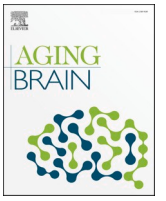
Aging Brain 6 (2024) 100130

Contents lists available at ScienceDirect

Aging Brain

journal homepage: www.elsevier.com/locate/nbas



Sleep discrepancy and brain glucose metabolism in community-dwelling older adults

Nadia Soh [a], Michael Weinborn [a,b], James D. Doecke [c], Rodrigo Canovas [d], Vincent Doré [d,e], Ying Xia [c], Jurgen Fripp [c], Kevin Taddei [f], Romola S. Bucks [a,g], Hamid R. Sohrabi [f,h,i], Ralph N. Martins [f,i], Melissa Ree [a], Stephanie R. Rainey-Smith [a,b,f,h,*]

[a] School of Psychological Science, University of Western Australia, Crawley, Western Australia, Australia
[b] Australian Alzheimer's Research Foundation, Sarich Neuroscience Research Institute, Nedlands, Western Australia, Australia
[c] Australian E-Health Research Centre, CSIRO, Herston, Queensland, Australia
[d] Australian E-Health Research Centre, CSIRO, Melbourne, Victoria, Australia
[e] Department of Molecular Imaging and Therapy, Centre for PET, Austin Health, Heidelberg, Victoria, Australia
[f] School of Medical and Health Sciences, Edith Cowan University, Joondalup, Western Australia, Australia
[g] School of Population and Global Health, University of Western Australia, Crawley, Western Australia, Australia
[h] Centre for Healthy Ageing, Health Futures Institute, Murdoch University, Murdoch, Western Australia, Australia
[i] Department of Biomedical Sciences, Macquarie University, New South Wales, Australia

ARTICLE INFO

Keywords:
Sleep
Sleep Discrepancy
Brain Health
Glucose Metabolism
Alzheimer's disease
FDG-PET

ABSTRACT

Sleep discrepancy (negative discrepancy reflects worse self-reported sleep than objective measures, such as actigraphy, and positive discrepancy the opposite) has been linked to adverse health outcomes. This study is first to investigate the relationship between sleep discrepancy and brain glucose metabolism (assessed globally and regionally via positron emission tomography), and to evaluate the contribution of insomnia severity and depressive symptoms to any associations. Using data from cognitively unimpaired community-dwelling older adults ($N = 68$), cluster analysis was used to characterise sleep discrepancy (for total sleep time (TST), wake after sleep onset (WASO), and sleep efficiency (SE)), and logistic regression was used to explore sleep discrepancy's associations with brain glucose metabolism, while controlling for insomnia severity and depressive symptoms. Lower glucose metabolism across multiple brain regions was associated with negative discrepancy for WASO and SE, and positive discrepancy for WASO only (large effect sizes; $\beta \geq 0.5$). Higher glucose metabolism in the superior parietal and posterior cingulate regions was associated with negative discrepancy for TST (large effect sizes; $\beta \geq 0.5$). These associations remained when controlling for insomnia severity and depressive symptoms, suggesting a unique role of sleep discrepancy as a potential early behavioural marker of brain health.

Abbreviations: OSA, obstructive sleep apnoea; TST, total sleep time; SE, sleep efficiency; WASO, wake after sleep onset.

* Corresponding author at: Centre for Healthy Ageing, Health Futures Institute, Murdoch University, 90 South Street, Murdoch, Western Australia 6150, Australia.

E-mail addresses: nadia.soh@research.uwa.edu.au (N. Soh), michael.weinborn@uwa.edu.au (M. Weinborn), james.doecke@csiro.au (J.D. Doecke), rodrigo.canovas@csiro.au (R. Canovas), vincent.dore@csiro.au (V. Doré), ying.xia@csiro.au (Y. Xia), jurgen.mejan-fripp@csiro.au (J. Fripp), k.taddei@ecu.edu.au (K. Taddei), romola.bucks@uwa.edu.au (R.S. Bucks), hamid.sohrabi@murdoch.edu.au (H.R. Sohrabi), ralph.martins@mq.edu.au (R.N. Martins), melissa.ree@uwa.edu.au (M. Ree), stephanie.raineysmith@murdoch.edu.au (S.R. Rainey-Smith).

https://doi.org/10.1016/j.nbas.2024.100130
Received 16 May 2024; Received in revised form 1 November 2024; Accepted 3 November 2024
Available online 20 November 2024

1. Introduction

Sleep discrepancy is the discordance between an individual's self-reported sleep compared to behavioural or physiological measures of sleep quantity/quality (e.g., sleep diaries or questionnaires vs. actigraphy or polysomnography). Greater sleep discrepancy is associated with adverse health outcomes, including insomnia [1], depression [2]), cognitive impairment [3], poor quality of life [4], and all-cause mortality [5]. Importantly, sleep discrepancy is common amongst older adults [6], with preliminary findings that greater sleep discrepancy is linked to poorer cognitive function [7,8]. However, research on sleep discrepancy and biomarkers of brain health in older adults is scant, despite evidence that indicators of brain pathology can precede observable cognitive decline by many years [9]. Therefore, the current study aims to explore sleep discrepancy in cognitively unimpaired community-dwelling older adults and its relationship to brain health as indexed by brain glucose metabolism measured with [18F]-fluoro-2-deoxyglucose positron emission tomography (FDG-PET).

Sleep discrepancy is typically operationalised using a difference score (e.g., sleep discrepancy = self-reported sleep – actigraphy-determined sleep) and may be evident across multiple parameters, including total sleep time (TST), sleep onset latency (SOL; i.e., amount of time taken to fall asleep), wake after sleep onset (WASO; i.e., amount of time spent awake after falling asleep), sleep efficiency (SE; i.e., ratio of TST to time in bed), and number of awakenings (NWAK) [10]. While a greater magnitude of discrepancy is often linked to worse health outcomes [4], discrepancy in a "negative" direction (i.e., where self-reported sleep is worse than suggested by behavioural or physiological measures), and discrepancy in a "positive" direction (i.e., where self-reported sleep is better than suggested by behavioural or physiological measures), have each been linked to somewhat distinct adverse health outcomes. For example, insomnia and depression have generally both been linked to negative discrepancy, while obstructive sleep apnoea (OSA) and cognitive decline have been associated with positive sleep discrepancy [11–13].

The existing literature appears to provide initial evidence for a relationship between sleep discrepancy and brain health [3,14–18]. For example, sleep discrepancy continues to increase in magnitude as neurodegenerative disease progresses, such as in early-moderate stage Alzheimer's disease (AD), where the predictive capacity of self-reported measures of sleep becomes virtually non-existent [15]. Furthermore, researchers have found sleep discrepancy to predict performance in certain cognitive domains, such as delayed memory, in older adult samples [7], including those with cognitive impairment [19]. Naturally, given the high incidence of sleep discrepancy, cognitive decline, and brain changes (e.g., due to neurodegeneration) in late life, it is reasonable to suggest that disruption to certain neural regions, such as those governing learning and memory (e.g., hippocampus), may be responsible for eliciting the cognitive dysfunction that underpins inaccurate reporting of one's sleep duration or quality, thus increasing sleep discrepancy. However, the mechanisms behind this proposed relationship between sleep discrepancy and brain changes have not been well-studied (nor the sleep measure – self-report or objective – that contributes most to the relationship determined), although it is speculated that sleep discrepancy may be a marker or risk factor for advancing neuropathology.

To our knowledge, prior studies investigating the relationship between sleep discrepancy and biomarkers of brain health are scarce, although some preliminary results have emerged. Specifically, a study by Kay et al. [20] evaluated the relationship between sleep discrepancy and brain glucose metabolism measured *during* sleep, finding that in both individuals with insomnia as well as "good sleepers" (N = 32 and 30, respectively), SOL discrepancy was associated with higher regional glucose metabolism across the right anterior insula and middle/posterior cingulate cortex. Notably, however, this sample was relatively young (i.e., mean ages of 37 and 39 for the insomnia and "good sleeper" groups, respectively). As such, while these findings provide initial evidence of a link between sleep discrepancy and biomarkers of brain health, it is difficult to interpret these results in the context of cognitive ageing and late-life neurodegenerative disease.

Recent research by Winer et al. [8] is perhaps more relevant in this regard; the authors examined the relationship between sleep discrepancy, cognition, and biomarkers of brain health in cognitively unimpaired community-dwelling older adults (N = 89). Regarding cognition, the authors found that greater absolute and negative discrepancy (i.e., poorer self-reported sleep quality, including TST, SE, and fragmentation, compared with actigraphy) was associated with poorer executive function (i.e., set-shifting), but not working memory or episodic memory. In addition, Winer et al. [8] found that greater absolute and negative discrepancy was associated with greater brain beta-amyloid (Aβ), but not tau, burden; two hallmarks of AD. It is theorised by some that the presence of brain Aβ may indicate the initial stage of a cascade of processes that ultimately results in AD [21], and a relationship between sleep discrepancy and Aβ may implicate the former as a sensitive behavioural marker of the disease process. Therefore, Winer et al.'s [8] findings provide intriguing initial evidence that sleep discrepancy may be associated with at least one biomarker of late-life neuropathology as well as, potentially, cognitive decline. In saying this, their analytical approach precluded answering certain questions. For instance, sleep discrepancy was evaluated in a linear manner (i.e., assuming that discrepancy in a more positive direction is associated with better clinical outcomes); this is a limitation as negative *and* positive forms of discrepancy may each be related to brain health, and perhaps in different ways. Indeed, previous research demonstrates associations between positive discrepancy and adverse health outcomes such as OSA [7,12] and cognitive impairment [3,15,19]. In such conditions, underestimation of sleep problems may arise due to undetected awakenings and disruptions to sleep cycles, or the effects of cognitive decline on accurate reporting of sleep [20]. Moreover, given Winer et al.'s [8] findings focus on Aβ as a biomarker of brain health, future research in older adults would benefit from incorporating other functional neuroimaging outcomes, such as brain glucose metabolism, assessed via FDG-PET.

The current study adds to the literature by thoroughly characterising the relationship between sleep discrepancy and brain glucose metabolism, a dynamic biomarker of brain health, in cognitively unimpaired community-dwelling older adults. This characterisation was achieved using a cluster analytic approach to analysing sleep discrepancy, which considered both the magnitude and direction of sleep discrepancy (i.e., negative and positive discrepancy), better and worse self-reported sleep and actigraphy-determined sleep, and

examined multiple nights of data across three sleep parameters (i.e., sleep diary vs. actigraphy for TST, WASO, and SE). This approach allowed us to identify groups of older adults with specific sleep discrepancy characteristics and accounts for some limitations of linear approaches [22].

Given that neurobiological changes precede cognitive decline, and the importance of early detection of neurodegenerative processes, the current study also extended upon previous work by examining an indicator of brain health that is more sensitive to early changes due to a variety of etiologies of neuropathology – namely, brain glucose metabolism as indexed by FDG-PET [23]. Further, the current study evaluated the contribution of important potential covariates – specifically, insomnia severity and depressive symptoms, which have significant theoretical/empirical overlap. In both insomnia and depression, the following has been found: a negative bias towards information processing [24,25], evidence of negative [6,26] and positive [27,28] sleep discrepancy, and associations with poorer cognitive function [29,30] and brain health [31–33]. Controlling for insomnia severity and depressive symptoms in the current study's analyses allowed for greater isolation of the sleep discrepancy construct, and evaluation of its clinical potential (e.g.,

Table 1
Demographic and health characteristics of the sample.

