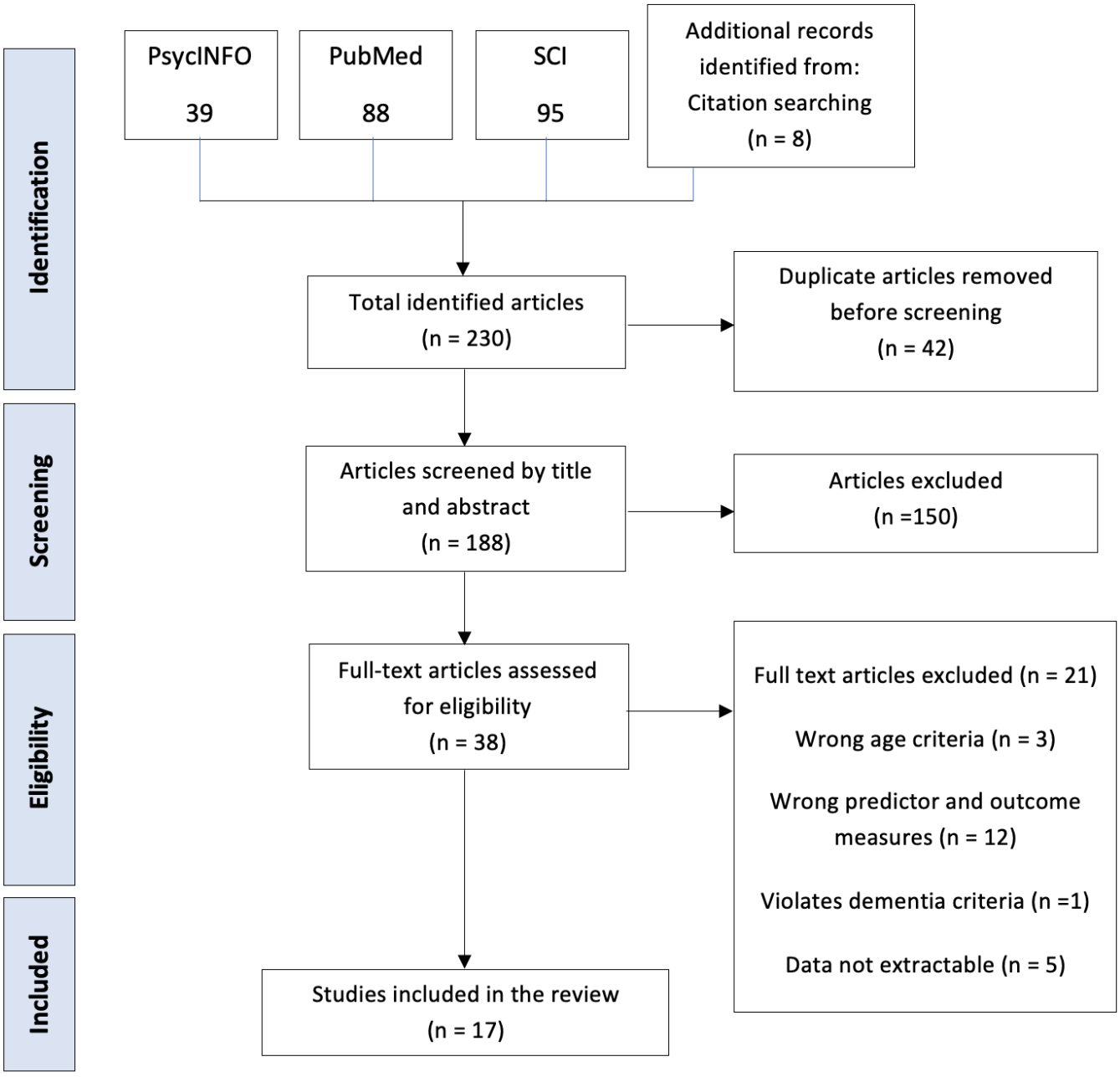


Table 1

Quality rating by study assessed by the Mixed Methods Appraisal Tool (MMAT)

Reference	S1	S2	RCT 2.1	RCT 2.2	RCT 2.3	RCT 2.4	RCT 2.5	Non RCT 3.1	Non RCT 3.2	Non RCT 3.3	Non RCT 3.4	Non RCT 3.5
Champetier et al 2023	Y	Y						CT	Y	Y	CT	Y
Cherdieu et al 2013	Y	Y						CT	Y	Y	CT	Y
Coutrot et al 2022	Y	Y						CT	Y	Y	Y	Y
Cox et al 2019	Y	Y						CT	Y	CT	Y	Y
Filipczyk et al 2021	Y	Y						CT	Y	CT	N	CT
Guan et al 2020	Y	Y						CT	Y	Y	Y	Y
Hamel et al 2025	Y	Y						CT	Y	Y	CT	Y
Iglesias et al 2012								CT	Y	CT	CT	Y

Li et al 2024	Y	Y	Y	Y	Y	Y	Y					
Maybrier et al 2024	Y	Y						CT	Y	CT	CT	Y
Mullins et al 2025	Y	Y						CT	Y	Y	CT	Y
Pasula et al 2018	Y	Y						CT	Y	Y	CT	Y
Qiu et al 2018	Y	Y						CT	Y	Y	Y	Y
Richards et al	Y	Y						CT	Y	CT	CT	Y
Seelye et al 2015	Y	Y						CT	Y	Y	Y	Y
Siddarth et al 2021	Y	Y						CT	Y	Y	Y	Y
Varga et al 2016	Y	Y						CT	Y	Y	CT	Y

Table 2

Characteristics and Summary of findings for the included studies

Study ID	Study design	Total study sample (N, age)	Sample used in SR	Sleep exposure (measure & window)	Cognitive outcome (task & construct)	Key result (direction only)	Effect estimate type	Effect size / p-value
Champetier et al., 2023	Observational, cross-sectional	N = 179; mean 34.5y (young), mean 69.3y (older)	N = 57 older adults	PSG; fast-spindle clustering & NREM fragmentation; single night	2-D object-location task; visuospatial memory consolidation	Greater fast-spindle clustering associated with better overnight visuospatial memory	Regression (β)	β = 0.29, p = .036
Cherdieu et al., 2013	Experimental, non-randomised (sleep vs wake)	N = 40; mean 22.1y (young), mean 68.9y (older)	N = 20 older adults	PSG; TST, sleep efficiency, REM, total cycle time; overnight	2-D object-location task; visuospatial memory	No difference in forgetting between sleep and wake in older adults	Mean difference	p = .53
Coutrot et al., 2022	Cross-sectional observational	N = 730,187; mean 38.7y Aged 19-70y	N = 191,791 aged 54–70y	Self-reported sleep duration (hours/night)	Virtual way-finding task; spatial navigation	Inverted-U association with optimal navigation at ~7h sleep, after which further sleep was linked to poorer navigation	Regression (linear & quadratic)	β_linear = 0.39; β_quad = −0.028
Cox et al., 2019	Longitudinal observational (3 waves)	N = 1,091; 7 Aged 70–76y	N = 664	Self-reported sleep duration, latency, quality, daytime sleep	Matrix Reasoning, Block Design, Spatial Span; visuospatial ability	Shorter sleep latency & less daytime sleep linked to better visuospatial ability	Regression (β)	β = −0.215, p = .003; β =−0.533, p = .007 β = -0.071, p < 0.001

Filipczyk et al., 2021	Pre–post single-group	N = 32; median 78.5y	N = 29	Athens Insomnia Scale; self-report	ROCFT; ACE-III visuospatial; MoCA visuospatial	No association between insomnia severity and visuospatial performance	Correlation (ρ)	ρ > .05 (NS)
Guan et al., 2020	Cross-sectional observational	N = 246; mean 67.1y	N = 246	PSQI total & components; past month	ROCFT copy/recall; CDT	Poorer sleep not linked visuospatial ability	Correlation / partial correlation	r = -0.12, p = 0.09
Hamel et al., 2025	Cross-sectional observational	N = 42; mean ≈68.8y	N = 42	In-home PSG; fast-spindle clustering & NREM fragmentation	Object-location task; visuospatial consolidation	Greater spindle clustering linked to better memory consolidation	Regression (β)	β = −3.15, p = .04
Iglesias et al., 2012	Pre–post CPAP intervention	N = 42; Age ≥60y	N = 13 OSAS	PSG-confirmed OSA; CPAP for 6 months	ROCFT; WMS Spatial Span; visuospatial memory	No significant improvement after CPAP	Pre–post mean comparison	p > .05
Li et al., 2024	RCT (Tai Chi vs control)	N = 56; mean 67.4y	N = 48 completed	ISI, PSQI daytime dysfunction; actigraphy SOL	Picture-location task; visuospatial memory	No association between sleep changes and visuospatial memory	Mediation / regression	ps > .05
Maybrier et al., 2024	Cross-sectional observational	N = 79; 37 aged 60–89y	N = 37 older adults	Actigraphy (1 week): fragmentation, TST, circadian variability	Virtual navigation; allocentric & egocentric	Greater fragmentation linked to worse virtual navigation	Regression (β)	β =−0.344, p = .022; β =−0.437, p = .005
Mullins et al., 2025	Observational cohort (OSA vs controls)	N = 52; mean 66.9y	N = 52	PSG: AHI, arousal index, SWA	Virtual 3-D maze; navigation learning	OSA linked to poorer overnight improvement; SWA beneficial in OSA	Mixed ANOVA; correlation	F(2,50) = 3.53, p= .03; r = .51, p= .02

Pasula et al., 2018	Counter-balanced crossover	N = 64; 33 (older) aged 59–82y	N = 33 older adults	36-h total sleep deprivation vs normal sleep	vsCRMT; visuospatial working memory	No visuospatial WM impairment after TSD in older adults	ANOVA / t-tests	t(24)= .93, p= .36
Qiu et al., 2018	Cross-sectional observational	N = 267,889; mean 57y	N = 267,889	Self-reported sleep duration	Card-matching task; visuospatial memory	Sleep duration not analysed as predictor; no association observed	Regression	NS
Richards et al., 2019	Cross-sectional observational	N = 512,823; aged 15-89y	N = 80,522 aged ≥55y	Self-reported habitual sleep duration	Memory Matrix game; visuospatial STM	Inverted-U in younger-old only; flat association in oldest group	Regression	Peak ≈7h; CIs overlap zero
Seelye et al., 2015	Exploratory cross-sectional	N = 63; mean 87y	N = 63	In-home sensors (30 days): TST, movement, variability (SD)	Block Design; Visual Reproduction; visuospatial ability	Greater sleep variability modestly associated to poorer visuospatial ability (week before and month before testing)	Spearman correlation	ρ = −0.29, p < .05 ρ = −0.30, p < .05
Siddarth et al., 2021	Cross-sectional observational	N = 203; mean 60.4y	N = 203	PSQI total & components	BVMT-R delayed; Buschke SRT	No association between subjective sleep quality and visuospatial memory	Regression (β)	β = −0.04, p = .57
Varga et al., 2016	Sleep-laboratory observational	N = 31; mean 20y (younger) mean 68.2y (older)	N = 13 older adults	PSG: SWS %, fragmentation, continuity	Virtual maze; navigation performance	No overnight navigation improvement	Pre–post comparison	p = .73

Note. AHI = Apnea–Hypopnea Index; AIS = Athens Insomnia Scale; BVMT-R = Brief Visuospatial Memory Test–Revised; CDT = Clock Drawing Test; CPAP = Continuous Positive Airway Pressure; EEG = Electroencephalography; EOG = Electro-oculography; EMG = Electromyography; ISI = Insomnia Severity Index; MCI = Mild Cognitive Impairment; MoCA = Montreal Cognitive Assessment; NREM = Non-rapid eye movement sleep; OSA/OSAS = Obstructive sleep apnea / obstructive sleep apnea syndrome; PSG = Polysomnography; PSQI = Pittsburgh Sleep Quality Index; REM = Rapid eye movement sleep; ROCFT = Rey–Osterrieth Complex Figure Test; SOL = Sleep onset latency; SR = Systematic review; STM = Short-term memory; SWA = Slow-wave activity; SWS = Slow-wave sleep; TSD = Total sleep deprivation; TST = Total sleep time; WM = Working memory; vsCRMT = Visuospatial Continuous Recognition Memory Test.

Chapter Three: Bridging Chapter

This chapter aims to summarise the key findings of the systematic review and provide some background and rational for the subsequent empirical paper.

The systematic review presented in chapter two examined the associations between sleep characteristics and visuospatial memory and spatial navigation in adults aged 50 years and older. Overall, findings across the included studies were mixed, with the majority reporting null findings for associations between sleep parameters and visuospatial and navigational outcomes. Where associations were observed, these were inconsistent in their direction and appeared to depend on the type of sleep measures that were used, as well as methodological factors such as sample size and design.

Importantly, most studies included in the review were cross-sectional, limiting understanding of how sleep and cognition may change together over time. This is particularly relevant in the context of dementia risk, as visuospatial memory and spatial navigation are increasingly recognised as early cognitive markers of neurodegenerative change (Coughlan et al., 2018; Coughlan et al., 2019; Heo et al., 2010, Wang et al., 2024). This review also highlights that mental health outcomes are rarely examined alongside sleep and cognition. This represents an important clinical gap, as sleep difficulties in older adults have been found to be closely linked to symptoms of depression and anxiety (Poole & Jackowska, 2017; Taylor et al., 2005), which may influence both quality of life and cognitive risk (Klepac et al., 2008).

The following empirical study therefore aims to address these gaps by adopting a longitudinal design to examine changes in sleep, psychological wellbeing, and cognition in older adults. In line with the systematic review, cognitive domains examined will include visuospatial memory and spatial navigation. This empirical paper will also examine whether these relationships differ according to APOE ε4 carrier status, a key genetic risk factor for Alzheimer's disease (Corder et al., 1993; Farrer et al., 1997).

Chapter Four: Empirical Research Paper

The Impact of Sleep on Cognitive and Mental Health Outcomes in Older Adults: A Longitudinal Study of Circadian Rhythms and Early Cognitive and Emotional Change

Prepared for submission to The Journal of Sleep Research

(Author Guidelines can be found in Appendix A)

The Impact of Sleep on Cognitive and Mental Health Outcomes in Older Adults: A Longitudinal Study of Circadian Rhythms and Early Cognitive and Emotional Change

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Abstract

The study examined longitudinal associations between sleep quality, cognition and psychological wellbeing in older adults at increased genetic risk for dementia.

A follow-up study was conducted in cognitively healthy older adults previously genotyped three to five years ago for the apolipoprotein E epsilon-4 (APOE ε4) allele. A total of 38 participants completed online self-report questionnaires assessing sleep quality, depressive and anxiety symptoms, quality of life, and subjective cognitive change, alongside cognitive tasks assessing visuospatial memory and spatial navigation, using the same measures as administered at baseline. A subset of participants also wore a wrist-worn actigraphy device for seven days and completed a daily sleep diary.

No differences were observed in APOE ε4 carriers and non-carriers in subjective or objective sleep over time, and carrier status did not moderate associations between sleep and cognitive or psychological outcomes. However, regression models using baseline-to-follow-up change scores found that poorer subjective sleep quality predicted increases in depressive and anxiety symptoms over the follow-up period. Although APOE ε4 status did not significantly moderate these relationships, associations were observed within the carrier group, where poorer subjective sleep quality was linked to worsening mood symptoms.

Overall, sleep was not associated with cognitive change in this sample, but may represent a modifiable factor for supporting psychological wellbeing in ageing populations at elevated risk for dementia.

Keywords: Sleep; APOE ε4; psychological wellbeing; ageing; actigraphy; cognition

Introduction

Research in the field of sleep has increased over the last two decades, with studies exploring how disrupted sleep impacts the body, including our cells, metabolism and gene expression (Worley, 2018). This growing body of research highlights that inadequate sleep is linked to a wide range of adverse outcomes across the lifespan, including cardiovascular morbidity (Gottlieb et al., 2016; Grandner et al., 2018; Reutrakul et al., 2018; Watson et al., 2017) and poorer mental health (Ben & Walker, 2018; Pell & Smith, 2018), as well as conditions associated with cognitive decline and dementia (Sprecher et al., 2017). This literature suggests sleep is important for brain health and cognitive ageing, and may be a modifiable target to support cognitive functioning in later life, providing a rationale for investigating sleep-cognition relationships in older adulthood. However, despite growing evidence for the role of sleep on brain health and cognitive ageing, important gaps remain in our understanding of how sleep quality interacts with genetic risk factors, such as the APOE-ε genotype (a well-established genetic risk factor for Alzheimer's disease), to influence psychological wellbeing and cognitive functioning over time in older adults.

Sleep and Cognitive Health

Older adults experience increased sleep disturbances, including more fragmented sleep and reduced time spent in deeper restorative stages (Mander et al., 2017). Evidence suggests that sleep disturbances may contribute to accelerated ageing, cognitive decline and dementia progression (Videnovic et al., 2014). This relationship also appears bidirectional, with neurodegenerative changes contributing to sleep problems (Wang and Holtzman 2019). Sleep disturbances linked to dementia risk include sleep fragmentation, reduced sleep efficiency, and altered sleep duration (Wu et al., 2017), with longitudinal evidence associating sleep disruption with later cognitive impairment (Musiek et al., 2022; Sabia et al., 2021). Together, this highlights the value of examining specific sleep parameters over time in relation to cognitive ageing.

Genetic factors may further influence both sleep quality and cognitive outcomes. Healthy adults with the APOE-ε genotype, the strongest genetic risk factor for late-onset Alzheimer's disease, have been found to

have higher objective measures of sleep disruptions than non-carriers of the gene (Drogos et al., 2016). Better sleep consolidation has also been linked to reduced Alzheimer's risk (Lim et al., 2013), supporting investigation of sleep as a modifiable in genetically at-risk older adults.

Sleep and Mental Health

In addition to its effects on cognitive functioning, disrupted sleep is strongly associated with poorer mental health outcomes (Scott et al., 2021). Individuals with insomnia are more likely to experience depressive and anxiety symptoms compared to those without sleep difficulties (Taylor et al., 2005). Sleep problems may also precipitate or exacerbate mental health difficulties (Jaussent et al., 2011). A systematic review of prospective studies found that depressed mood is one of the most consistent independent predictors of future sleep disturbances in older adults (Smagula et al., 2016), highlighting the bidirectional relationship between sleep and mental health. These associations are clinically relevant for ageing populations, where affective symptoms are common and may interact with sleep disturbances to increase vulnerability to cognitive decline and reduced quality of life.

Dementia and Mental Health

Research demonstrates a close, multifaceted relationship between mental health and Dementia. Neuropsychiatric symptoms, particularly depression and anxiety, are highly prevalent across stages of dementia, and often emerge before disease onset (Lyketsos et al., 2011, as cited in Jia et al., 2022; Wise et al., 2019). In a substantial proportion of individuals, affective symptoms appear years before a formal dementia diagnosis, suggesting that depression and anxiety could act as early indicators or risk factors for subsequent cognitive decline (Da Silva et al., 2013).