Variable	Mean (SD) or N (%)	Range
Age, years	70.00 (7.09)	55–89
Sex, *N* = female (%)	43 (63.24)	–
Education, years	14.12 (2.60)	8–20
MMSE Total Score	27.84 (1.54)	23–30
BMI, kg/m^2	26.94 (3.78)	18.92–38.06
DASS-21 Score		
Depression[#]	4.85 (5.03)	0–24
Anxiety[#]	3.91 (3.76)	0–18
Stress[#]	10.00 (6.46)	0–30
Berlin Risk Score, *N* = low OSA risk (%)	55 (80.88)	–
ISI Total Score	6.54 (5.13)	0–19
Sleep Diary		
TST, minutes	407.94 (57.37)	225.23–558.57
WASO, minutes	27.40 (24.36)	0.86–116.31
SE, %	79.09 (10.88)	38.71–100.00
Actigraphy		
TST, minutes	415.00 (52.65)	242.17–597.77
WASO, minutes	42.52 (22.18)	6.14–95.57
SE, %	90.10 (4.49)	78.00–98.01
Sleep Discrepancy^		
TST, minutes	−7.29 (51.36)	−258.27–100.16
WASO, minutes	15.12 (28.90)	−53.31–82.50
SE, %	−10.99 (11.54)	−48.10–10.91
FDG-PET, SUVR		
Neocortex	1.03 (0.07)	0.85–1.22
Frontal cortex	1.06 (0.08)	0.85–1.27
Temporal cortex	0.79 (0.05)	0.67–0.92
Inferior parietal cortex	1.06 (0.08)	0.91–1.35
Left superior parietal cortex	1.09 (0.10)	0.89–1.43
Right superior parietal cortex	1.06 (0.10)	0.74–1.39
Left posterior cingulate cortex	1.21 (0.10)	1.03–1.51
Right posterior cingulate cortex	1.20 (0.09)	0.98–1.48
Left entorhinal cortex	0.58 (0.08)	0.39–0.74
Right entorhinal cortex	0.60 (0.08)	0.44–0.81
Left hippocampus	0.73 (0.05)	0.60–0.84
Right hippocampus	0.74 (0.05)	0.64–0.88
Left amygdala	0.68 (0.06)	0.54–0.82
Right amygdala	0.71 (0.05)	0.59–0.82
Sleep assessment to PET scan, weeks	11.87 (11.19)	0.43–45.29

Note. *N* = 68. Abbreviations: Berlin = Berlin Questionnaire, measure of obstructive sleep apnoea risk; BMI = Body Mass Index (kilograms/metres^2); DASS-21 = Depression Anxiety and Stress Scales, where higher scores indicate greater depression, anxiety, and stress symptoms, respectively; FDG-PET = [18F]-fluoro-2-deoxyglucose positron emission tomography, measure of brain glucose metabolism; ISI = Insomnia Severity Index, where higher scores indicate greater insomnia severity; MMSE = Mini Mental State Examination, where higher scores indicate greater global cognitive function; OSA = Obstructive Sleep Apnoea; SD = standard deviation; SE = Sleep Efficiency, ratio of total sleep time to time in bed (%); SUVR = standardized update value ratio; TST = Total Sleep Time, amount of time spent asleep (minutes); WASO = Wake After Sleep Onset, amount of time spent awake after falling asleep (minutes).

^Sleep discrepancy was calculated using difference scores (i.e., sleep diary–actigraphy). [#]Scores were multiplied by two, such that higher scores indicate greater symptomology. Note, WASO discrepancy scores were reversed as higher WASO indicates poorer sleep, while higher TST and SE reflect better sleep. Negative values for TST, WASO, and SE discrepancy reflect a negative sleep discrepancy, where self-reported sleep is worse than objective sleep, whilst positive values reflect a positive sleep discrepancy, where self-reported sleep is better than objective sleep. Mean values (≥5 nights) were used for all sleep parameters.

independent associations with brain health).

Specifically, the current exploratory study investigated the relationship between sleep discrepancy and brain glucose metabolism, an indicator of brain health, in a sample of cognitively unimpaired community-dwelling older adults, while controlling for relevant demographic and sleep-related factors found to be associated with suboptimal brain health and poor sleep/sleep discrepancy (e.g., age, sex, education, and OSA risk). We investigated 1) whether clusters characterised by greater sleep discrepancy (negative or positive) and/or poor sleep (self-report and/or actigraphy-determined) are associated with lower global or regional brain glucose metabolism; and 2) whether there is a unique relationship between sleep discrepancy and global or regional brain glucose metabolism when controlling for insomnia severity and depressive symptoms, respectively, as covariates. To further isolate the sleep discrepancy construct, post-hoc analyses were conducted controlling for actigraphy-determined sleep.

2. Method

2.1. Participants

The current study used cross-sectional archival data from the Western Australia Memory Study (WAMS), an ongoing observational study of age-related cognitive change in community-dwelling older adults, conducted at the Australian Alzheimer's Research Foundation (AARF; now Alzheimer's Research Australia (ARA)) in Perth, Western Australia. From the larger WAMS cohort, cognitively unimpaired individuals who had undergone FDG-PET and participated in a sleep and thinking skills sub-study in collaboration with the Healthy Ageing Research Project (HARP) at the University of Western Australia (UWA) were included in the current study ($N = 68$). These participants are a subset of those included in a previous study exploring the relationship between sleep discrepancy and cognitive function in older adults ($N = 221$) [7]. Participants were recruited to WAMS and HARP in several ways, including public information sessions and word of mouth. Data were collected between 2014 and 2017. Study approval was obtained from the UWA Human Research Ethics Office (2019/RA/4/1/8884 and 2021/ET000261). Written informed consent was obtained from individuals prior to study participation.

Exclusion criteria for the current study were as follows: significant psychiatric (e.g., bipolar disorder, psychosis) or neurological (e.g., stroke, acquired brain injury) disorders that could impact cognitive performance; previous loss of consciousness for over 30 min; less than five valid nights of concurrent sleep diary and actigraphy data, following American Academy of Sleep Medicine recommendations [34]. We did not implement exclusion based on cognitive scores suggestive of cognitive impairment (e.g., Mini Mental State Examination [MMSE] score < 24; $N = 1$), to increase generalizability to community-dwelling older adults; however, no participants met criteria for dementia. Demographic and health characteristics of the sample are shown in Table 1.

2.2. Materials

2.2.1. Self-reported sleep

Self-reported sleep was measured with the Consensus Sleep Diary [35], a 15-item self-report measure of daily sleep patterns over seven consecutive nights. The current study examined the following self-reported sleep parameters: TST (minutes), WASO (minutes), and SE (%). TST was calculated by subtracting the sum of WASO ("In total, how long did these awakenings last?") and SOL ("How long did it take you to fall asleep?") from the sleep period ("What time did you try to go to sleep?" – "What time was your final awakening?"). SE was calculated by dividing TST by time in bed ("What time did you get into bed?" – "What time did you get out of bed for the day?").

2.2.2. Actigraphy-determined sleep

Our 'objective' measure of sleep was derived from wrist-worn actigraphy (Tri-axial wGT3X-BT activity monitor, Actigraph LLC, FL, USA). Actigraphy data were automatically scored using the ActiLife software (version 6.13.4) and Cole-Kripke algorithm, [36] over 24-hour periods and in 60-second epochs. Autoscored bed/rise times were defined according to sleep diary estimates (i.e., "What time did you try to go to sleep?" and "What time was your final awakening?", respectively). Data were then visually inspected for missing or unusual values. If sleep diary bed/rise times were missing, or actigraphy data differed from sleep diary estimates of the sleep period by > 60 min, visual manual scoring was conducted in accordance with the Society of Behavioural Sleep Medicine guidelines [37], whereby both sleep diary estimates and typical movement patterns of bed/rise times were considered to define the sleep period. Additionally, nights with non-wear time within five minutes of bed/rise time, and those with fewer than 300 min of sleep opportunity, were excluded from analyses, due to questionable validity of the sleep period.

All sleep parameters were continuous variables, with higher WASO, and lower TST and SE, indicating worse self-reported and actigraphy-determined sleep. Mean values ($\geq$5 nights) were used for all sleep parameters.

2.2.3. Brain glucose metabolism

Brain glucose metabolism was indexed by [18F]-fluoro-2-deoxyglucose positron emission tomography (FDG-PET), which was performed and analysed per standard protocols, described previously [38]. To summarise, FDG retention was quantified using a standardised uptake value ratio (SUVR); that is, tracer uptake divided by the average uptake in the cerebellum as the reference region. The SUVR for the neocortex was calculated as the mean SUVR in the grey matter masked neocortical region, comprising of the frontal, superior parietal, lateral temporal, occipital, as well as anterior and posterior cingulate regions. SUVRs were also calculated for regions of interest, which were selected *a priori* based on existing literature regarding their relevance to sleep and brain health (reviewed in

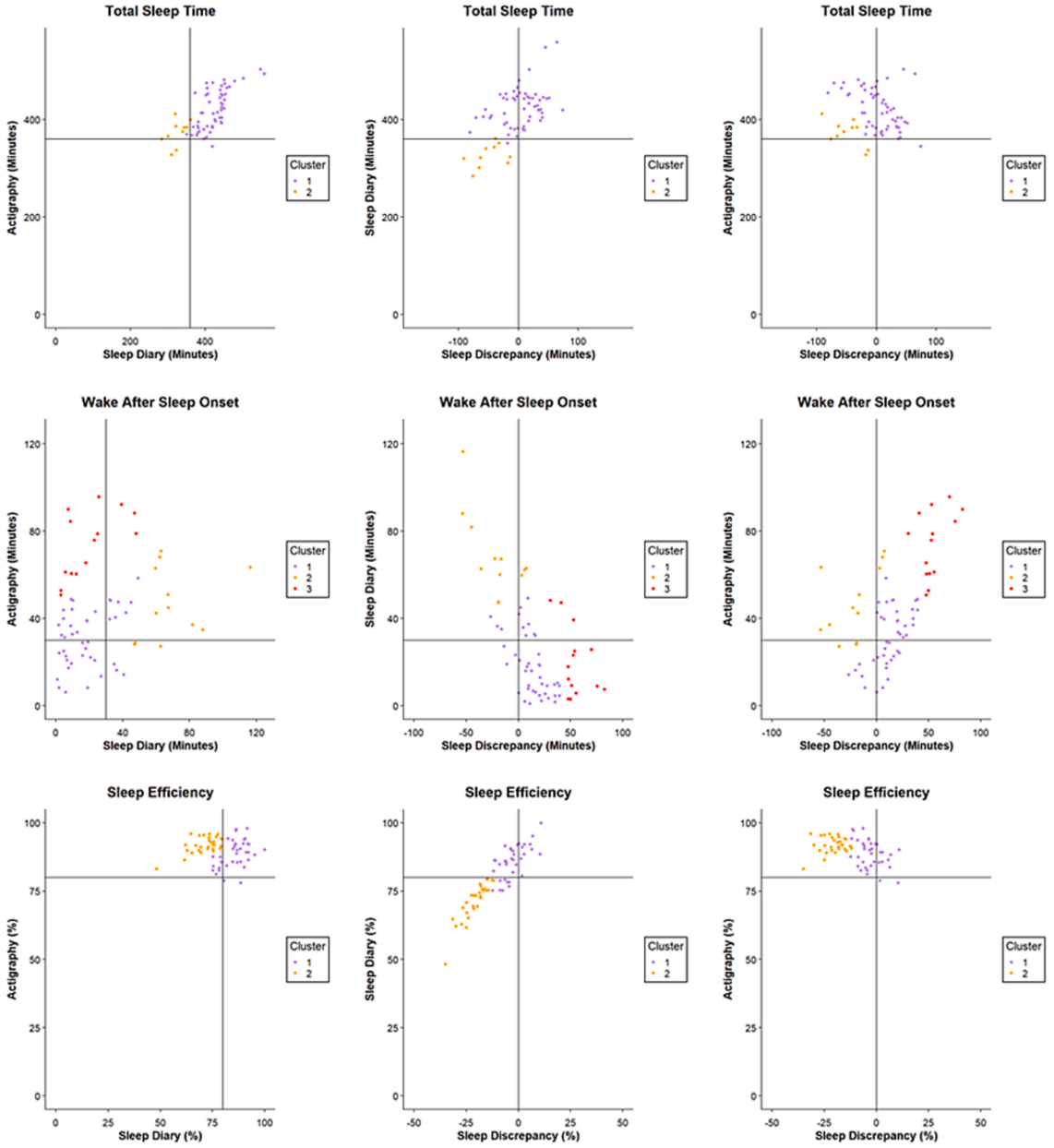


Fig. 1. Scatter plots of self-reported sleep (i.e., sleep diary), objective sleep (i.e., actigraphy), and sleep discrepancy clusters for each sleep parameter. Mean values (≥5 nights) were used for all sleep parameters. Abbreviations: SE, Sleep Efficiency (ratio of total sleep time to time in bed, %); TST, Total Sleep Time (amount of time spent asleep, minutes); WASO, Wake After Sleep Onset (amount of time spent awake after falling asleep, minutes). The colouring scheme depicts a two-cluster solution for TST, where, Cluster 1 (purple) = "TST 1: no sleep discrepancy and longer sleep duration"; Cluster 2 (orange) = "TST 2: negative sleep discrepancy and shorter sleep duration". For WASO, there is a three-cluster solution, where, Cluster 1 (purple) = "WASO 1: no sleep discrepancy and good sleep quality"; Cluster 2 (orange) = "WASO 2: negative sleep discrepancy and poor sleep quality"; Cluster 3 (red) = "WASO 3: positive sleep discrepancy and poor sleep quality". For SE, there is a two-cluster solution, where, Cluster 1 (purple) = "SE 1: no sleep discrepancy and good self-reported sleep quality"; Cluster 2 (orange) = "SE 2: negative sleep discrepancy and poor self-reported sleep quality". Sleep discrepancy was calculated using difference scores (i.e., sleep diary – actigraphy). Note, WASO discrepancy scores were reversed as higher WASO indicates poorer sleep, while higher TST and SE reflect better sleep. Negative values for TST, WASO, and SE discrepancy reflect a negative sleep discrepancy, where self-reported sleep is worse than objective sleep, whilst positive values reflect a positive sleep discrepancy, where self-reported sleep is better than objective sleep. Solid black horizontal and vertical lines correspond to cut-offs consistent with National Sleep Foundation guidelines for adequate sleep for sleep diary and actigraphy values. Solid black horizontal and vertical lines for sleep discrepancy correspond to a cut-off of 0. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

[39]): frontal cortex (sum of SUVRs for the dorsolateral prefrontal cortex, ventrolateral prefrontal cortex, orbitofrontal cortex, and gyrus rectus, averaged by the number of regions included), temporal cortex (sum of SUVRs for the temporooccipital cortex, temporal cortex, inferior temporal cortex, amygdala, hippocampus, parahippocampus, fusiform gyrus, and entorhinal cortex, averaged by the number of regions included), and inferior parietal cortex (sum of SUVRs for the supramarginal gyrus and angular gyrus, averaged by the number of regions included), as well as the bilateral superior parietal cortex, posterior cingulate cortex, entorhinal cortex, hippocampus, and amygdala.

2.2.4. Covariates

Covariates included insomnia severity, depressive symptoms, OSA risk, age, sex, education, and time between sleep data collection and FDG-PET. Insomnia severity was measured using the Insomnia Severity Index (ISI) [40], a self-report questionnaire assessing insomnia symptoms over the past two weeks, with higher scores (scores range from 0 to 28) indicating greater insomnia severity; continuous scores were included in analyses. Depressive symptoms were measured using the depression subscale of the Depression, Anxiety, and Stress Scale (DASS-21) [41], a self-report questionnaire evaluating depressive, anxiety, and stress symptoms over the past week. The depression subscale was summed and multiplied by two, such that higher scores (scores range from 0 to 42) indicate greater depressive symptoms; continuous scores were included in analyses. OSA risk was measured using the Berlin Questionnaire [42], a self-report measure that categorises individuals as being "high risk" or "low risk" for OSA, based on snoring, excessive daytime sleepiness, and high blood pressure, and obesity (defined based on body mass index). "High risk" and "low risk" for OSA were parameterised as 1 and 0, respectively, in the current study. Age (years), sex (male/female), and education (years) were determined via participant self-report.

2.3. Procedure

Participants underwent a comprehensive neuropsychological assessment for approximately three hours, including completion of several questionnaires (e.g., ISI, DASS-21, and Berlin Questionnaire). Participants were then given sleep measures (i.e., sleep diary and actigraphy) to complete/wear at home across seven consecutive nights. Participants completed FDG-PET either before or after the sleep study. Upon completion of data collection, participants were reimbursed for their time and travel expenses. All measures were selected due to their wide use and adequate psychometric properties [40,43–46].

2.4. Statistical analysis

All statistical analyses were conducted using the R programming language (version 4.3.1) [47]. Outliers for continuous variables were winzorised based on a cut-off of greater/less than 3 *SD* from the mean ($N = 1$ value for DASS-21 depression subscale). Sleep discrepancy was calculated using difference scores (i.e., sleep diary – actigraphy). WASO difference scores were reversed as higher WASO indicates poorer sleep, while higher TST and SE reflect better sleep. Negative values for TST, WASO, and SE discrepancy reflect a negative sleep discrepancy, whilst positive values reflect a positive sleep discrepancy. Per our previous study, which included sleep data from the current sample [7], SOL and NWAK were omitted from cluster analyses as all participants had a negative SOL discrepancy, which may reflect a tendency for actigraphy to overestimate sleep in older adults [48], and all participants had a positive NWAK discrepancy, which may reflect an inability for individuals to recall awakenings less than a certain duration [49].

Patterns of sleep discrepancy for the sleep parameters of TST, WASO, and SE were defined via agglomerative hierarchical clustering using a Euclidean distance and complete linkage method, performed on diary/actigraphy/discrepancy data for each of the three sleep parameters. Participants' cluster assignments in the current study ($N = 68$) were allocated based on those described in Soh et al. [7] given the overlap of samples: two clusters for TST and SE, and three clusters for WASO. TST, WASO, and SE clusters are shown in Fig. 1. Demographic and health summary statistics across each sleep parameter cluster are shown in Table 2. For continuous variables, independent samples *t*-tests were performed to compare means across TST and SE clusters, while a one-way between-subjects analysis of variance was conducted to compare group means across WASO clusters. For categorical variables, Fisher's exact tests were performed to compare proportions of sex (female/male) and OSA risk (low/high) across clusters. See Soh et al. [7] for further information on the data cleaning/preparation and cluster analytic approach.

Given the sample size of the current study, stepwise model selection (forward and backward selection) by Akaike Information Criteria (AIC; stepAIC function from the Modern Applied Statistics with S [MASS] package) [50] was performed, to select an optimal set of features from the following covariates: age, sex, education, OSA risk, and time between sleep diary/actigraphy and FDG-PET. Subsequently, education was used to model TST, age and education to model WASO, and age to model SE. FDG-PET (SUVR) variables were *z*-transformed to improve model stability. To address our exploratory aims, three models were performed for each sleep parameter (i.e., TST, WASO, SE):

1) Sleep parameter cluster ~ SUVR + covariates.

2) Sleep parameter cluster ~ SUVR + insomnia severity + covariates.

3) Sleep parameter cluster ~ SUVR + depressive symptoms + covariates.

Binary logistic regressions were performed for analyses involving TST and SE, while Multinomial logistic regressions were performed for analyses involving WASO. Separate models were performed for each of the 14 brain regions of interest.

After completion of the planned analyses, questions regarding the role of actigraphy-determined sleep were identified and a post-hoc analysis to address this was conducted. Specifically, to further isolate the sleep discrepancy construct, a model with the inclusion of actigraphy-determined sleep was performed for each sleep parameter:

Table 2
Demographic and health characteristics across Total Sleep Time, Wake After Sleep Onset, and Sleep Efficiency clusters.

	Total Sleep Time (N = 65)				Wake After Sleep Onset (N = 68)						Sleep Efficiency (N = 67)			
	Cluster 1 (N = 55)		Cluster 2 (N = 10)		Cluster 1 (N = 42)		Cluster 2 (N = 12)		Cluster 3 (N = 14)		Cluster 1 (N = 38)		Cluster 2 (N = 29)	
Demographics	Mean (SD) or N (%)	Range	Mean (SD) or N (%)	Range	Mean (SD) or N (%)	Range	Mean (SD) or N (%)	Range	Mean (SD) or N (%)	Range	Mean (SD) or N (%)	Range	Mean (SD) or N (%)	Range
Age, years	71.40 (6.45)	63–83	69.75 (7.34)	55–89	71.00 (7.07)	56–89	70.33 (7.62)	55–83	66.71 (6.08)	55–77	68.66 (6.27)	55–83	71.93 (7.81)	55–89
Sex, female, *N* (%)	7 (70.00)	–	33 (60.00)	–	27 (64.29)	–	9 (75.00)	–	7 (50.00)	–	22 (57.89)	–	20 (68.97)	–
Education, years	12.80 (3.49)	8–20	14.31 (2.42)	10–20	14.50 (2.71)	10–20	13.33 (2.53)	8–16	13.64 (2.24)	10–18	13.92 (2.46)	10–20	14.31 (2.82)	8–20
Health														
MMSE Total Score	28.20 (1.69)	25—30	27.75 (1.53)	23–30	27.98 (1.35)	25–30	27.58 (1.62)	25–30	27.64 (2.02)	23–30	27.74 (1.57)	23–30	27.97 (1.57)	25–30
BMI, kg/m^2	25.29 (3.28)	19.42–29.41	27.29 (3.78)	18.92–38.06	26.53 (3.40)*	18.92–35.83	25.47 (3.38)*	21.19–33.13	29.43 (4.29)*	23.45–38.06	27.3 (4.12)	18.92–38.06	26.36 (3.13)	19.42–33.13
DASS-21 Score														
Depression[#]	6.60 (4.99)	0–12	4.58 (5.14)	0–24	3.57 (3.41)**	0–14	6.00 (5.46)**	0–16	7.71 (7.31)**	0–24	5.00 (5.48)	0–24	4.76 (4.55)	0–16
Anxiety[#]	6.00 (5.89)	0–18	3.53 (3.20)	0–14	3.29 (3.64)	0–18	5.83 (4.39)	0–14	4.14 (3.18)	0–12	3.63 (3.83)	0–18	4.14 (3.70)	0–14
Stress[#]	10.80 (6.41)	2–22	10.11 (6.50)	2–30	9.33 (5.79)	2–26	10.33 (7.85)	0–28	11.71 (7.27)	2–30	10.11 (6.88)	2–30	10.07 (6.01)	0–28
Sleep Measures														
Berlin, low OSA risk, *N* (%)	9 (90.00)	–	43 (78.18)	–	35 (83.33)	–	11 (91.67)	–	9 (64.29)	–	30 (78.95)	–	24 (82.76)	–
ISI Total Score	9.00 (3.74)*	1–9	6.05 (5.01)*	0–19	5.64 (4.87)	0–16	8.92 (5.55)	1–19	7.21 (5.6)	1–19	5.21 (4.75)*	0–19	7.86 (4.85)*	0–16
Sleep Diary	426.00 (39.95)**	351.62–558.57	325.71 (23.78)**	284.03–361.29	18.20 (13.84)	0.86–49.29	68.57 (19.06)	47.14–116.31	19.70 (15.71)	3.00–48.14	86.10 (6.01)**	75.20–100.00	71.30 (6.91)**	48.19–79.47
Actigraphy	421.14 (41.13)**	344.71–502.86	373.00 (26.05)**	328.00–411.43	30.90 (13.43)**	6.14–58.43	46.59 (16.27)**	27.14–70.86	73.89 (15.23)**	50.71–95.57	88.78 (5.01)**	78.00–98.01	91.94 (2.97)**	83.15–96.01
Sleep Discrepancy[^]	4.86 (33.26)**	−81.00–74.64	−49.22 (25.23)**	−91.34–−13.91	12.69 (15.95)**	−26.57–39.57	−21.98 (21.33)**	−53.31–7.89	54.18 (13.55)**	30.71–82.50	−2.65 (5.90)**	−12.36–10.91	−20.64 (5.70)**	−34.96–−11.87
FDG-PET, SUVR														
Neocortex	1.05 (0.08)	0.94–1.22	1.03 (0.07)	0.90–1.22	1.04 (0.07)	0.92–1.22	0.98 (0.07)	0.85–1.10	1.01 (0.07)	0.90–1.15	1.04 (0.07)	0.90–1.22	1.01 (0.07)	0.85–1.22
Frontal cortex	8.66 (0.56)	7.93–9.84	8.43 (0.61)	7.33–10.15	8.58 (0.61)	7.42–10.15	8.08 (0.60)	6.82–9.18	8.34 (0.58)	7.33–9.49	8.55 (0.61)	7.33–10.15	8.31 (0.64)	6.82–9.84
Temporal cortex	12.60 (0.76)	11.32–13.99	12.64 (0.80)	11.20–14.76	12.74 (0.74)	11.20–14.76	12.07 (0.66)	10.72–12.96	12.66 (1.00)	11.30–14.65	12.82 (0.86)*	11.30–14.76	12.33 (0.67)*	10.72–13.99
Inferior parietal cortex	4.35 (0.42)	3.94–5.38	4.22 (0.30)	3.67–5.13	4.31 (0.34)*	3.67–5.38	4.07 (0.25)*	3.62–4.54	4.14 (0.27)*	3.75–4.72	4.30 (0.30)	3.75–5.13	4.15 (0.33)	3.62–5.38

(*continued on next page*)

Table 2 (*continued*)