Genetic vulnerability may modulate this relationship. The APOE-ε allele has been linked to increased dementia risk and elevated anxiety and depression symptoms (Holmes et al., 2016). These symptoms are also associated with poorer quality of life and an increased risk of dementia even in the absence of cognitive impairments. One proposed mechanism underlying this association can be partly explained by stress-related increases in cortisol, in that elevated cortisol levels in anxiety and depression have been linked to brain

changes, namely the accumulation of amyloid plaques, which may contribute to neurodegeneration (Holmes et al., 2016). Together, these findings highlight mental health as a clinically relevant factor in dementia risk, particularly when considered alongside genetic susceptibility.

Aims of the Study

Despite growing evidence that sleep disturbance, mental health and genetic vulnerability are each associated with an increased risk of dementia, these factors have largely been examined in isolation. Research has started to investigate early biological markers of dementia, with memory and spatial navigation emerging as particularly sensitive indicators of early change (Mamani et al., 2017; Alvi et al., 2023; Laczó et al., 2023). However, the understanding of how sleep quality interacts with genetic risk to influence both cognitive and psychological wellbeing outcomes longitudinally remains limited and has not been comprehensively studied.

The present study aimed to examine the longitudinal interplay between sleep quality, mental health and cognitive functioning in older adults, and to determine how these relationships are modulated by the genetic risk for Alzheimer's disease, as indexed by the APOE- ε4 genotype. By examining these factors within a longitudinal model and incorporating early cognitive markers, like memory and spatial navigation, this study aims to enhance understanding of dementia risk processes and inform clinically relevant approaches for early identification and prevention.

Research Questions and Hypotheses

The study examined the following research questions and hypotheses:

Research Question 1: How does the APOEe4 genotype influence longitudinal changes in sleep quality among older adults?

Hypothesis 1: Individuals with the APOEe4 genotype will experience a greater decline in sleep quality compared to those without the genotype.

Research Question 2: Does APOE ε4 carrier status moderate the association between longitudinal changes in sleep quality and longitudinal changes in psychological wellbeing in older adults?

Hypothesis 2: A decline in sleep quality will be associated with increased levels of depression and anxiety among the APOEe4 carriers.

Research Question 3: Does APOE ε4 carrier status moderate the association between longitudinal changes in sleep quality and longitudinal changes in cognitive functioning in older adults?

Hypothesis 3: Changes in sleep quality will have a greater impact on spatial navigation and memory in individuals with the APOE-ε genotype compared to those without.

Methods

Ethical Considerations

Ethical approval for this study was obtained from the Faculty of Medicine and Health Sciences Research Ethics Committee at the University of East Anglia (ref: ETH2425-0281; See Appendix A for approval letter).

Design

This study employed a longitudinal follow-up design, extending data from an earlier cross-sectional observational study conducted approximately three to five years prior in cognitively healthy older adults, who had been genotyped for the apolipoprotein E (APOE) ε polymorphism. These participants were invited to complete a follow-up assessment that repeated key measures collected at baseline, allowing for the examination of longitudinal changes in sleep quality, psychological wellbeing, and cognitive functioning. Genetic group (APOE-ε4 carriers vs. non-carriers) was treated as a between-subjects factor, while time (baseline vs. follow-up) was treated as a within-subject factor. This design allowed the examination of longitudinal changes in sleep, psychological wellbeing and cognitive outcomes within individuals, and to assess whether these changes differed according to genetic risk for dementia. By examining change over time across these domains, the study aimed to identify potential early markers associated with cognitive decline in ageing populations.

Participants

Participants were recruited from a database derived from a pilot study conducted three to five years ago, which included 129 cognitively healthy older adults genotyped for the APOE- ε polymorphism. This database included APOE-ε4 carriers and non-carriers who had consented to be re-contacted for future research. Eligible participants were contacted via their preferred method of communication (email or telephone) and provided with information about the follow-up study.

Inclusion criteria included: aged 60 years or above, cognitively healthy at baseline as established during the original screening, and prior consent to be re-contacted. Exclusion criteria included: a diagnosis of dementia, current use of medication known to significantly affect sleep, and major neurological or medical conditions likely to interfere with sleep or cognitive functioning (e.g., stroke, traumatic brain injury, chronic pain conditions, or progressive neurological disorders). Eligibility was confirmed through self-report at recruitment.

An a priori power analysis using G*Power 3.1 (Faul et al., 2009) indicated that a minimum sample size of 36 participants was needed to detect medium-sized effects ($f = 0.25$) with 80% power at $\alpha = .05$. Allowing for attrition and feasibility, the recruitment target was approximately 40 participants. This target was comparable to prior longitudinal studies examining genotype-related differences in sleep and cognition in older adults (e.g., Drogos et al., 2016).

Measures

The same psychological, cognitive and sleep measures administered at baseline were repeated at follow-up, alongside collected demographics (including sex, age, APOE status) and health-related lifestyle information for the screening stage.

Psychological Measures

Depression severity was assessed using the Patient Health Questionnaire (PHQ-9; Kroenke et al., 2001), rated on a 4-point Likert Scale ranging from 0 (*not at all*) to 3 (*nearly every day*) with a total score ranging from 0-27. This measure is brief, easy to administer, and demonstrates strong psychometric

properties, including good internal validity and efficacy for monitoring depressive symptoms (Kroenke et al., 2001; Rancans et al., 2018).

Anxiety symptoms were assessed using the Generalised Anxiety Disorder–7 (GAD-7; Spitzer et al., 2006), a 7-item self-report questionnaire rated on the same 4-point scale, with total scores ranging from 0-21. The PHQ-9 and GAD-7 are widely used and demonstrate good reliability and validity in older adult populations.

Quality of life was assessed using the 12-Item Short Form Health Survey (SF-12; Ware et al., 1996), which generates Physical Component Summary (PCS) and Mental Component Summary (MCS) scores. The SF-12, a validated shorter version of the SF-36, was selected to reduce participant burden while retaining robust psychometric properties.

All psychological questionnaires were completed online via Microsoft Forms.

Cognitive measures

Subjective cognitive change was assessed using the Cognitive Change Index (CCI; Rattanabannakit et al., 2014), a 20-item self-report questionnaire assessing perceived changes in cognitive change over time, rated on a 5-point Likert scale (higher scores indicating greater perceived decline). The CCI was completed online via Microsoft Forms.

Spatial navigation was assessed using the Supermarket Task (Tu et al., 2015), a virtual navigation task requiring participants to locate items within a simulated supermarket. This task demonstrates good reliability and ecological validity and is sensitive to early spatial navigation difficulties in older adults. The Supermarket test was completed online via a link to the task.

Visuospatial memory was assessed using the three-minute Rey–Osterrieth Complex Figure Test (ROCFT; Rey, 1941; Osterrieth, 1944), requiring participants to copy and recall a complex figure after three minutes. Performance was scored according to standard accuracy and organisation criteria. The ROCFT was administered via video call with the researcher.

Sleep Measures

Subjective sleep quality was assessed using the Pittsburgh Sleep Quality Index (PSQI; Buysse et al., 1989), a 19-item self-report questionnaire yielding a total score from 0-21 (higher scores indicating poorer sleep quality). The PSQI assesses sleep on seven components (sleep quality, sleep disturbances, sleep latency, sleep duration, habitual sleep efficiency, use of sleep medications and daytime dysfunction), and demonstrates good internal consistency (Cronbach's $\alpha = .83$) and sensitivity to change over time (Krakow et al., 2004). The PSQI is widely used and validated in older adult populations and was administered online via Microsoft Forms.

Objective sleep parameters were assessed using wrist-worn actigraphy (MotionWatch 8; Cambridge Neurotechnology Ltd., Cambridge, UK), worn continuously for seven days. The actigraphy estimates sleep–wake patterns by recording movement and provides proxy measures of sleep–wake timing, sleep duration, and sleep efficiency, derived using MotionWare Sleep Analysis software (Aili et al., 2017). Actigraphy is practical and ecologically valid for naturalistic assessment of habitual sleep, and demonstrates good agreement with polysomnography for key sleep parameters (Ancoli-Israel et al., 2003; Martin & Hakim, 2011). Participants also completed the Karolinska Sleep Diary (KSD; Gillberg et al., 1994) each morning to support interpretation of actigraphy data.

Procedure

Participants were contacted by email and provided with a brief study overview. Interested individuals were sent a Participant Information Sheet and completed an online consent form before participation. Eligibility was confirmed through self-report screening questions covering inclusion and exclusion criteria. Data collection was conducted remotely. Participants first completed online questionnaires via Microsoft Forms assessing sleep quality (PSQI), psychological wellbeing (PHQ-9, GAD-7, SF-12) and subjective cognitive change (CCI), and were then provided with a link to complete the Supermarket Task. Participants subsequently completed the three-minute Rey–Osterrieth Complex Figure Test during a live video call with the researcher. Objective sleep was assessed last, where participants were sent an actigraphy

device and provided with written instructions and asked to wear it continuously on their non-dominant hand for seven consecutive days, alongside completing the Karolinska Sleep Diary each morning.

Upon completing all study components, participants were debriefed and thanked for their involvement.

Statistical Analysis

All statistical analyses were conducted in IBM SPSS Statistics (Version 31.0.0.0).

Prior to analysis, data were screened for completeness and accuracy. Descriptive statistics were examined, and the distribution of continuous variables was assessed for normality using the Shapiro–Wilk test. Visual inspection of histograms and Q–Q plots was also undertaken. For regression and general linear models, assumptions of linearity, homoscedasticity, independence of errors, and normality of residuals were evaluated using residual plots and standardised residuals. Multicollinearity was assessed using tolerance values and variance inflation factors (VIF), which indicated no significant multicollinearity.

Longitudinal change scores were calculated for sleep, psychological, and cognitive outcomes by subtracting baseline values from follow-up values. APOE-ε4 status (carriers vs. non-carriers) was treated as a between-subjects variable in all analyses.