	Total Sleep Time (N = 65)				Wake After Sleep Onset (N = 68)						Sleep Efficiency (N = 67)			
	Cluster 1 (N = 55)		Cluster 2 (N = 10)		Cluster 1 (N = 42)		Cluster 2 (N = 12)		Cluster 3 (N = 14)		Cluster 1 (N = 38)		Cluster 2 (N = 29)	
Demographics	Mean (SD) or N (%)	Range	Mean (SD) or N (%)	Range	Mean (SD) or N (%)	Range	Mean (SD) or N (%)	Range	Mean (SD) or N (%)	Range	Mean (SD) or N (%)	Range	Mean (SD) or N (%)	Range
Left superior parietal cortex	1.12 (0.11)	0.89–1.30	1.09 (0.10)	0.90–1.43	1.12 (0.09)*	0.90–1.43	1.05 (0.10)*	0.89–1.18	1.06 (0.09)*	0.90–1.23	1.10 (0.11)	0.90–1.43	1.09 (0.09)	0.89–1.30
Right superior parietal cortex	1.12 (0.13)	0.92–1.39	1.05 (0.10)	0.74–1.28	1.08 (0.11)	0.74–1.39	1.01 (0.08)	0.88–1.13	1.03 (0.07)	0.91–1.18	1.06 (0.10)	0.85–1.28	1.05 (0.12)	0.74–1.39
Left posterior cingulate cortex	1.27 (0.11)	1.10–1.51	1.20 (0.09)	1.04–1.41	1.23 (0.09)*	1.09–1.51	1.17 (0.09)*	1.03–1.31	1.17 (0.09)*	1.04–1.35	1.21 (0.10)	1.04–1.41	1.20 (0.10)	1.03–1.51
Right posterior cingulate cortex	1.25 (0.10)	1.11–1.48	1.20 (0.09)	1.01–1.42	1.22 (0.09)*	1.06–1.48	1.16 (0.09)*	0.98–1.29	1.17 (0.09)*	1.01–1.32	1.21 (0.09)	1.01–1.42	1.19 (0.10)	0.98–1.48
Left entorhinal cortex	0.58 (0.10)	0.39–0.73	0.58 (0.08)	0.42–0.74	0.58 (0.08)	0.39–0.73	0.56 (0.10)	0.42–0.73	0.58 (0.08)	0.46–0.74	0.59 (0.08)	0.45–0.74	0.57 (0.09)	0.39–0.73
Right entorhinal cortex	0.58 (0.09)	0.45–0.69	0.61 (0.08)	0.44–0.81	0.61 (0.07)	0.45–0.81	0.56 (0.07)	0.44–0.65	0.62 (0.09)	0.45–0.78	0.62 (0.08)*	0.45–0.81	0.58 (0.07)*	0.44–0.70
Left hippocampus	0.72 (0.06)	0.64–0.83	0.73 (0.05)	0.65–0.84	0.73 (0.04)	0.66–0.84	0.69 (0.05)	0.60–0.78	0.73 (0.05)	0.65–0.82	0.73 (0.05)	0.65–0.84	0.72 (0.05)	0.60–0.83
Right hippocampus	0.74 (0.05)	0.67–0.83	0.75 (0.05)	0.66–0.88	0.75 (0.05)	0.66–0.88	0.71 (0.04)	0.64–0.78	0.75 (0.05)	0.69–0.85	0.76 (0.05)*	0.68–0.88	0.73 (0.04)*	0.64–0.83
Left amygdala	0.66 (0.05)	0.57–0.73	0.69 (0.05)	0.54–0.82	0.69 (0.05)	0.54–0.80	0.64 (0.05)	0.54–0.71	0.70 (0.07)	0.59–0.82	0.69 (0.06)*	0.54–0.82	0.66 (0.04)*	0.54–0.73
Right amygdala	0.70 (0.06)	0.61–0.79	0.71 (0.05)	0.61–0.82	0.72 (0.05)	0.61–0.80	0.67 (0.04)	0.59–0.75	0.72 (0.06)	0.65–0.82	0.72 (0.05)*	0.65–0.82	0.69 (0.05)*	0.59–0.79
Sleep assessment to PET scan, weeks	8.43 (7.35)	1.00–22.14	11.98 (11.48)	0.43–45.29	11.31 (11.92)	0.43–45.29	15.10 (10.50)	1.71–37.00	10.80 (9.58)	1.14–33.86	10.28 (10.01)	0.71–36.57	13.09 (11.82)	0.43–45.29

Note. Abbreviations: Berlin = Berlin Questionnaire, measure of obstructive sleep apnoea risk; BMI = Body Mass Index (kilograms/metres^2); DASS-21 = Depression Anxiety and Stress Scales, where higher scores indicate greater depression, anxiety, and stress symptoms, respectively; FDG-PET SUVR = [18F]-fluoro-2-deoxyglucose positron emission tomography, measure of brain glucose metabolism; ISI = Insomnia Severity Index, where higher scores indicate greater insomnia severity; MMSE = Mini Mental State Examination, where higher scores indicate better global cognitive function; OSA = Obstructive Sleep Apnoea; SD = standard deviation; SE = Sleep Efficiency, ratio of total sleep time to time in bed (%); SUVR = standardized update value ratio; TST = Total Sleep Time, amount of time spent asleep (minutes); WASO = Wake After Sleep Onset, amount of time spent awake after falling asleep (minutes). For TST, there is a two-cluster solution, where Cluster 1 = "TST 1: no sleep discrepancy and longer sleep duration"; Cluster 2 = "TST 2: negative sleep discrepancy and shorter sleep duration". For WASO, there is a three-cluster solution, where Cluster 1 = "WASO 1: no sleep discrepancy and good sleep quality"; Cluster 2 = "WASO 2: negative sleep discrepancy and poor sleep quality"; Cluster 3 = "WASO 3: positive sleep discrepancy and poor sleep quality". For SE, there is a two-cluster solution, where Cluster 1 = "SE 1: no sleep discrepancy and good self-reported sleep quality"; Cluster 2 = "SE 2: negative sleep discrepancy and poor self-reported sleep quality".

[#]Scores were multiplied by two, such that higher scores indicate greater symptomology.

[^]Sleep discrepancy was calculated using difference scores (i.e., sleep diary – actigraphy). Note, WASO discrepancy scores were reversed as higher WASO indicates poorer sleep, while higher TST and SE reflect better sleep. Negative values for TST, WASO, and SE discrepancy reflect a negative sleep discrepancy, where self-reported sleep is worse than objective sleep, whilst positive values reflect a positive sleep discrepancy, where self-reported sleep is better than objective sleep. Independent-samples t-tests and analysis of variance (ANOVA) were performed to compare continuous variable means across clusters, whilst Fisher's exact tests were used to compare categorical variables across clusters.

*$p < 0.05$, **$p < 0.01$.

Table 3
Binary logistic regression analyses exploring brain glucose metabolism as a predictor of Total Sleep Time cluster membership.

Total Sleep Time (TST; Negative vs. No Sleep Discrepancy)																
	Model 1				Model 2				Model 3				Model 4			
Brain region	*β*	*SE*	*OR [95 % ECI]*	*p*	*β*	*SE*	*OR [95 % ECI]*	*p*	*β*	*SE*	*OR [95 % ECI]*	*p*	*β*	*SE*	*OR [95 % ECI]*	*p*
Neocortex	0.42	0.37	0.66 [0.31, 1.39]	0.26	0.44	0.39	0.64 [0.30, 1.41]	0.26	0.45	0.38	1.57 [0.74, 3.35]	0.23	0.17	0.43	1.19 [0.49, 2.73]	0.69
Frontal cortex	0.44	0.38	0.64 [0.30, 1.38]	0.25	0.54	0.41	0.58 [0.25, 1.31]	0.19	0.49	0.39	1.63 [0.75, 3.62]	0.22	0.19	0.46	1.20 [0.47, 2.95]	0.69
Temporal cortex	−0.08	0.38	1.09 [0.53, 2.47]	0.82	−0.17	0.42	1.19 [0.54, 2.88]	0.68	−0.08	0.38	0.93 [0.41, 1.91]	0.84	−0.45	0.42	0.64 [0.26, 1.40]	0.28
Inferior parietal cortex	0.50	0.36	0.61 [0.29, 1.27]	0.17	0.52	0.37	0.59 [0.28, 1.27]	0.16	0.54	0.37	1.72 [0.82, 3.62]	0.14	0.38	0.40	1.46 [0.63, 3.23]	0.35
Left superior parietal cortex	0.40	0.37	0.67 [0.32, 1.37]	0.27	0.34	0.39	0.71 [0.33, 1.55]	0.39	0.42	0.37	1.52 [0.74, 3.24]	0.26	0.24	0.44	1.27 [0.53, 3.11]	0.59
Right superior parietal cortex	0.90	0.40	0.41 [0.18, 0.88]	**0.03***	0.83	0.41	0.44 [0.19, 0.97]	**0.05***	0.92	0.41	2.51 [1.16, 5.88]	**0.02***	0.72	0.46	2.06 [0.84, 5.32]	0.12
Left posterior cingulate cortex	0.87	0.39	0.42 [0.18, 0.88]	**0.03***	0.88	0.40	0.43 [0.18, 0.88]	**0.03***	0.89	0.39	2.44 [1.16, 5.60]	**0.02***	0.79	0.43	2.20 [0.96, 5.49]	0.07
Right posterior cingulate cortex	0.70	0.39	0.50 [0.22, 1.06]	0.07	0.70	0.39	0.50 [0.22, 1.07]	0.08	0.74	0.39	2.10 [0.99, 4.76]	0.06	0.60	0.43	1.82 [0.79, 4.49]	0.17
Left entorhinal cortex	−0.09	0.38	1.10 [0.51, 2.37]	0.81	−0.25	0.40	1.29 [0.59, 2.91]	0.53	−0.11	0.39	0.90 [0.41, 1.93]	0.78	−0.55	0.46	0.58 [0.22, 1.37]	0.23
Right entorhinal cortex	−0.42	0.37	1.53 [0.76, 3.26]	0.25	−0.57	0.39	1.76 [0.84, 4.00]	0.15	−0.50	0.38	0.61 [0.27, 1.26]	0.19	−1.19	0.56	0.30 [0.08, 0.79]	**0.03***
Left hippocampus	−0.12	0.39	1.12 [0.53, 2.52]	0.77	−0.26	0.41	1.30 [0.59, 3.09]	0.53	−0.12	0.39	0.89 [0.40, 1.88]	0.77	−0.46	0.45	0.63 [0.25, 1.49]	0.31
Right hippocampus	−0.16	0.39	1.17 [0.57, 2.65]	0.68	−0.14	0.41	1.15 [0.53, 2.72]	0.73	−0.12	0.40	0.89 [0.39, 1.90]	0.77	−0.35	0.46	0.70 [0.27, 1.66]	0.44
Left amygdala	−0.62	0.41	1.86 [0.86, 4.40]	0.13	−0.78	0.46	2.18 [0.93, 5.75]	0.09	−0.63	0.42	0.53 [0.22, 1.17]	0.13	−1.01	0.49	0.36 [0.12, 0.86]	**0.04***
Right amygdala	−0.28	0.39	1.33 [0.63, 3.04]	0.48	−0.38	0.42	1.46 [0.67, 3.57]	0.36	−0.26	0.40	0.77 [0.33, 1.65]	0.51	−0.63	0.44	0.53 [0.20, 1.19]	0.15

Note. Abbreviations: β = standardized beta-weight; *ECI* = exponentiated confidence interval; *OR* = odds ratio; *SE* = standard error; TST = Total Sleep Time, amount of time spent asleep (minutes). Sleep discrepancy was calculated using difference scores (i.e., sleep diary – actigraphy). Negative values for TST discrepancy reflect a negative sleep discrepancy, where self-reported sleep is worse than objective sleep, whilst positive values reflect a positive sleep discrepancy, where self-reported sleep is better than objective sleep. Brain glucose metabolism was assessed using [18F]-fluoro-2-deoxyglucose positron emission tomography (FDG-PET) standardized update value ratio. Insomnia severity was assessed with the Insomnia Severity Index. Depressive symptoms were assessed with the depression subscale of the Depression, Anxiety, and Stress Scales. For TST, there is a two-cluster solution, where Cluster 1 = "TST 1: no sleep discrepancy and longer sleep duration"; Cluster 2 = "TST 2: negative sleep discrepancy and shorter sleep duration". Model 1 = glucose metabolism in each brain region predicting TST discrepancy cluster membership, controlling for education (years). Model 2 = glucose metabolism in each brain region predicting TST discrepancy cluster membership, controlling for education (years) and insomnia severity. Model 3 = glucose metabolism in each brain region predicting TST discrepancy cluster membership, controlling for education (years) and depressive symptoms. Model 4 = glucose metabolism in each brain region predicting TST discrepancy cluster membership, controlling for education (years) and objective TST. *$p < 0.05$, **$p < 0.01$.

Table 4
Multinomial logistic regression analyses exploring brain glucose metabolism as a predictor of Wake After Sleep Onset cluster membership.

Wake After Sleep Onset (WASO; Negative vs. No Sleep Discrepancy)

	Model 1				Model 2				Model 3				Model 4			
Brain region	β	SE	OR [95 % ECI]	p	β	SE	OR [95 % ECI]	p	β	SE	OR [95 % ECI]	p	β	SE	OR [95 % ECI]	p
Neocortex	−1.42	0.52	0.24 [0.09, 0.66]	**0.01***	−1.69	0.80	0.19 [0.06, 0.59]	**0.004****	−1.38	0.52	0.25 [0.09, 0.69]	**0.01****	−1.81	0.77	0.16 [0.04, 0.73]	**0.02***
Frontal cortex	−1.33	0.50	0.26 [0.10, 0.70]	**0.01****	−1.40	0.53	0.25 [0.09, 0.70]	**0.01****	−1.32	0.50	0.27 [0.10, 0.72]	**0.01****	−1.64	0.76	0.26 [0.04, 0.87]	**0.03***
Temporal cortex	−1.35	0.52	0.26 [0.09, 0.71]	**0.01****	−1.59	0.57	0.20 [0.07, 0.63]	**0.01****	−1.31	0.51	0.27 [0.10, 0.74]	**0.01***	−1.48	0.62	0.23 [0.07, 0.77]	**0.02***
Inferior parietal cortex	−1.33	0.54	0.26 [0.09, 0.76]	**0.01***	−1.59	0.61	0.20 [0.06, 0.68]	**0.01****	−1.28	0.54	0.28 [0.10, 0.80]	**0.02***	−1.85	0.75	0.16 [0.04, 0.68]	**0.01***
Left superior parietal cortex	−0.96	0.43	0.38 [0.16, 0.89]	**0.03***	−1.33	0.51	0.26 [0.10, 0.72]	**0.01****	−0.94	0.44	0.39 [0.17, 0.92]	**0.03***	−1.54	0.65	0.21 [0.06, 0.76]	**0.02***
Right superior parietal cortex	−1.01	0.45	0.36 [0.15, 0.87]	**0.02***	−1.44	0.54	0.24 [0.08, 0.69]	**0.01****	−0.99	0.46	0.37 [0.15, 0.91]	**0.03***	−1.40	0.58	0.25 [0.08, 0.78]	**0.02***
Left posterior cingulate cortex	−0.75	0.41	0.47 [0.21, 1.04]	0.06	−0.94	0.46	0.39 [0.16, 0.96]	**0.04***	−0.71	0.41	0.49 [0.22, 1.09]	0.08	−0.91	0.51	0.40 [0.15, 1.10]	0.08
Right posterior cingulate cortex	−1.03	0.43	0.36 [0.15, 0.84]	**0.02***	−1.30	0.50	0.27 [0.10, 0.72]	**0.01****	−0.97	0.44	0.38 [0.16, 0.89]	**0.03***	−1.25	0.61	0.29 [0.09, 0.94]	**0.04***
Left entorhinal cortex	−0.33	0.36	0.72 [0.36, 1.44]	0.35	−0.41	0.36	0.66 [0.33, 1.35]	0.26	−0.34	0.37	0.72 [0.35, 1.47]	0.36	−0.23	0.41	0.80 [0.36, 1.77]	0.58
Right entorhinal cortex	−0.78	0.38	0.46 [0.22, 0.97]	**0.04***	−0.83	0.40	0.43 [0.20, 0.94]	**0.03***	−0.86	0.40	0.42 [0.19, 0.93]	**0.03***	−1.01	0.52	0.37 [0.13, 1.02]	0.06
Left hippocampus	−1.29	0.48	0.28 [0.11, 0.71]	**0.01****	−1.50	0.53	0.22 [0.08, 0.63]	**0.01****	−1.27	0.49	0.28 [0.11, 0.73]	**0.01****	−1.08	0.52	0.34 [0.12, 0.95]	**0.04***
Right hippocampus	−1.18	0.49	0.31 [0.12, 0.80]	**0.02***	−1.30	0.54	0.27 [0.09, 0.79]	**0.02***	−1.12	0.49	0.33 [0.12, 0.86]	**0.02***	−0.95	0.49	0.39 [0.15, 1.02]	0.06
Left amygdala	−1.03	0.40	0.36 [0.16, 0.78]	**0.01****	−1.11	0.43	0.33 [0.14, 0.77]	**0.01****	−1.04	0.40	0.35 [0.16, 0.78]	**0.01****	−1.17	0.51	0.31 [0.11, 0.84]	**0.02***
Right amygdala	−1.39	0.50	0.25 [0.09, 0.66]	**0.01****	−1.68	0.57	0.19 [0.06, 0.56]	**0.003****	−1.39	0.51	0.25 [0.09, 0.67]	**0.01****	−1.28	0.55	0.28 [0.10, 0.82]	**0.01***

Wake After Sleep Onset (WASO; Positive vs. No Sleep Discrepancy)

	Model 1				Model 2				Model 3				Model 4			
Brain region	β	SE	OR [95 % ECI]	p	β	SE	OR [95 % ECI]	p	β	SE	OR [95 % ECI]	p	β	SE	OR [95 % ECI]	p
Neocortex	−0.78	0.44	0.46 [0.19, 1.09]	0.08	−0.59	0.45	0.45 [0.18, 1.09]	0.08	−0.75	0.45	0.47 [0.19, 1.16]	0.10	−1.59	0.90	0.20 [0.03, 1.20]	0.08
Frontal cortex	−0.79	0.44	0.46 [0.19, 1.08]	0.07	−0.77	0.44	0.46 [0.19, 1.10]	0.08	−0.79	0.46	0.45 [0.18, 1.12]	0.09	−1.36	0.89	0.26 [0.04, 1.48]	0.13
Temporal cortex	−0.23	0.35	0.79 [0.40, 1.58]	0.51	−0.23	0.35	0.79 [0.40, 1.59]	0.51	−0.23	0.37	0.79 [0.38, 1.64]	0.53	−0.30	0.75	0.74 [0.17, 3.23]	0.69
Inferior parietal cortex	−0.99	0.48	0.37 [0.15, 0.95]	**0.04***	−1.01	0.49	0.36 [0.14, 0.95]	**0.04***	−0.90	0.48	0.41 [0.16, 1.05]	0.06	−2.04	0.96	0.13 [0.02, 0.84]	**0.03***
Left superior parietal cortex	−0.96	0.43	0.38 [0.16, 0.90]	**0.03***	−1.10	0.47	0.33 [0.13, 0.84]	**0.02***	−0.99	0.45	0.37 [0.15, 0.90]	**0.03***	−2.12	0.91	0.12 [0.02, 0.71]	**0.02***
Right superior parietal cortex	−0.97	0.45	0.38 [0.16, 0.92]	**0.03***	−1.08	0.48	0.34 [0.13, 0.86]	**0.02***	−0.94	0.46	0.39 [0.16, 0.97]	**0.04***	−2.19	1.03	0.11 [0.01, 0.85]	**0.03***

(*continued on next page*)

Table 4 (*continued*)

Wake After Sleep Onset (WASO; Negative vs. No Sleep Discrepancy)

	Model 1				**Model 2**				**Model 3**				**Model 4**			
Brain region	β	SE	OR [95 % ECI]	p	β	SE	OR [95 % ECI]	p	β	SE	OR [95 % ECI]	p	β	SE	OR [95 % ECI]	p
Left posterior cingulate cortex	−0.80	0.41	0.45 [0.20, 1.00]	**0.05***	−0.85	0.42	0.43 [0.19, 0.98]	**0.04***	−0.77	0.42	0.46 [0.20, 1.05]	0.06	−1.74	0.83	0.18 [0.03, 0.89]	**0.04***
Right posterior cingulate cortex	−0.91	0.42	0.40 [0.18, 0.92]	**0.03***	−0.98	0.44	0.37 [0.16, 0.89]	**0.03***	−0.83	0.43	0.44 [0.19, 1.02]	0.06	−1.66	0.80	0.19 [0.04, 0.91]	**0.04***
Left entorhinal cortex	−0.17	0.35	0.84 [0.43, 1.66]	0.62	−0.19	0.35	0.82 [0.41, 1.64]	0.58	−0.21	0.37	0.81 [0.39, 1.68]	0.57	0.61	0.65	1.84 [0.51, 6.65]	0.35
Right entorhinal cortex	0.01	0.34	1.01 [0.52, 1.96]	0.98	0.003	0.34	1.00 [0.51, 1.96]	0.99	−0.07	0.37	0.93 [0.46, 1.91]	0.86	0.77	0.80	2.15 [0.45, 10.22]	0.34
Left hippocampus	−0.19	0.34	0.82 [0.42, 1.61]	0.57	−0.21	0.34	0.81 [0.42, 1.59]	0.55	−0.22	0.36	0.81 [0.40, 1.63]	0.55	0.37	0.63	1.45 [0.42, 5.01]	0.55
Right hippocampus	−0.13	0.34	0.88 [0.45, 1.70]	0.70	−0.10	0.35	0.90 [0.46, 1.78]	0.77	−0.01	0.36	0.99 [0.49, 2.00]	0.98	0.36	0.61	1.43 [0.43, 4.68]	0.56
Left amygdala	0.18	0.34	1.20 [0.61, 2.35]	0.60	0.22	0.36	1.25 [0.62, 2.50]	0.54	0.29	0.39	1.33 [0.63, 2.84]	0.45	0.85	0.79	2.35 [0.50, 11.01]	0.28
Right amygdala	−0.11	0.34	0.90 [0.46, 1.75]	0.76	−0.11	0.35	0.90 [0.45, 1.78]	0.76	−0.04	0.37	0.96 [0.47, 1.98]	0.91	0.16	0.64	1.18 [0.34, 4.10]	0.80

Note. Abbreviations: β = standardized beta-weight; *ECI* = exponentiated confidence interval; *OR* = odds ratio; *SE* = standard error; WASO = Wake After Sleep Onset, amount of time spent awake after falling asleep (minutes). Sleep discrepancy was calculated using difference scores (i.e., sleep diary – actigraphy). WASO discrepancy scores were reversed given that higher WASO indicates worse sleep quality. Negative values for WASO discrepancy reflect a negative sleep discrepancy, where self-reported sleep is worse than objective sleep, whilst positive values reflect a positive sleep discrepancy, where self-reported sleep is better than objective sleep. Brain glucose metabolism was assessed using [18F]-fluoro-2-deoxyglucose positron emission tomography (FDG-PET) standardized update value ratio. Insomnia severity was assessed with the Insomnia Severity Index. Depressive symptoms were assessed with the depression subscale of the Depression, Anxiety, and Stress Scales. For WASO, there is a three-cluster solution, where Cluster 1 = "WASO 1: no sleep discrepancy and good sleep quality"; Cluster 2 = "WASO 2: negative sleep discrepancy and poor sleep quality"; Cluster 3 = "WASO 3: positive sleep discrepancy and poor sleep quality". Negative and positive sleep discrepancy clusters were compared to the no sleep discrepancy cluster as a reference. Model 1 = glucose metabolism in each brain region predicting WASO discrepancy cluster membership, controlling for age (years) and education (years). Model 2 = glucose metabolism in each brain region predicting WASO discrepancy cluster membership, controlling for age (years), education (years), and insomnia severity. Model 3 = glucose metabolism in each brain region predicting WASO discrepancy cluster membership, controlling for age (years), education (years), and depressive symptoms. Model 4 = glucose metabolism in each brain region predicting WASO discrepancy cluster membership, controlling for age (years), education (years), and objective WASO. *$p < 0.05$, **$p < 0.01$.

Table 5
Binary logistic regression analyses exploring brain glucose metabolism as a predictor of Sleep Efficiency cluster membership.