Assumptions

Several baseline variables (PHQ-9, GAD-7, CCI, and Supermarket egocentric performance) deviated from normality based on Shapiro–Wilk tests (see *Table 1*). Outliers were identified using boxplots and classified according to SPSS conventions (1.5 × IQR for outliers; 3 × IQR for extreme outliers) (see *Table 2*), and were retained as plausible within bounded symptom and cognitive scales rather than indicative of data entry error.

Regression assumptions were therefore evaluated using scatterplots and normal P–P plots of standardised residuals for each model, which indicated acceptable linearity, homoscedasticity, and approximately normal residual distributions. Minor deviations are expected with the use of longitudinal change scores and small sample size. Bootstrapped confidence intervals and data transformations were

explored but not retained due to instability with the small APOE ε4 subsample. Analyses therefore used untransformed change scores, and findings were interpreted with appropriate caution.

For moderation analyses, interaction terms between sleep change variables and APOE ε4 status were entered into relevant linear regression models to test whether carrier status moderated associations between changes in sleep and psychological wellbeing. Assumptions for these models were evaluated using the same residual-based examination and were considered adequately met.

Research Question 1

To examine changes in sleep characteristics over time, and whether these changes differed as a function of APOE ε4 carrier status, a series of repeated-measures analyses of variance (RM-ANOVAs) were conducted. Time (baseline vs. follow-up) was entered as a within-subjects factor, and APOE ε4 status (carrier vs. non-carrier) as a between-subjects factor.

Research Question 2

To examine longitudinal associations between changes in sleep and psychological wellbeing, a linear regression analysis using change scores was conducted in the full sample. This allowed examination of whether changes in sleep quality were associated with changes in depressive symptoms (PHQ-9), anxiety symptoms (GAD-7), and mental health–related quality of life (SF-12 Mental Component Summary). Where associations were identified, moderation analyses were subsequently conducted to test whether effects differed by APOE ε4 status.

Research Question 3

To examine whether APOE ε4 status moderated associations between changes in sleep quality and changes in cognitive functioning, including subjective cognition (CCI), visuospatial memory (ROCFT Immediate Recall), and spatial navigation performance (Supermarket Task, egocentric and allocentric measures), a linear regression analysis was conducted, with sleep variables mean-centred before analysis.

Change scores for sleep variables were entered as predictors, and change scores for cognitive outcomes were entered as dependent variables. Given the modest sample size for actigraphy-derived

parameters and the reduced power associated with interaction testing, models were first conducted in the full sample without APOE ε4 status to identify any sleep–cognition associations before testing moderation effects. Follow-up analyses were conducted, repeating the model with a sleep x APOE ε4 interaction, and another analysis additionally adjusting for age and sex.

Statistical significance was set at $\alpha = .05$ (two-tailed). Effect sizes are reported alongside p-values, and where applicable, model fit indices and confidence intervals are presented.

Results

Sample Characteristics

A total of 38 participants completed the questionnaire and cognitive components. Of these, 32 participants also completed the actigraphy, and comparable actigraphy baseline data were available for 18 participants.

Participants had a mean age of 72.9 years (SD = 6.6, range = 62–93). The sample included 11 male (28.9%) and 27 female participants (71.1%). Fourteen participants (36.8%) were APOE-ε4 carriers, while 24 participants (63.2%) were non-carriers.

Research question 1

Subjective Sleep Quality

There was a significant main effect of time on subjective sleep quality (PSQI), indicating that PSQI scores increased from baseline to follow-up (see *Table 3*). There was no main effect of APOE ε4 carrier status, and no time × APOE ε4 interaction, indicating that subjective sleep quality did not differ by genotype and that change over time was comparable for carriers and non-carriers (See *Table 4).*

Objective Sleep

There was a significant main effect of time for sleep duration and sleep efficiency, both of which increased from baseline to follow-up (see *Table 3*). Sleep fragmentation did not change significantly over time. Across objective sleep outcomes, there was no main effect of APOE ε4 carrier status and no time ×

APOE ε4 interaction, indicating no evidence that objective sleep differed by genotype or changed differently over time for carriers versus non-carriers (See *Table 4).*

Assumptions

RM-ANOVA assumptions were assessed and were adequately met (Levene's tests, all ps > .05). Normality of residuals was considered acceptable based on visual inspection of residual plots, and sphericity was assumed given the two time points. Analyses were restricted to participants with complete baseline and follow-up actigraphy data.

Table 3

Descriptive Statistics for Sleep Outcomes by APOE ε4 Carrier Status and Time

Outcome	APOE ε4 Status	Baseline M (SD)	Follow-up M (SD)
Subjective Sleep Quality (PSQI)	Non-carrier	5.21 (2.75)	6.54 (3.93)
	ε4 carrier	5.29 (2.84)	6.36 (3.15)
Sleep Duration (minutes)	Non-carrier	398.69 (24.06)	439.81 (25.99)
	ε4 carrier	403.38 (39.55)	414.89 (29.97)
Sleep Efficiency (%)	Non-carrier	77.29 (4.45)	81.84 (4.68)
	ε4 carrier	77.10 (4.85)	79.93 (6.57)
Sleep Fragmentation Index	Non-carrier	34.25 (9.87)	29.83 (12.73)
	ε4 carrier	35.01 (14.10)	39.09 (12.17)

Table 4

Repeated-Measures ANOVA Results for Sleep Variables by APOE

Outcome	Effect	F(df1, df2)	p	ηp^2
Subjective Sleep Quality (PSQI)	Time	F(1, 36) = 4.97	.032*	.12
	APOE ε4	F(1, 36) = 0.003	.956	.000
	Time × APOE ε4	F(1, 36) = 0.06	.810	.002
Sleep Duration (min)	Time	F(1, 16) = 12.38	.003*	.44

	APOE ε4	F(1, 16) = 0.68	.422	.041
	Time × APOE ε4	F(1, 16) = 3.92	.065	.20
Sleep Efficiency (%)	Time	F(1, 16) = 5.59	.031*	.259
	APOE ε4	F(1, 16) = 0.31	.585	.019
	Time × APOE ε4	F(1, 16) = 0.30	.590	.019
Sleep Fragmentation Index	Time	F(1, 16) = 0.003	.961	.000
	APOE ε4	F(1, 16) = 1.12	.306	.065
	Time × APOE ε4	F(1, 16) = 1.61	.222	.091

Moderate to large effect sizes for the main effect of time were observed, reflecting a trend toward improved subjective quality, sleep duration and sleep efficiency (see *Table 4*). However, the absence of significant interaction effect sizes for subjective sleep quality and sleep efficiency indicated that this change was not differentially associated with APOE ε4 status. The Time × APOE ε4 for sleep duration was non-significant but observed to have a larger effect size. This should be interpreted cautiously given the sample size.

Research Question 2

Subjective Sleep

Worsening subjective sleep quality (increases in PSQI) significantly predicted increases in depressive symptoms (PHQ-9) and anxiety symptoms (GAD-7) at follow-up. Associations with mental health–related quality of life (SF-12 MCS) were not significant. Results are presented in *Table 5*.

Across models, no significant sleep × APOE ε4 interactions were observed; the PSQI X APOE interaction did not significantly predict changes in PHQ-9 (B = 0.149, SE = 0.251, β = .10, p = .558) or GAD-7 (B = 0.269, SE = 0.208, β = .21, p = .204).

Objective Sleep

Changes in actigraphy-derived sleep outcomes (efficiency, duration and fragmentation) were not significantly associated with changes in psychological wellbeing (PHQ-9, GAD-7 and SF-12 MCS). Sleep

efficiency showed a non-significant trend with depressive symptom change, such that reductions in sleep efficiency were associated with increases in PHQ-9 scores, although this did not reach statistical significance. Results are presented in *Table 5*.

Table 5

Linear Regression Analyses Examining Changes in Sleep and Psychological Wellbeing

Sleep variable	Outcome	B	SE	β	p
Subjective sleep					
PSQI	PHQ-9	0.445	0.115	.54	< .001*
PSQI	GAD-7	0.227	0.109	.33	.044*
PSQI	SF-12 (MCS)	0.440	0.320	.23	.178
Objective sleep					
Sleep efficiency	PHQ-9	−0.270	0.680	−.42	.079
Sleep efficiency	GAD-7	−0.060	0.070	−.21	.399
Sleep efficiency	SF-12 (MCS)	0.161	0.222	.19	.481
Sleep duration	PHQ-9	0.000	0.000	−.15	.556
Sleep duration	GAD-7	4.48×10^{-5}	0.000	.05	.852
Sleep duration	SF-12 (MCS)	0.001	0.001	.33	.212
Sleep fragmentation	PHQ-9	0.020	0.033	.15	.592
Sleep fragmentation	GAD-7	0.020	0.033	.15	.547
Sleep fragmentation	SF-12 (MCS)	0.020	0.110	.06	.838

Note. Higher PSQI scores reflect poorer subjective sleep quality

Sensitivity analysis

Models were repeated with covariates (age, sex and APOE-4; see *Table 6*).

Research Question 3

Subjective Sleep Quality

Changes in subjective sleep quality (PSQI) were not significantly associated with longitudinal changes in s subjective cognition (CCI), visuospatial memory (ROCFT Immediate Recall), and egocentric navigation performance and allocentric navigation performance (Supermarket task), (all *ps* > .10). Effect sizes were

small, with models explaining between 0.2% and 7.0% of the variance in cognitive change outcomes. Visual inspection of residual plots and normal P–P plots indicated no major violations of linearity, homoscedasticity, or normality, and collinearity diagnostics were within acceptable limits (VIFs = 1.00 across models).

Objective Sleep Parameters

Changes in objectively measured sleep duration, sleep efficiency, and sleep fragmentation were not significantly associated with longitudinal changes in subjective cognitive decline (CCI) or visuospatial memory performance (ROCFT Immediate Recall) *(all* s > .30*)*, and were similarly not associated with changes in egocentric or allocentric spatial navigation performance. Across allocentric navigation models, age and sex accounted for a significant proportion of variance in performance change; however, sleep parameters did not contribute additional explanatory value, and interaction effects remained non-significant (ΔR^2s ≤ .036, all ps > .366). Given the smaller subsample available for actigraphy-based analyses, findings should be interpreted with caution.

Summary of Findings

Across subjective and objective sleep measures, there was no evidence that changes in sleep were associated with changes in cognitive performance over time, and no evidence that these relationships differed by APOE ε4 status. Findings remained non-significant when models were repeated to include APOE ε4 (*Table 8*) and covariates (*Table 9*).

Table 7

Changes in Sleep and Cognitive outcomes

Sleep predictor	Cognitive outcome	B	β	R^2	p
Subjective Sleep					
PSQI	CCI	0.56	.26	.070	.109
PSQI	ROCFT Immediate Recall	−0.30	−.18	.034	.269
PSQI	Supermarket Egocentric	−0.07	−.04	.002	.800
PSQI	Supermarket Allocentric	−0.48	−.17	.028	.326

Objective Sleep					
Sleep Duration	CCI	-.04	-.31	.10	.205
Sleep Fragmentation	CCI	0.10	.40	.16	.103
Sleep Efficiency	CCI	-0.18	-.31	.09	.216
Sleep Duration	ROCFT Immediate Recall	.01	.03	.001	.900
Sleep Fragmentation	ROCFT Immediate Recall	.10	.26	.068	.295
Sleep Efficiency	ROCFT Immediate Recall	-.07	-.80	.006	.751
Sleep Duration	Supermarket Egocentric	-.04	-.24	.055	.347
Sleep Fragmentation	Supermarket Egocentric	-.001	-.004	.000	.988
Sleep Efficiency	Supermarket Egocentric	-.10	-.12	.013	.649
Sleep Duration	Supermarket Allocentric	-.03	-.13	.017	.611
Sleep Fragmentation	Supermarket Allocentric	.03	.044	.002	.864
Sleep Efficiency	Supermarket Allocentric	-.34	-.256	.066	.305

Discussion

This study explored longitudinal relationships between sleep, psychological wellbeing and cognitive functions in cognitively healthy older adults with and without APOE ε4 genetic risk for Alzheimer's disease. Contrary to initial hypotheses, APOE ε4 status did not predict longitudinal changes in subjective or objective sleep, nor did it moderate associations between sleep and cognitive outcomes. In contrast, worsening subjective sleep quality and reductions in actigraphy-derived sleep efficiency were associated with poorer psychological wellbeing over time. Overall, sleep-cognition associations were not detectable in this sample, whereas sleep-psychological wellbeing associations were more consistent.

Findings did not support the hypothesis that APOE ε4 carriers would show greater decline in sleep quality over time. Carriers and non-carriers demonstrated broadly similar patterns of sleep quality change, suggesting that age-related processes rather than genetic risk may account for observed changes in cognitively healthy older adults. One possible explanation is that genetically related differences become more apparent closer to the onset of cognitive difficulties, or in combination with other biological risk factors not examined in this study.

In line with the second hypothesis, declines in subjective sleep quality predicted increases in depressive and anxiety symptoms, independent of participants' APOE ε4 status. Reductions in actigraphy-derived sleep efficiency also predicted worsening mood symptoms. These findings are clinically relevant in older adulthood, where affective symptoms are common and may contribute to subjective cognitive concerns. For example, Saint Martin et al. (2012) reported largely null sleep-cognition associations and found that subjective cognitive complaints were more strongly related to anxiety and depression than to subjective sleep quality. Wider evidence also suggests that psychological symptoms can precede dementia and may be associated with subsequent cognitive decline (Da Silva et al., 2013), although the current study cannot determine whether affective symptoms are early markers of neurodegenerative change. Notably, associations between sleep efficiency and psychological outcomes were observed after controlling for age and sex, suggesting that demographic factors accounted for meaningful variance and that adjustment likely improved sensitivity to detect sleep-mood relationships.

The third hypothesis was not supported, finding no sleep × APOE ε4 interaction across cognitive outcomes, and with findings remaining the same when the analyses were repeated with covariates. Several factors could explain these null findings. First, participants remained cognitively healthy at baseline and follow-up, potentially limiting the ability to detect small or subtle cognitive changes. Consistent with this, Kronholm et al. (2009) found that sleep variables often explain only a small proportion of variance in objective cognitive performance in large community samples, and when analyses were repeated in a healthier subgroup and adjusted for sociodemographic factors, sleep duration was no longer associated with objective cognition. This highlights that sleep–cognition associations can be influenced by health factors and confounding factors. Second, sleep-cognition associations may be sensitive to how sleep is measured and may be clearer when looking at sleep continuity or in individuals with greater cognitive vulnerability. This interpretation is consistent with the broader literature showing heterogeneous findings, like studies reporting small or non-linear associations between self-reported sleep duration and cognition (Blackwell et al., 2011), and others reporting largely null findings in cognitively healthy older adults (Saint Martin et al.,

2012). Prospective studies indicate that sleep continuity and variability may be more sensitive predictors of later cognitive impairment and risk of developing dementia, including actigraphy-derived sleep latency and variability in sleep duration (Diem et al., 2016; Kiel et al., 2023).

Strengths and Limitations

Several limitations should be considered. The actigraphy sample was smaller than the subjective sleep, psychological, and cognitive samples, reducing power for objective sleep effects and increasing vulnerability to individual variability. The use of change scores may also have introduced additional measurement error in a modestly sized longitudinal sample, potentially limiting sensitivity to detect small effects.

Strengths include the longitudinal design, allowing the examination of within-person changes over time, and the inclusion of both objective and subjective sleep measures, addressing a limitation identified in the systematic review. To the author's knowledge, this study is among the first to examine longitudinal interrelationships between sleep quality, psychological wellbeing, and early cognitive markers in relation to APOE ε4 status in cognitively healthy older adults.

Conclusion

APOE ε4 status did not predict sleep change over time or moderate sleep-cognition associations in this cognitively healthy sample. However, worsening sleep, particularly in subjective sleep quality and sleep efficiency, was associated with poorer psychological wellbeing. These findings support sleep as a clinically relevant and potentially modifiable factor for mental health in later life. Findings further suggest that detecting sleep-cognition associations in genetically vulnerable and healthy samples may require larger samples, longer follow-up periods or more sensitive indices of sleep continuity and variability.

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Chapter 5: Extended Discussion and Critical Evaluation Chapter

Discussion and Critical Evaluation

The aim of this thesis portfolio was to examine the role of sleep in cognitive functioning and psychological wellbeing in later life, with particular consideration of genetic risk for Alzheimer's disease. Sleep disturbances are highly prevalent in older adulthood and have been linked to poorer mental health and increased risk of cognitive decline (Baglioni et al., 2016; Musiek et al., 2022; Scott et al., 2021; Schubert et al., 2002; Wu et al., 2017). However, important gaps remain regarding which sleep parameters are most relevant to specific cognitive domains, and whether genetic vulnerability modifies these associations.

To address these gaps, this thesis portfolio included two complementary studies. First, a systematic review which synthesised evidence on associations between sleep characteristics and visuospatial and spatial navigational performance in adults aged 50 years and older. Second, an empirical longitudinal follow-up study which examined whether changes in subjective and objective (actigraphy-derived) sleep were associated with changes in cognitive functioning and psychological wellbeing over time, and whether these associations were moderated by the APOE ε4 carrier status (a well-established genetic risk factor for Alzheimer's disease).

This chapter presents a critical evaluation of principal findings from both studies, an appraisal of the overall research process, including strengths, limitations, and methodological choices, and considers theoretical and clinical implications alongside recommendations for future research.

Principal Findings

Systematic Review

Across 17 studies, the systematic review found that the evidence was predominantly characterised by null findings, with only a few studies reporting associations between sleep parameters and visuospatial or navigation outcomes. Where associations were observed, they related to sleep continuity and sleep

architecture, such as sleep spindles, rather than other sleep parameters, like sleep duration. Overall, the findings revealed that sleep is not a consistent predictor of visuospatial memory or spatial navigation in adults aged 50 and above, with observed effects seen as small, task-specific and dependent on the type of sleep measures used. Several methodological limitations were also identified, particularly heterogeneity of sleep measures, cognitive tasks and sample characteristics, as well as the studies predominantly involving cross-sectional designs, which may limit inferences about directionality and change over time.

Taken together, this review suggests that future research would benefit from greater standardisation of sleep and spatial cognitive measures, as well as from longitudinal research designs that examine within-person change.

Empirical Study

The empirical study extended this review by using a longitudinal design in cognitively healthy adults previously genotyped for APOE ε4 status, with follow-up assessments conducted between three to five years after baseline, using the same measures to ensure direct comparison.

Overall, findings were again predominantly null for the domain of cognition. APOE ε4 status did not predict longitudinal changes in subjective or objective sleep quality, and did not moderate associations between sleep change and cognitive outcomes (subjective cognition, visuospatial memory and spatial navigation). In contrast, sleep was more consistently linked to psychological wellbeing. Declines in subjective sleep quality and sleep efficiency were associated with worsening depression and anxiety symptoms over time. APOE ε4 status did not moderate these associations, and effects for objectively measured sleep efficiency were evident only after controlling for age and sex, suggesting that demographic factors accounted for meaningful variance in psychological outcomes, and adjusted models improved sensitivity to detect these relationships.