Sleep Efficiency (Negative vs. No Sleep Discrepancy)																
	Model 1				Model 2				Model 3				Model 4			
Brain region	β	SE	OR [95 % ECI]	p	β	SE	OR [95 % ECI]	p	β	SE	OR [95 % ECI]	p	β	SE	OR [95 % ECI]	p
Neocortex	−0.32	0.27	0.73 [0.41, 1.22]	0.24	−0.33	0.29	0.72 [0.39, 1.23]	0.25	−0.33	0.28	0.72 [0.40, 1.22]	0.24	−0.53	0.30	0.59 [0.31, 1.03]	0.07
Frontal cortex	−0.31	0.27	0.73 [0.42, 1.23]	0.26	−0.26	0.28	0.77 [0.43, 1.33]	0.36	−0.31	0.27	0.73 [0.41, 1.23]	0.26	−0.54	0.30	0.58 [0.31, 1.02]	0.07
Temporal cortex	−0.65	0.31	0.52 [0.27, 0.92]	**0.04***	−0.72	0.32	0.49 [0.24, 0.89]	**0.03***	−0.65	0.31	0.52 [0.27, 0.92]	**0.04***	−0.90	0.36	0.41 [0.19, 0.77]	**0.01***
Inferior parietal cortex	−0.45	0.29	0.64 [0.34, 1.09]	0.12	−0.47	0.31	0.63 [0.32, 1.11]	0.14	−0.46	0.30	0.63 [0.33, 1.09]	0.12	−0.69	0.32	0.50 [0.25, 0.90]	**0.03***
Left superior parietal cortex	0.01	0.26	1.01 [0.60, 1.67]	0.98	−0.07	0.27	0.93 [0.54, 1.57]	0.80	0.01	0.26	1.01 [0.60, 1.68]	0.98	−0.10	0.28	0.91 [0.51, 1.55]	0.72
Right superior parietal cortex	0.02	0.26	1.02 [0.60, 1.71]	0.94	−0.12	0.28	0.89 [0.51, 1.52]	0.67	0.02	0.26	1.02 [0.60, 1.72]	0.93	−0.13	0.28	0.88 [0.49, 1.52]	0.64
Left posterior cingulate cortex	−0.05	0.26	0.95 [0.57, 1.57]	0.85	−0.06	0.26	0.94 [0.55, 1.57]	0.81	−0.05	0.26	0.95 [0.57, 1.58]	0.85	−0.20	0.27	0.82 [0.47, 1.39]	0.46
Right posterior cingulate cortex	−0.10	0.26	0.90 [0.53, 1.48]	0.68	−0.13	0.26	0.88 [0.51, 1.46]	0.61	−0.11	0.26	0.90 [0.53, 1.49]	0.69	−0.27	0.27	0.76 [0.44, 1.29]	0.32
Left entorhinal cortex	−0.15	0.26	0.86 [0.51, 1.43]	0.56	−0.31	0.28	0.73 [0.41, 1.26]	0.27	−0.15	0.26	0.86 [0.51, 1.43]	0.56	−0.17	0.27	0.84 [0.49, 1.43]	0.53
Right entorhinal cortex	−0.49	0.28	0.61 [0.34, 1.04]	0.08	−0.62	0.32	0.54 [0.28, 0.97]	0.05	−0.49	0.28	0.61 [0.34, 1.04]	0.08	−0.54	0.30	0.58 [0.31, 1.02]	0.07
Left hippocampus	−0.27	0.27	0.76 [0.44, 1.28]	0.32	−0.33	0.28	0.72 [0.40, 1.23]	0.24	−0.27	0.27	0.76 [0.44, 1.28]	0.31	−0.41	0.29	0.66 [0.36, 1.16]	0.16
Right hippocampus	−0.49	0.28	0.61 [0.34, 1.03]	0.08	−0.45	0.29	0.64 [0.34, 1.10]	0.12	−0.50	0.28	0.60 [0.34, 1.03]	0.07	−0.66	0.31	0.52 [0.27, 0.92]	**0.03***
Left amygdala	−0.65	0.31	0.52 [0.26, 0.92]	**0.04***	−0.70	0.34	0.50 [0.24, 0.91]	**0.04***	−0.65	0.31	0.52 [0.26, 0.92]	**0.04***	−0.87	0.38	0.42 [0.18, 0.82]	**0.02***
Right amygdala	−0.66	0.29	0.52 [0.28, 0.89]	**0.03***	−0.76	0.33	0.47 [0.23, 0.85]	**0.02***	−0.67	0.30	0.51 [0.27, 0.89]	**0.02***	−0.91	0.34	0.40 [0.19, 0.75]	**0.01****

Note. Abbreviations: β = standardized beta-weight; *ECI* = exponentiated confidence interval; *OR* = odds ratio; *SE* = standard error. Sleep Efficiency refers to the ratio of total sleep time to time in bed (%). Sleep discrepancy was calculated using difference scores (i.e., sleep diary – actigraphy). Negative values for Sleep Efficiency discrepancy reflect a negative sleep discrepancy, where self-reported sleep is worse than objective sleep, whilst positive values reflect a positive sleep discrepancy, where self-reported sleep is better than objective sleep. Brain glucose metabolism was assessed using [18F]-fluoro-2-deoxyglucose positron emission tomography (FDG-PET) standardized update value ratio. Insomnia severity was assessed with the Insomnia Severity Index. Depressive symptoms were assessed with the depression subscale of the Depression, Anxiety, and Stress Scales. For Sleep Efficiency, there is a two-cluster solution, where Cluster 1 = "Sleep Efficiency 1: no sleep discrepancy and good self-reported sleep quality"; Cluster 2 = "Sleep Efficiency 2: negative sleep discrepancy and poor self-reported sleep quality". Model 1 = glucose metabolism in each brain region predicting Sleep Efficiency discrepancy cluster membership, controlling for age (years). Model 2 = glucose metabolism in each brain region predicting Sleep Efficiency discrepancy cluster membership, controlling for age (years) and insomnia severity. Model 3 = glucose metabolism in each brain region predicting Sleep Efficiency discrepancy cluster membership, controlling for age (years) and depressive symptoms. Model 4 = glucose metabolism in each brain region predicting Sleep Efficiency discrepancy cluster membership, controlling for age (years) and objective Sleep Efficiency. *$p < 0.05$, **$p < 0.01$.

4) Sleep parameter cluster ~ SUVR + actigraphy-determined sleep + covariates.

Given that the current study is exploratory in nature and involves a small sample size, adjustment for multiple comparisons was not performed [51].

To aid the interpretability of the FDG-PET data, tests of normality (Shapiro-Wilk) [52] and skewness (test.skew from the statpsych package; a monte carlo *p*-value based on 250,000 replications) [53] were performed on the SUVR values, for all brain regions and the neocortex.

3. Results

Tests of normality and skewness performed on the FDG-PET SUVR data, were non-significant for all brain regions (data not shown), suggesting glucose metabolism remains within the "normal" range for all participants.

As shown in Table 2, there were no significant differences across TST and SE clusters with respect to demographic, cognitive, mood and health measures. Across WASO clusters, however, there were significant differences in BMI and DASS depression subscale scores. For WASO, FDG-PET SUVR values differed across clusters for the inferior parietal cortex, left superior parietal cortex, and bilateral posterior cingulate cortex. Across SE clusters, there were differences in FDG-PET SUVR values for the temporal cortex, right entorhinal cortex, left hippocampus, and bilateral amygdala. As expected, differences were observed for sleep measures across TST, WASO and SE clusters. Specifically, there were differences in actigraphy and sleep discrepancy measures across clusters for all three sleep parameters. While TST and SE clusters exhibited differences in sleep diary measures, WASO clusters did not. Moreover, there were differences in ISI total scores across TST and SE, but not WASO, clusters.

3.1. Predicting sleep discrepancy cluster membership with brain glucose metabolism

3.1.1. Total sleep time

A summary of regression output for the TST models, including standardized beta-weights, odds ratios, and *p*-values, is shown in Table 3. Higher glucose metabolism in the right superior parietal and left posterior cingulate regions was associated with a greater likelihood of belonging to the "TST 2: negative sleep discrepancy and shorter sleep duration" versus "TST 1: no sleep discrepancy and longer sleep duration" cluster, with large effect sizes observed (Model 1). Neither insomnia severity nor depressive symptoms (Models 2 and 3, respectively) had significant effects on the relationship between TST discrepancy and brain glucose metabolism. See Supplementary Tables 1.1–1.3 for models including covariates (i.e., education, insomnia severity, and depressive symptoms) across TST clusters.

3.1.2. Wake after sleep onset

A summary of regression output for the WASO models, including standardized beta-weights, odds ratios, and *p*-values, is shown in

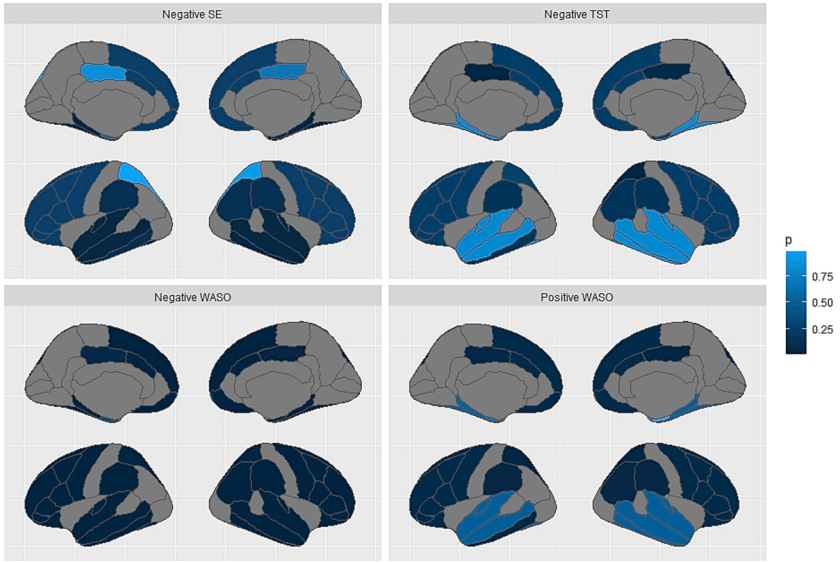


Fig. 2. Visual representation of logistic regression models, with regional brain glucose metabolism predicting sleep discrepancy cluster membership, for each sleep parameter. Regions are shaded on a Desikan-Killiany atlas, representing the magnitude of the *p*-value for each region analysed as a predictor of cluster membership. Within each quadrant, the top two images represent a mid-sagittal view of the left and right hemisphere, respectively, while the bottom two images represent a lateral view of the left and right hemisphere, respectively. The figure was generated using ggseg in R. Abbreviations: SE, Sleep Efficiency (ratio of total sleep time to time in bed, %); TST, Total Sleep Time (amount of time spent asleep, minutes); WASO, Wake After Sleep Onset (amount of time spent awake after falling asleep, minutes).

Table 4. Lower glucose metabolism in most brain regions (neocortex, frontal cortex, temporal cortex, inferior parietal cortex, bilateral superior parietal cortex, right posterior cingulate cortex, right entorhinal cortex, bilateral hippocampus, and bilateral amygdala) was associated with a greater likelihood of belonging to the "WASO 2: negative sleep discrepancy and poor sleep quality" versus "WASO 1: no sleep discrepancy and good sleep quality" cluster, with large effect sizes observed (Model 1). For most brain regions, neither insomnia severity nor depressive symptoms (Models 2 and 3, respectively) had significant effects on the relationship between WASO discrepancy and brain glucose metabolism.

Lower glucose metabolism in the inferior parietal cortex, bilateral superior parietal cortex, and bilateral posterior cingulate cortex was associated with a greater likelihood of belonging to the "WASO 3: positive sleep discrepancy and poor sleep quality" versus "WASO 1: no sleep discrepancy and good sleep quality" cluster, with large effect sizes observed (Model 1); the same pattern of results was found when controlling for insomnia severity (Model 2). When controlling for depressive symptoms, lower glucose metabolism in the bilateral superior parietal cortex remained significantly associated with a greater likelihood of belonging to the "WASO 3: positive sleep discrepancy and poor sleep quality" versus "WASO 1: no sleep discrepancy and good sleep quality" cluster, with large effect sizes evident, but the association with inferior parietal cortex glucose metabolism disappeared (Model 3). See Supplementary Tables 2.1–2.3 for models including covariates (i.e., age, education, insomnia severity, and depressive symptoms) across WASO clusters.

3.1.3. Sleep efficiency

A summary of regression output for the SE models, including standardized beta-weights, odds ratios, and *p*-values, is shown in Table 5. Lower glucose metabolism in the temporal cortex and bilateral amygdala was associated with a greater likelihood of belonging to the "SE 2: negative sleep discrepancy and poor self-reported sleep quality" versus "SE 1: no sleep discrepancy and good self-reported sleep quality" cluster, with large effect sizes observed (Model 1). Neither insomnia severity nor depressive symptoms (Models 2 and 3, respectively) had significant effects on the relationship between SE discrepancy and brain glucose metabolism. See Supplementary Tables 3.1–3.3 for models including covariates (i.e., age, insomnia severity, and depressive symptoms) across SE clusters.