Integrated Conclusion

When considered together, the systematic review and empirical study highlight similarities in finding no strong evidence for sleep predicting cognitive change over time, and that sleep may not be a robust predictor of measurable visuospatial and spatial navigational performance decline in cognitively healthy adults.

Additionally, empirical findings highlight that sleep appears more consistently linked to mental health outcomes than cognitive performance in this population. The portfolio therefore, enhances our understanding of sleep in later life by suggesting that sleep may be a more clinically actionable factor for emotional wellbeing than an early marker of decline in specific cognitive domains examined in the study. Although findings contrast with research linking sleep difficulties with global cognitive decline, it may be more of a reflection of the domain-specific focus of this thesis. Finally, much of the existing research focuses on global cognition, whereas visuospatial memory and spatial navigation may be influenced by different factors or may need different measurements to detect subtle longitudinal changes in healthy samples.

Strengths and Limitations

Strengths

A key strength of the empirical study was its longitudinal design, which addressed a gap identified in the systematic review where much of the evidence is cross-sectional. Additionally, the integration of subjective and objective sleep measures provided another strength, also mentioned in the limitations of the systematic review, where almost all studies relied on self-report or objective sleep measures in isolation. This strengthened the ecological validity of sleep assessment, allowing sleep data to be gathered in more naturalistic settings.

Another key strength involved the inclusion of psychological wellbeing measures alongside cognitive outcomes, which is rarely discussed alongside sleep-cognition literature. Finally, by focusing on visuospatial memory and spatial navigation, domains recognised as sensitive to early neurodegenerative change and

important for everyday independence, this portfolio addressed a gap in the literature that typically relies on global cognitive measures when examining sleep-cognition associations.

Limitations

Despite these strengths, several limitations must be acknowledged, and highlight directions for future research.

Sample Size and Power. Whilst a total of 32 participants completed actigraphy measures at follow-up, baseline data to compare with were only available for 18 participants. This smaller subsample size of actigraphy measures reduced power to detect associations involving objective sleep parameters and moderation testing. Null findings, especially for objective sleep measures and APOE ε4 interaction effects, should therefore be interpreted with caution.

Change Scores. Change scores were calculated by subtracting baseline values from follow-up values for sleep, psychological and cognitive outcomes. While this approach aligns with the portfolio's longitudinal aim, this could introduce additional measurement error and reduce sensitivity to detect small longitudinal associations. This is particularly relevant in this population, where the aim is to detect subtle preclinical changes in cognitively healthy individuals.

Cognitive Change. Finally, participants were cognitively healthy at baseline and follow-up, which is a strength when addressing preclinical ageing, but this also means that measurable cognitive change, especially in specific domains, may be small over a three to five-year prior. It is plausible that sleep-related cognitive effects may become more apparent when individuals begin to show more obvious signs of cognitive impairment nearer to the onset of neurodegenerative symptoms, or when sleep is considered alongside additional health factors or biological risk markers not measured in this study.

Theoretical and Clinical Implications

Overall, findings suggest that sleep problems may not be clear early warning signs of decline in visuospatial memory or navigation skills in cognitively healthy older adults. Although previous research links sleep difficulties to changes in the hippocampus and neurodegeneration (Bódizs et al., 2008; Nguyen et al., 2013), the predominantly null findings across both studies indicate that sleep efficiency, duration and fragmentation may not be sufficient on their own to produce measurable change in these cognitive measures within this population.

This thesis specifically examined visuospatial memory and spatial navigation, considered sensitive to early neurodegenerative change (Coughlan et al., 2018; Coughlan et al., 2019; Heo et al., 2010; Wang et al., 2024), as well as subjective cognition. However, no consistent longitudinal sleep-cognition associations were observed within these domains. A key implication is that sleep may not operate as a standalone predictor of visuospatial and navigational cognitive decline. Instead, future models may need to integrate sleep alongside other factors, such as biological markers, physical health and psychological wellbeing.

More consistent associations were found between sleep quality and psychological wellbeing, with poorer sleep linked to worsening depressive and anxiety symptoms over time. These findings align with established evidence linking sleep disturbances with low mood in older adults (Baglioni et al., 2016; Scott et al., 2021), and suggest that sleep may play a more immediate role in emotional stability than in cognitive change.

The absence of APOE ε4 moderation in the empirical study further suggests that genetic vulnerability does not necessarily strengthen sleep–cognition associations in cognitively healthy adults, when using the current measures. It may be that APOE-related differences may emerge later, or that more sensitive sleep measures are needed to detect early biological changes.

The most consistent finding in this portfolio was that poorer sleep was associated with worsening psychological wellbeing over time, consistent with the wider evidence. These findings highlight the value of routine sleep assessments in older adults, especially when presenting with mood difficulties. With studies

suggesting that affective symptoms can precede dementia diagnosis (Da Silva et al., 2013), addressing sleep disturbances could support psychological wellbeing and possibly reduce affective disorders. Importantly, this portfolio does not demonstrate that improving sleep could prevent cognitive decline, but rather strengthens the idea that sleep is a modifiable target that could support emotional resilience and quality of life in ageing populations, including those with elevated genetic risk.

Suggestions for Future Research

Future research would benefit from longer follow-up intervals and multiple assessment periods, to determine whether sleep-related cognitive changes emerge over extended time frames. Additionally, larger samples with increased statistical power are also needed to detect small effects, particularly when examining moderation effects of APOE ε4 status. This could be done whilst also combining actigraphy with sleep-architecture measures, such as with PSG devices looking at spindles, whilst incorporating relevant health markers to better identify conditions under which sleep relates to cognition.

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- Up to six keywords;
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Appendix B: Ethical Approval Letter for the Empirical Research Paper

University of East Anglia

Study title: Longitudinal investigation of the interrelationships between sleep, mental health and cognition and their modulation by the genetic risk of Alzheimer's Disease in older adults

Application ID: ETH2425-0281

Dear Romane,

Your application was considered on 20th December 2024 by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee).

The decision is: **approved**.

You are therefore able to start your project subject to any other necessary approvals being given.

This approval will expire on **30th September 2026**.

Please note that your project is granted ethics approval only for the length of time identified above. Any extension to a project must obtain ethics approval by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) before continuing.

It is a requirement of this ethics approval that you should report any adverse events which occur during your project to the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) as soon as possible. An adverse event is one which was not anticipated in the research design, and which could potentially cause risk or harm to the participants or the researcher, or which reveals potential risks in the treatment under evaluation. For research involving animals, it may be the unintended death of an animal after trapping or carrying out a procedure.

Any amendments to your submitted project in terms of design, sample, data collection, focus etc. should be notified to the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) in advance to ensure ethical compliance. If the amendments are substantial a new application may be required.

Approval by the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee) should not be taken as evidence that your study is compliant with the UK General Data Protection Regulation (UK GDPR) and the Data Protection Act 2018. If you need guidance on how to make your study UK GDPR compliant, please contact the UEA Data Protection Officer (dataprotection@uea.ac.uk).

Please can you send your report once your project is completed to the FMH S-REC (fmh.ethics@uea.ac.uk).

I would like to wish you every success with your project.

On behalf of the FMH S-REC (Faculty of Medicine and Health Sciences Research Ethics Subcommittee)

Yours sincerely,

Dr Paul Linsley

Ethics ETH2425-0281 : Miss Romane De Tauzia-Lahiner

Appendix C: Participant Information Sheet

School of Psychology

Title of research: Longitudinal investigation of the interrelationships between sleep, mental health and cognition and their modulation by the genetic risk of Alzheimer's Disease in older adults

Participant Information Sheet

Thank you for showing interest in our study. Please take the time to read the following information thoroughly before deciding whether to participate. You may reach out and ask any questions you might have or if you need further information (this document is yours to keep).

What is the purpose of this study?

We are interested in investigating how sleep quality affects people over a long period of time. Specifically, we are interested in whether there are changes in cognitive abilities and mental health changes in people with a genetic risk of dementia.

Why have I been asked to participate?

Having previously participated in the pilot study and consented to being contacted for future studies, we would like to do a follow up on this data to see how measures of sleep, cognition and mental wellbeing have changed this then.

Do I have to participate?

It is up to you whether you chose to take part in this study after reading through the description of the study in this document. You will be asked to provide written informed consent before participating, and you are free to withdraw at any time, without giving a specific reason or it is affecting you in any way.

What will happen if I take part in this study?

If you agree to take part, you will complete several online questionnaires and neuropsychological tasks which will measure your mental health, cognitive function, and sleep quality. You will have one week to complete these questionnaires and tasks remotely, with an additional 48 hours to complete one of the cognitive tests online via Teams with a facilitator. Additionally, you will be asked whether you are willing to wear an

actigraphy device, in the shape of a wristwatch, for one week to monitor sleep patterns and complete a daily sleep diary. Please note that many factors can explain performance on certain tests, and that researchers on this team are not trained to interpret neuropsychological tests in a clinical setting or offer a clinical diagnosis.

Are there any risks in taking part?

Filling out questionnaires and taking part in online cognitive tasks, may cause some fatigue, but you will be given plenty of time to complete these and allow for regular breaks. Some questions about your mental health and sleep may cause some emotional discomfort for certain participants. In taking part in the actigraphy measures you may experience some mild discomfort from wearing the watch over the week, for which you will be compensated 10GBP in the form of a voucher. If you experience any inconvenience or issues during the study, you can choose to stop at any time. If any participant discloses information indicating immediate risk of harm to themselves or others, the research team will follow safeguarding procedures, including contacting emergency services if necessary.

Are there any benefits from taking part?

While you will not directly benefit, your participation will contribute to valuable research for the field of sleep and dementia.

If you would like to request feedback regarding your subjective and objective sleep measures from the questionnaires and actigraphy measures you undertook, please contact the lead researcher. Please note that the feedback will not serve as a way to receive clinical advice, assessment or treatment.

Will my information be kept confidential?

Yes, all identifiable personal data you provide (such as your name, phone number, and email) will be anonymized and stored securely in accordance with the General Data Protection Regulation (GDPR) and the Data Protection Act (2018). The research team will have access to your anonymized study data, which will be identified by an alphanumeric code rather than personal details, for the duration of this study. The Principal Investigator will be responsible for the anonymous research data (data collected from questionnaires and tests), which will be stored indefinitely to adhere to open practice standards. Any identifiable personal information, including consent forms, will be stored separately in a password-protected file and will be securely disposed of once it is no longer needed.

How will the data be used?

The information collected will be kept for future scientific research and could be presented at scientific conferences and published in scientific journals. Your name or any identifying details will never appear in any public documents. The results presented will be based on group data, ensuring that your individual information remains confidential.

What happens if I agree to take part, but change my mind later?

You can withdraw from the study at any time during the study, and without providing a reason, and your data will be destroyed. Your decision to withdraw will not affect your relationship with the establishment.

How do I know that this research is safe for me to take part in?

All research conducted at the University is reviewed by an independent group of people, known as a Research Ethics Committee. This committee ensures that the study follows to strict ethical standards and that your participation is safe. The study will seek ethics approval from the FMH Research Ethics Committee at the University of East Anglia. This approval means that the study has been carefully evaluated for potential risks and benefits, and safeguards are in place to protect you throughout your participation.

Will I receive compensation for participating?

You will receive compensation of 10GBP in the form of a voucher for your time and any inconvenience caused by wearing the actiwatch. If you withdraw from the study after having taking part in some of the testing, your compensation will not be affected.

What if I have more questions?

If you have any further questions or concerns, you can contact the research team. Please see details below.
You are under no obligation to agree to take part in this research. If you do agree you can withdraw at any time without giving a reason.

Researchers contact details:

Dr Alpar Lazar, Principal Investigator & Project Supervisor, a.lazar@uea.ac.uk

Romane de Tauzia, ClinPsyD Lead Researcher r.detauzia@uea.ac.uk

Dr Sarah Reeve, Research Supervisor a.lazar@uea.ac.uk

Dr Michael Hornberger, Research Supervisor,

Please feel free to contact us if you have any worries or concerns about this research. Please feel free to contact us if you have any worries or concerns about this research.

Appendix D: Consent Form

School of Psychology

University of East Anglia

Consent form

Title of Research Project: Longitudinal investigation of the interrelationships between sleep, mental health and cognition and their modulation by the genetic risk of Alzheimer's Disease in older adults

Researcher: Romane de Tauzia, ClinPsyD Lead Researcher

Please tick each box with an **X**

1. I confirm that I have read and understood the Participant Information Sheet for the above study and have had the opportunity to ask questions and have had these answers satisfactorily. ☐
2. I understand that my participation is voluntary, and I can withdraw from the study at any time without giving a reason, and without any negative consequences ☐
3. I understand how my data will be kept confidential and protected, and that no personal information will be shared outside of the research team or published in any final report(s) from the research ☐
4. I understand that the information collected about me will be used to support other research in the future and may be shared anonymously with other researchers. ☐
5. I am aware of any potential risks or discomforts and benefits of participating in this study. ☐
6. I agree to take part in the above study. ☐

Participant's signature …… Date……

Researchers contact details:

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Appendix E: Measures

The Patient Health Questionnaire (PHQ-9)

PHQ-9

Over the last 2 weeks, how often have you been bothered by any of the following problems?	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

The Generalised Anxiety Disorder Assessment (GAD-7)

GAD-7

Over the last 2 weeks, how often have you been bothered by any of the following problems?	**Not at all**	**Several days**	**More than half the days**	**Nearly every day**
1. Feeling nervous, anxious, or on edge	0	1	2	3
2. Not being able to stop or control worrying	0	1	2	3
3. Worrying too much about different things	0	1	2	3
4. Trouble relaxing	0	1	2	3
5. Being so restless that it's hard to sit still	0	1	2	3
6. Becoming easily annoyed or irritable	0	1	2	3
7. Feeling afraid as if something awful might happen	0	1	2	3

The Short Form Health Survey (SF-12)

SF-12 Health Survey

INSTRUCTIONS: this survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Please answer every question by marking one box. If you are unsure about how to answer, please give the best answer you can.

---

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
☐	☐	☐	☐	☐

The following items are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much?

	Yes, Limited A Lot	Yes, Limited A Little	No, Not Limited At All
2. Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐	☐	☐
3. Climbing several flights of stairs	☐	☐	☐

During the <u>past 4 weeks</u>, have you had any of the following problems with your work or other regular daily activities <u>as a result of your physical health?</u>

	Yes	No
4. Accomplished less than you would like	☐	☐
5. Were limited in the kind of work or other activities	☐	☐

	Yes	No
6. Accomplished less than you would like	☐	☐
7. Didn't do work or other activities as carefully as usual	☐	☐

During the <u>past 4 weeks</u>, have you had any of the following problems with your work or other regular daily activities <u>as a result of any emotional problems</u> (such as feeling depressed or anxious)?

8. During the last 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

Excellent	Very good	Good	Fair	Poor
☐	☐	☐	☐	☐

These questions are about how you feel and things have been with you <u>during the past 4 weeks</u>. For each question, please give the one answer that comes closest to the way you have been feeling.
How much of the time during <u>the past 4 weeks</u> –

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	None of the Time
9. Have you felt calm and peaceful?	☐	☐	☐	☐	☐
10. Did you have a lot of energy	☐	☐	☐	☐	☐
11. Have you felt downhearted and blue?	☐	☐	☐	☐	☐

12. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	Most of the time	Some of the time	A little of the time	None of the time
☐	☐	☐	☐	☐

Pittsburgh Sleep Quality Index (PSQI)

Instructions: The following questions relate to your usual sleep habits during the past month only. Your answers should indicate the most accurate reply for the majority of days and nights in the past month. **Please answer all questions**.

1. During the past month, what time have you usually gone to bed at night? _____
2. During the past month, how long (in minutes) has it usually taken you to fall asleep each night? _____
3. During the past month, what time have you usually gotten up in the morning? _____
4. During the past month, how many hours of actual sleep did you get at night? (This may be different than the number of hours you spent in bed.) _____

5. During the past month, how often have you had trouble sleeping because you…	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week
a. Cannot get to sleep within 30 minutes				
b. Wake up in the middle of the night				
c. Have to get up to use the bathroom				
d. Cannot breathe comfortably				
e. Cough or snore loudly				
f. Feel too cold				
g. Feel too hot				
h. Have bad dreams				
i. Have pain				
j. Other reason(s), please describe:				
6. During the past month, how often have you taken medicine to help you sleep (prescribed or "over the counter")?				
7. During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?				

	No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem
8. During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?				
	Very good	Fairly good	Fairly bad	Very bad
9. During the past month, how would you rate your sleep quality overall?				

Karolinska Sleep Diary (KSD)

Instructions: Please refer to your last overnight sleep episode, i.e. not a daytime nap, when answering the following questions. Please indicate whether the time is am or pm.

What time did you go to bed?		AM/PM
What time did you try starting to sleep at?		AM/PM
How long did it take you to fall asleep? (min)		
How many times did you wake up?		
How long were you awake for? (min) Please estimate the time and duration of each night awakening.		
What time did you wake up?		AM/PM
What time did you get up?		AM/PM
Did your alarm clock wake you up?		
Did you do any strenuous activity during the last 24 hours (if yes, please specify)		

How would you rate your quality of sleep?

Best sleep ever **Worst sleep ever**

1 2 3 4 5 6 7 8 9

How difficult did you find to wake up/get up?

1 2 3 4 5 6 7 8 9

Very easy **Quite hard**

Cognitive Change Index (CCI-20-S) (Self-Report Version)

Participant identification code ..... Date of birth ...../...../.....

A. Do you feel like your memory is becoming worse? (Check only one)

☐ No ☐ Yes, but this does not worry me ☐ Yes and this worries me

B. Instructions:

This self-rating scale asks about your abilities, problem areas, daily functioning and activities. Please rate your **current** level of ability **compared to 5 years ago** and the severity of any current problems. Remember, you are describing how you are functioning now (meaning during the past month including today) compared to 5 years ago. Please rate any changes in your ability on the following 5-point scale, choosing the best fitting rating for each item describing a cognitive function or ability:

1. **Normal Ability (No Change or Better than 5 years ago):** not a problem; no effect on daily activities; no assistance needed

2. **Slight/Occasional Problem (Minimal Change from 5 years ago):** subtle; occurs less than once a week; may be slightly slower or less efficient; no assistance needed with ability; probably not noticeable to most other people

3. **Mild Problem (Some Change from 5 years ago):** A bit worse, may perform related activity more slowly or less efficiently; occasionally may need a little help; may be noticeable to others

4. **Moderate Problem (Clearly Noticeable Change from 5 years ago):** frequent problem; may affect complex activities on a daily basis or several times per week; often needs some assistance to perform complex activity

5. **Severe Problem (Much Worse than 5 years ago):** continuous problem; unable to independently perform complex activity; requires ongoing assistance or supervision

Circle the number that best fits your current ability level compared to 5 years ago, using the scale from 1 to 5 below. Select the best choice for each item and *please do not skip any questions*:

Normal Ability	**Slight/Occasional Problem**	**Mild Problem**	**Moderate Problem**	**Severe Problem**
No Change *(compared to 5 years ago)*	Minimal Change *(compared to 5 years ago)*	Some Change *(compared to 5 years ago)*	Clearly Noticeable Change *(compared to 5 years ago)*	Much Worse *(compared to 5 years ago)*
1	2	3	4	5