A visual representation of logistic regression results is shown in Figs. 2 and 3. Fig. 2 uses a Desikan-Killiany atlas [54] to illustrate *p*-value magnitudes across the frontal, temporal, inferior parietal, left and right superior parietal, left and right posterior cingulate, and left and right entorhinal cortices. Fig. 3 uses an automatic subcortical segmentation atlas [55] to visualise *p*-values for subcortical regions, namely the left and right hippocampus, and left and right amygdala. As Figs. 2 and 3 illustrate, the significant brain regions of interest varied across the three sleep parameters. For example, lower glucose metabolism across most brain regions assessed was

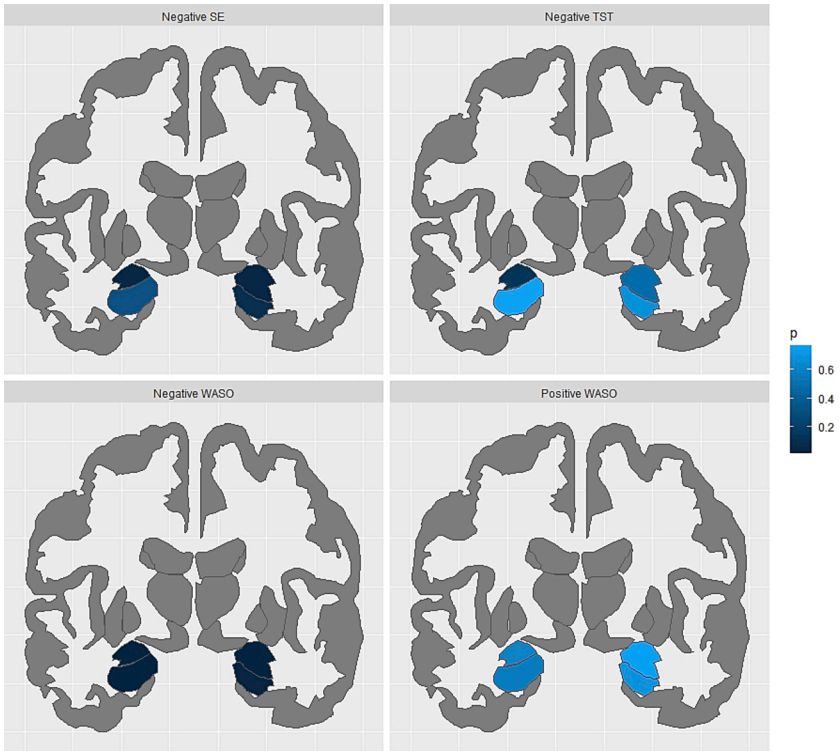


Fig. 3. Visual representation of logistic regression models, with regional brain glucose metabolism predicting sleep discrepancy cluster membership, for each sleep parameter. Regions are shaded on an automatic subcortical segmentation (aseg) atlas, representing the magnitude of the *p*-value for each subcortical structure analysed as a predictor of cluster membership. The figure was generated using ggseg in R. Abbreviations: SE, Sleep Efficiency (ratio of total sleep time to time in bed, %); TST, Total Sleep Time (amount of time spent asleep, minutes); WASO, Wake After Sleep Onset (amount of time spent awake after falling asleep, minutes).

associated with negative WASO discrepancy, while higher/lower brain glucose metabolism across fewer brain regions was associated with negative TST discrepancy (i.e., right superior parietal and left posterior cingulate), and negative SE discrepancy (i.e., temporal cortex and bilateral amygdala).

3.1.4. Post-Hoc exploratory analyses with actigraphy-determined sleep

For TST, when controlling for actigraphy-determined sleep, lower glucose metabolism in the right entorhinal cortex and left amygdala was associated with a greater likelihood of belonging to the "TST 2: negative sleep discrepancy and shorter sleep duration" versus: "TST 1: no sleep discrepancy and longer sleep duration" cluster, with large effect sizes seen (Table 3, Model 4).

For WASO, when controlling for actigraphy-determined sleep, lower glucose metabolism in the neocortex, frontal cortex, temporal cortex, inferior parietal cortex, bilateral superior parietal cortex, right posterior cingulate cortex, left hippocampus, and bilateral amygdala was associated with a greater likelihood of belonging to the "WASO 2: negative sleep discrepancy and poor sleep quality" versus "WASO 1: no sleep discrepancy and good sleep quality" cluster (Table 4, Model 4). In addition, for WASO, lower glucose metabolism in the inferior parietal cortex, bilateral superior parietal cortex, and bilateral posterior cingulate cortex was associated with a greater likelihood of belonging to the "WASO 3: positive sleep discrepancy and poor sleep quality" versus "WASO 1: no sleep discrepancy and good sleep quality" cluster (Table 4, Model 4).

For SE, when controlling for actigraphy-determined sleep, lower glucose metabolism in the temporal cortex, inferior parietal cortex, right hippocampus, and bilateral amygdala was associated with a greater likelihood of belonging to the "SE 2: negative sleep discrepancy and poor self-reported sleep quality" versus "SE 1: no sleep discrepancy and good self-reported sleep quality" cluster (Table 5, Model 4). See Supplementary Tables 1.4, 2.4, and 3.4 for models including covariates and actigraphy-determined sleep, across TST, WASO and SE clusters.

4. Discussion

In a sample of cognitively unimpaired community-dwelling older adults, the current exploratory study investigated the relationship between sleep discrepancy and brain glucose metabolism (both global and regional), an indicator of brain health, by examining: 1) whether clusters characterised by greater sleep discrepancy (either negative or positive) and/or poor sleep (self-reported and/or actigraphy-determined) are associated with lower brain glucose metabolism; and 2) whether there is a unique relationship between sleep discrepancy and brain glucose metabolism when controlling for insomnia severity and depressive symptoms, respectively, as covariates. To further isolate the sleep discrepancy construct, post-hoc analyses were conducted controlling for actigraphy-determined sleep. Analyses focussed on the sleep parameters of TST, WASO, and SE.

For TST, somewhat unexpectedly, higher glucose metabolism in the right superior parietal and left posterior cingulate cortex was associated with a greater likelihood of belonging to the cluster characterised by a negative sleep discrepancy (versus no sleep discrepancy). The superior parietal and posterior cingulate regions form part of the default mode network (DMN), a group of brain regions that is active during idle mental states. Higher neural activation in these regions, which can be reflected by higher levels of glucose metabolism, may represent a "compensatory" process (i.e., an attempt to compensate for the decrease in activity in DMN areas) or an inability to deactivate the DMN, and is observed in pre-clinical cases of neurodegenerative disease, such as AD. For example, individuals with MCI and early AD, compared to healthy controls, show hyperactivation in core areas of the DMN [56]). In the current study, higher activation in the superior parietal and posterior cingulate cortex was associated with negative TST discrepancy. Together with previous findings that positive TST discrepancy may predict cognitive impairment [6], our results suggest TST discrepancy in either direction may be a prognostic marker of AD risk. Although, it should be noted that other aspects of the DMN were not directly examined; future research is needed to replicate the current study and further explore the role of TST discrepancy.

For SE, lower glucose metabolism in the temporal cortex and bilateral amygdala was associated with a greater likelihood of belonging to the cluster characterised by a negative sleep discrepancy (versus no sleep discrepancy). That is, there appears to be an association between negative SE discrepancy and *lower* glucose metabolism in brain regions central to emotional functioning and learning/memory – this is the opposite pattern to that observed for TST in the current study, and is somewhat surprising, given that SE is calculated as TST divided by time in bed. This pattern may therefore implicate the time in bed variable as responsible for the shift in direction of effect and brain regions involved. For example, longer time in bed may represent greater time spent ruminating about sleep throughout the night. Alternatively, discordant findings may be because SE is more difficult to estimate than other sleep parameters. SE involves summation of multiple pieces of information, and findings may reflect poorer cognitive capacity impacting accurate recall of sleep, resulting in sleep discrepancy. This notion is consistent with not only the regions linked to negative SE discrepancy in the current study, but also our previous study [7], where we found negative SE discrepancy to be associated with poorer delayed memory in cognitively unimpaired older adults.

For WASO, lower glucose metabolism in most brain regions (neocortex, frontal cortex, temporal cortex, inferior parietal cortex, bilateral superior parietal cortex, right posterior cingulate cortex, right entorhinal cortex, bilateral hippocampus, and bilateral amygdala) was associated with a greater likelihood of belonging to the negative sleep discrepancy (versus no sleep discrepancy) cluster. This suggests a relationship between negative WASO discrepancy and lower glucose metabolism across almost the entire cortex, which is consistent with the negative association observed in the neocortex. In comparison, for positive WASO discrepancy, there were associations with glucose metabolism across fewer brain regions. Specifically, lower glucose metabolism in the inferior parietal cortex, bilateral superior parietal cortex, and bilateral posterior cingulate cortex was associated with a greater likelihood of belonging to the cluster characterised by a positive sleep discrepancy (versus no sleep discrepancy). Hypometabolism in these regions associated with positive WASO discrepancy has previously been identified as a biomarker for early AD [57,58]. It is possible that this

may constitute a link between positive WASO discrepancy and early AD-related brain changes, although such a notion is speculative and pending replication given the exploratory nature of the current study and the novelty of this research area.

When controlling for insomnia severity and depressive symptoms, the same pattern of results was largely found across TST, WASO, and SE analyses. That is, insomnia severity and depressive symptoms did not appear to affect the relationship, suggesting a unique association between sleep discrepancy and brain glucose metabolism. Further, when controlling for actigraphy-determined sleep, results remained mostly consistent for WASO and SE analyses. This suggests that the link between WASO and SE discrepancy and brain glucose metabolism may not simply be due to the deleterious neurobiological effects of poor objective sleep on brain health (e.g., less clearance of neurotoxic waste products during sleep) [59]. Instead, the remaining two components of the clusters – self-reported sleep and the difference score – appear to be the driving factors behind the relationship between sleep discrepancy and brain glucose metabolism for WASO and SE. It is possible that perceived poor sleep may contribute towards high levels of allostatic load, the cumulative burden of chronic stress and physiological dysregulation of multiple body systems [60]. Specifically, the stress of perceiving oneself as sleep-deprived may contribute to negative health outcomes [61–63] such as lower brain glucose metabolism. Alternatively, some have proposed that perception of sleep may confer a kind of "placebo" effect, such that perception of sleep quantity/quality on a given night can lead to better or worse neurobiological function the next day depending on the direction (i.e., negative or positive) of sleep discrepancy [64–66].

As noted before, negative TST discrepancy was associated with several nodes in the DMN; interestingly, controlling for actigraphy-determined sleep resulted in a different pattern of findings, where associations with DMN nodes were lost, and instead, lower glucose metabolism in the right entorhinal cortex and left amygdala was associated with a greater likelihood of belonging to the cluster characterised by a negative sleep discrepancy (versus no sleep discrepancy). As such, it is possible that the relationship between sleep discrepancy and altered DMN activity is attributable to actigraphy-determined TST, at least in part, while self-reported TST and/or the difference score may be contributing towards altered activity in regions involved in emotional functioning and learning/memory. Again, while speculative, these hypotheses provide, at least, some framework by which to understand the construct of sleep discrepancy and its relationship with neurobiological systems, although more theoretical development is required in this area.

To our knowledge, only one previous study has directly explored the relationship between sleep discrepancy and neuroimaging biomarkers of brain health in community-dwelling older adults [8]. In a sample similar to the current study, Winer et al. [8] found that greater absolute and negative sleep discrepancy was associated with greater brain Aβ, but not tau, burden. Given that changes in regional brain glucose metabolism and Aβ deposition (relative to tau accumulation) may represent early stages in the AD process [21,67], our findings and those of Winer et al. [8] suggest that sleep discrepancy may be a prognostic marker for early AD. In line with this, greater sleep discrepancy, as well as both negative [3,7,8] and positive [6,15,19] forms of sleep discrepancy, are associated with poorer cognitive function in cognitively unimpaired older adults and commonly occur in MCI/AD samples. While collectively, these findings are intriguing, as mentioned previously, the role of sleep discrepancy as a marker or risk factor for AD remains tentative and any conclusions are pending support from future research, especially where the limitations of the current study are addressed.

In the current study, the use of wrist-mounted actigraphy meant that 'objective' sleep measurement was constrained by participants' self-reported estimate of their in-bed and out-of-bed times, as reported in their sleep diary. Moreover, actigraphy as a proxy for objective sleep has some drawbacks, given that it infers sleep through lack of movement. Although in saying this, research has shown actigraphy to demonstrate high accuracy (i.e., >80 %) compared to polysomnography [68], which is recognised as the "gold standard" objective measure of sleep. Of note, polysomnography also shows some degree of inaccuracy, and is more resource-intensive and challenging to implement across multiple nights, making it less amenable to the seven-day "averaging" method of sleep discrepancy employed in the current study. This "averaging" approach is particularly important, given that there is considerable night-to-night variability in sleep discrepancy in older adults [69], and measurement across one or two nights via polysomnography might yield unrepresentative estimates. Future sleep discrepancy research would benefit from using wearables that are both easy to use, but also address limitations by incorporating additional measures, such as heart rate, as well as offering independent bed/rise time detection.