1. Recalling information when I really try	1	2	3	4	5
2. Remembering names and faces of new people I meet:	1	2	3	4	5

3. Remembering things that have happened recently:	1	2	3	4	5
4. Recalling conversations a few days later:	1	2	3	4	5
5. Remembering where things are usually kept:	1	2	3	4	5
6. Remembering new information told to me:	1	2	3	4	5
7. Remembering where I placed familiar objects:	1	2	3	4	5
8. Remembering what I intended to do:	1	2	3	4	5
9. Remembering names of family members and friends:	1	2	3	4	5
10. Remembering without notes and reminders:	1	2	3	4	5
11. People who know me would find that my memory is:	1	2	3	4	5
12. Remembering things compared to my age group:	1	2	3	4	5
13. Making decisions about everyday matters:	1	2	3	4	5
14. Reasoning through a complicated problem:	1	2	3	4	5
15. Focusing on goals and carrying out a plan:	1	2	3	4	5
16. Shifting easily from one activity to the next:	1	2	3	4	5
17. Organizing my daily activities:	1	2	3	4	5
18. Understanding conversations:	1	2	3	4	5

19. Expressing myself when speaking:	1	2	3	4	5
20. Following a story in a book, movie or TV:	1	2	3	4	5

Appendix F: Debrief form

School of Psychology

Debrief Form

Study Title: Longitudinal investigation of the interrelationships between sleep, mental health and cognition and their modulation by the genetic risk of Alzheimer's Disease in older adults

Thank you for participating in our study!

Purpose of the Study: The purpose of this study is to investigate how sleep quality and the APOE-ε genotype interact to influence psychological wellbeing, as well as cognitive functions such as memory and spatial navigation in older adults. This study will help us understand the potential early markers and predictors of dementia onset.

Further Information: If you have any questions or concerns regarding this study, please feel free to contact the researcher of project supervisors.

Support: If participating in this study has raised any issues or concerns for you, we recommend seeking support from your General Practitioner, as they will be able to signpost you to local resources in your area. Information on additional resources and support services can also be found on the resources pack poster provided.

Thank You! We sincerely appreciate your time and effort in contributing to this research. Your participation is invaluable.

Researchers contact details:

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Romane de Tauzia, ClinPsyD Lead Researcher r.detauzia@uea.ac.uk

Dr Sarah Reeve, Research Supervisor a.lazar@uea.ac.uk

Dr Michael Hornberger, Research Supervisor,

Please feel free to contact us if you have any worries or concerns about this research. Many thanks again for your contribution!

Appendix G: Supplementary Results

Test of normality for baseline variables

Table 1

Test of normality for baseline variables

Variable	N	Shapiro–Wilk *W*	*p*
Sleep Efficiency Total Change	18	.931	.202
Sleep Fragmentation Total Change	18	.955	.503
Total Sleep Duration Change (minutes)	18	.929	.188
PSQI Total Change	35	.952	.127
PHQ-9 Total Change	35	.816	< .001
GAD-7 Total Change	35	.790	< .001
CCI Total Change	35	.828	< .001
ROCFT Immediate Total Change	35	.979	.743
Supermarket Egocentric Total Change	35	.876	< .001
Supermarket Allocentric Total Change	35	.973	.532
SF-12 Mental Health Total Change	35	.976	.641

Summary of findings

Shapiro–Wilk tests indicated significant departures from normality for several measures utilised in the analysis, including PHQ-9, GAD-7, CCI Total score, and Supermarket Egocentric (all *ps* < .05). In contrast, all other values did not significantly deviate from normality, including sleep duration, sleep efficiency, and sleep fragmentation index (all *ps* > .05).

Outliers Identified at Baseline

Table 2

Outliers Identified in Change Score Variables

Variable	N	Outliers (○)	Extreme Outliers (*)	Direction	Decision
PSQI Total Change	35	1	None	Upper	
PHQ-9 Total Change	35	1	None	Upper	
GAD-7 Total Change	35	3	4	Upper & Lower	Retained as Bounded symptom scale; higher scores plausible
CCI Total Change	35	3	1	Upper & Lower	Retained as in cognitive change index; high values plausible
SF-12 Mental Health Change	35	1	None	Upper	
Sleep duration change	35	1	None	Lower	

Note. Outliers (○) were defined as values exceeding 1.5 × IQR, and extreme outliers (*) as values exceeding 3 × IQR. Case numbers refer to SPSS-labelled observations.

Summary of findings

The presence of outliers was consistent with the expected distribution of symptom measures in a sample of largely cognitively healthy, community-dwelling older adults. Clustering at the lower end of scales with some occasional higher scores is common. This distribution likely reflects genuine individual differences rather than data errors or limitations of the measurement tools. Finally, removal of outliers would have further reduced an already modest sample size, increasing the risk of biased estimates and loss of clinically meaningful variance.

RQ2 Sensitivity Analysis (controlling for sex and age)

Table 6

Multiple Linear Regression Examining Changes in Sleep and Psychological Wellbeing for APOEe4 Carriers

Sleep variable	Outcome	B	SE	β	*p*
Subjective sleep					
PSQI	PHQ-9	0.55	0.19	.68	.016*
PSQI	GAD-7	0.24	0.16	.37	.169
PSQI	SF12 (MCS)	0.21	0.63	.10	.749
Objective sleep					
Sleep efficiency	PHQ-9	−0.30	0.11	−1.07	.036*
Sleep efficiency	GAD-7	−0.21	0.07	−.90	.033*
Sleep Efficiency	SF12 (MCS)	0.17	0.30	.34	.615
Sleep duration	PHQ-9	−0.001	<.001	−.73	.181
Sleep duration	GAD-7	<.001	<.001	−.56	.227
Sleep duration	SF12 (MCS)	0.002	0.001	1.32	.112
Sleep fragmentation	PHQ-9	0.08	0.09	.57	.376
Sleep fragmentation	GAD-7	0.07	0.06	.54	.315
Sleep fragmentation	SF12 (MCS)	0.05	0.24	.17	.844

Note. Higher PSQI scores reflect poorer subjective sleep quality

Summary of findings:

In these adjusted models, associations between subjective sleep quality (PSQI) and anxiety symptoms were no longer statistically significant, whereas reductions in objectively measured sleep efficiency emerged as significant predictors of both depressive and anxiety symptoms. This suggests that covariate adjustment influenced which sleep parameters were most strongly associated with psychological wellbeing.

RQ3 Linear Regression controlling for APOE ε4 Status (without age and sex)

Table 8

Summary of Sleep × APOE ε4 Interaction Effects on Cognitive Outcomes

Sleep Parameter	Cognitive Outcome	R^2	p
Subjective Sleep (PSQI)			
PSQI	CCI Total	.168	.278
PSQI	ROCFT Immediate Recall	.099	.348
PSQI	Supermarket Egocentric	.094	.837
PSQI	Supermarket Allocentric	.149	.059
Objective Sleep			
Sleep Duration	CCI	.261	.228
Sleep Efficiency	CCI	.238	.559
Sleep Fragmentation	CCI	.327	.195
Sleep Duration	ROCFT Immediate Recall	.006	.812
Sleep Efficiency	ROCFT Immediate Recall	.058	.396
Sleep Fragmentation	ROCFT Immediate Recall	.088	.638
Sleep Duration	Allocentric Navigation	.029	.750
Sleep Duration	Egocentric Navigation	.180	.790
Sleep Efficiency	Allocentric Navigation	.068	.968
Sleep Efficiency	Egocentric Navigation	.064	.957
Sleep Fragmentation	Allocentric Navigation	.052	.406
Sleep Fragmentation	Egocentric Navigation	.055	.728

Summary of findings

Controlling for APOE ε4 status did not meaningfully alter the pattern of findings for most of the models. Across both subjective and objective sleep parameters, sleep × APOE ε4 interaction terms remained

non-significant, and effect sizes were comparable to those observed in the baseline model as well as the covariate-adjusted analyses.

However, one trend-level effect emerged for subjective sleep quality (PSQI) in relations to allocentric navigation performance. The interaction term accounted approached statistical significance ($p = .059$) compared to the baseline model ($p = .326$) and the covariate-adjusted model ($p = .072$). However, this effect did not meet conventional threshold for significance and should therefore be interpreted with caution.

RQ3 Linear Regression with APOE moderation and Controlling for Age and Sex Covariates

Table 9

Summary of Subjective (PSQI) sleep × APOE ε4 Interaction Effects on Cognitive Outcomes (Adjusted for Age and Sex)

Sleep Parameter	Cognitive Outcome	R^2	p
Subjective Sleep (PSQI)			
PSQI	CCI Total	.171	.305
PSQI	ROCFT Immediate Recall	.140	.426
PSQI	Supermarket Egocentric	.100	.811
PSQI	Supermarket Allocentric	.328	.072
Objective Sleep			
Sleep Duration	CCI	.265	.264
Sleep Efficiency	CCI	.244	.576
Sleep Fragmentation	CCI	.373	.134
Sleep Duration	ROCFT Immediate Recall	.028	.840
Sleep Efficiency	ROCFT Immediate Recall	.066	.467
Sleep Fragmentation	ROCFT Immediate Recall	.104	.634
Sleep Duration	Allocentric Navigation	.440	.854
Sleep Duration	Egocentric Navigation	.256	.876
Sleep Efficiency	Allocentric Navigation	.460	.975
Sleep Efficiency	Egocentric Navigation	.118	.933
Sleep Fragmentation	Allocentric Navigation	.507	.366
Sleep Fragmentation	Egocentric Navigation	.112	.966

Summary of Findings

Across both subjective and objective sleep measures, no significant sleep × APOE ε4 interaction effects were observed for any cognitive outcome after adjusting for age and sex.