Another potential limitation of the current study relates to the operationalisation of the sleep discrepancy clusters. These were labelled based on a series of validation steps, including comparison to consensus guidelines for sleep quantity/quality, contingency tables, visual inspection, and mean comparisons of discrepancy values across clusters – while most of these metrics aligned with our cluster labels, other factors, such as the range of discrepancy between clusters, are overlapping, and suggests that the clusters themselves may not completely map onto discrete discrepancy subtypes.

In the current study, brain scans and sleep measures were not conducted simultaneously; however, stepwise model selection (see Statistical Analysis Methods) suggested that time between brain scan and sleep assessment not be included in subsequent analysis. An additional consideration relates to multiple comparisons, which were not performed given that the current study is exploratory in nature and comprised a small sample [51]. Nevertheless, our findings represent an important contribution to this area of research, identifying potential relationships of interest (e.g., with specific brain regions) to investigate further in larger samples. Finally, the cross-sectional design of the current study precludes understanding of temporal relationships; future research would benefit from investigating the link between sleep discrepancy and biomarkers of brain health longitudinally.

In summary, this study was the first to explore the relationship of sleep discrepancy to brain glucose metabolism, a dynamic biomarker of brain health, in community-dwelling older adults. Specifically, we found associations between sleep discrepancy and higher/lower resting-state glucose metabolism across multiple brain regions in community-dwelling older adults. This is a novel finding and provides preliminary evidence to support the idea that sleep discrepancy may constitute a marker or risk factor for early brain changes in older adults. This could potentially provide a foundation from which to further understand the higher incidence of sleep discrepancy in older adult populations, which also tends to increase alongside the advancement of neurodegenerative disease. The current study also showed that associations between sleep discrepancy and brain glucose metabolism survived correction for

insomnia severity and depressive symptoms, suggesting that sleep discrepancy itself may impact neurobiological function independently of these related constructs. However, any conclusions described herein should be considered in the context of the study limitations described above. Nevertheless, effect sizes observed in the current study were typically large, and future research into this area is clearly warranted. In the case where our preliminary findings are supported by future studies, this may implicate sleep discrepancy as a unique and salient predictor of brain changes in later life.

CRediT authorship contribution statement

Nadia Soh: Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Conceptualization. **Michael Weinborn:** Writing – review & editing, Supervision, Methodology, Conceptualization. **James D. Doecke:** Writing – review & editing, Supervision, Methodology, Formal analysis. **Rodrigo Canovas:** Writing – review & editing, Supervision, Methodology, Formal analysis. **Vincent Doré:** Writing – review & editing, Data curation. **Ying Xia:** Data curation. **Jurgen Fripp:** Data curation. **Kevin Taddei:** Resources, Project administration. **Romola S. Bucks:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Hamid R. Sohrabi:** Writing – review & editing. **Ralph N. Martins:** Project administration. **Melissa Ree:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Stephanie R. Rainey-Smith:** Writing – review & editing, Supervision, Methodology, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We thank all those who participated in this research project, and their families, for their commitment to ageing and Alzheimer's research.

Disclosure Statement

NS is supported by an Australian Government Research Training Project (RTP) stipend. SRRS is supported by a National Health and Medical Research Council (NHMRC) Investigator Grant (GNT1197315). This work was supported by grants awarded to SRRS by The Yulgilbar Foundation (Yulgilbar Alzheimer's Research Program), the Brain Foundation, and the Government of Western Australia (Department of Health/Future Health WA Merit Award).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nbas.2024.100130.

References

[1] Kay DB, Buysse DJ, Germain A, Hall M, Monk TH. Subjective–objective sleep discrepancy among older adults: associations with insomnia diagnosis and insomnia treatment. J Sleep Res 2015;24(1):32–9. https://doi.org/10.1111/jsr.12220.
[2] Tsuchiyama K, Nagayama H, Kudo K, Kojima K, Yamada K. Discrepancy between subjective and objective sleep in patients with depression. Psychiatry Clin Neurosci 2003;57(3):259–64. https://doi.org/10.1046/j.1440-1819.2003.01114.x.
[3] Hita-Yanez E, Atienza M, Cantero JL. Polysomnographic and subjective sleep markers of mild cognitive impairment. Sleep 2013;36(9):1327–34. https://doi.org/10.5665/sleep.2956.
[4] Cho S-E, Kang JM, Ko K-P, Lim W-J, Redline S, Winkelman JW, et al. Association between subjective-objective discrepancy of sleeping time and health-related quality of life: a community-based polysomnographic study. Psychosom Med 2022;84(4):505–12. https://doi.org/10.1097/PSY.0000000000001070.
[5] Utsumi T, Yoshiike T, Kaneita Y, Aritake-Okada S, Matsui K, Nagao K, et al. The association between subjective–objective discrepancies in sleep duration and mortality in older men. Sci Rep 2022;12(1):18650. https://doi.org/10.1038/s41598-022-22065-8.
[6] Van Den Berg JF, Van Rooij FJ, Vos H, Tulen JH, Hofman A, Miedema HM, et al. Disagreement between subjective and actigraphic measures of sleep duration in a population-based study of elderly persons. J Sleep Res 2008;17(3):295–302. https://doi.org/10.1111/j.1365-2869.2008.00638.x.
[7] Soh N, Rainey-Smith SR, Ree MJ, Bucks RS, Doecke J, Canovas R, et al. Sleep discrepancy and cognitive function in community-dwelling older adults. J Sleep Res 2024. https://doi.org/10.1111/jsr.14288.
[8] Winer JR, Morehouse A, Fenton L, Harrison TM, Ayangma L, Reed M, et al. Tau and β-amyloid burden predict actigraphy-measured and self-reported impairment and misperception of human sleep. J Neurosci 2021;41(36):7687–96. https://doi.org/10.1523/JNEUROSCI.0353-21.2021.
[9] Sperling RA, Karlawish J, Johnson KA. Preclinical Alzheimer disease-the challenges ahead. Nat Rev Neurol 2013;9(1):54–8. https://doi.org/10.1038/nrneurol.2012.241.
[10] Ohayon MM, Carskadon MA, Guilleminault C, Vitiello MV. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. Sleep 2004;27(7):1255–73. https://doi.org/10.1093/sleep/27.7.1255.
[11] Benz F, Riemann D, Domschke K, Spiegelhalder K, Johann AF, Marshall NS, et al. How many hours do you sleep? A comparison of subjective and objective sleep duration measures in a sample of insomnia patients and good sleepers. J Sleep Res 2023;32(2):e13802. https://doi.org/10.1111/jsr.13802.
[12] Ma Y, Goldstein MR, Davis RB, Yeh GY. Profile of subjective-objective sleep discrepancy in patients with insomnia and sleep apnea. J Clin Sleep Med 2021;17(11):2155–63. https://doi.org/10.5664/jcsm.9348.

[13] Trajanovic NN, Radivojevic V, Kaushansky Y, Shapiro CM. Positive sleep state misperception–a new concept of sleep misperception. Sleep Med 2007;8(2):111–8. https://doi.org/10.1016/j.sleep.2006.08.013.
[14] Li Y, Zou G, Shao Y, Yao P, Liu J, Zhou S, et al. Sleep discrepancy is associated with alterations in the salience network in patients with insomnia disorder: an EEG-fMRI study. Neuroimage Clin 2022;35:103111. https://doi.org/10.1016/j.nicl.2022.103111.
[15] Most EI, Aboudan S, Scheltens P, Van Someren EJ. Discrepancy between subjective and objective sleep disturbances in early-and moderate-stage Alzheimer disease. Am J Geriatr Psychiatry 2012;20(6):460–7. https://doi.org/10.1097/JGP.0b013e318252e3ff.
[16] Spiegelhalder K, Regen W, Baglioni C, Nissen C, Riemann D, Kyle SD. Neuroimaging insights into insomnia. Curr Neurol Neurosci Rep 2015;15(3):9. https://doi.org/10.1007/s11910-015-0527-3.
[17] Tadokoro K, Ohta Y, Hishikawa N, Nomura E, Wakutani Y, Takao Y, et al. Discrepancy of subjective and objective sleep problems in Alzheimer's disease and mild cognitive impairment detected by a home-based sleep analysis. J Clin Neurosci 2020;74:76–80. https://doi.org/10.1016/j.jocn.2020.01.085.
[18] Wu Y, Zhuang Y, Qi J. Explore structural and functional brain changes in insomnia disorder: A PRISMA-compliant whole brain ALE meta-analysis for multimodal MRI. Medicine 2020;99(14):e19151.
[19] DiNapoli EA, Gebara MA, Kho T, Butters MA, Gildengers AG, Albert SM, et al. Subjective-objective sleep discrepancy in older adults with MCI and subsyndromal depression. J Geriatr Psychiatry Neurol 2017;30(6):316–23. https://doi.org/10.1177/0891988717731827.
[20] Kay DB, Karim HT, Soehner AM, Hasler BP, James JA, Germain A, et al. Subjective-objective sleep discrepancy is associated with alterations in regional glucose metabolism in patients with insomnia and good sleeper controls. Sleep 2017;40(11):zsx155.
[21] Hardy JA, Higgins GA. Alzheimer's disease: the amyloid cascade hypothesis. Science 1992;256(5054):184–5. https://doi.org/10.1126/science.1566067.
[22] Shanock LR, Baran BE, Gentry WA, Pattison SC, Heggestad ED. Polynomial regression with response surface analysis: a powerful approach for examining moderation and overcoming limitations of difference scores. J Bus Psychol 2010;25(4):543–54. https://doi.org/10.1007/s10869-010-9183-4.
[23] Mosconi L, Tsui WH, Herholz K, Pupi A, Drzezga A, Lucignani G, et al. Multicenter standardized 18F-FDG PET diagnosis of mild cognitive impairment, Alzheimer's disease, and other dementias. J Nucl Med 2008;49(3):390–8. https://doi.org/10.2967/jnumed.107.045385.
[24] Beck AT, Bredemeier K. A unified model of depression: Integrating clinical, cognitive, biological, and evolutionary perspectives. Clin Psychol Sci 2016;4(4):596–619. https://doi.org/10.1177/2167702616628523.
[25] Harvey AG. A cognitive model of insomnia. Behav Res Ther 2002;40(8):869–93. https://doi.org/10.1016/s0005-7967(01)00061-4.
[26] Lovato N, Micic G, Lack L. Sleep misestimation among older adults suffering from insomnia with short and normal objective sleep duration and the effects of cognitive behavior therapy. Sleep 2021;44(5):zsaa250. https://doi.org/10.1093/sleep/zsaa250.
[27] Rotenberg VS, Indursky P, Kayumov L, Sirota P, Melamed Y. The relationship between subjective sleep estimation and objective sleep variables in depressed patients. Int J Psychophysiol 2000;37(3):291–7. https://doi.org/10.1016/s0167-8760(00)00110-0.
[28] Yoon G, Lee MH, Oh SM, Choi J-W, Yoon SY, Lee YJ. Negative and positive sleep state misperception in patients with insomnia: factors associated with sleep perception. J Clin Sleep Med 2022;18(7):1789–95. https://doi.org/10.5664/jcsm.9974.
[29] Fortier-Brochu É, Beaulieu-Bonneau S, Ivers H, Morin CM. Insomnia and daytime cognitive performance: a meta-analysis. Sleep Med Rev 2012;16(1):83–94. https://doi.org/10.1016/j.smrv.2011.03.008.
[30] McDermott LM, Ebmeier KP. A meta-analysis of depression severity and cognitive function. J Affect Disord 2009;119(1–3):1–8. https://doi.org/10.1016/j.jad.2009.04.022.
[31] Bagherzadeh-Azbari S, Khazaie H, Zarei M, Spiegelhalder K, Walter M, Leerssen J, et al. Neuroimaging insights into the link between depression and insomnia: a systematic review. J Affect Disord 2019;258:133–43. https://doi.org/10.1016/j.jad.2019.07.089.
[32] Kay DB, Karim HT, Soehner AM, Hasler BP, Wilckens KA, James JA, et al. Sleep-wake differences in relative regional cerebral metabolic rate for glucose among patients with insomnia compared with good sleepers. Sleep 2016;39(10):1779–94. https://doi.org/10.5665/sleep.6154.
[33] Long Y, Cao H, Yan C, Chen X, Li L, Castellanos FX, et al. Altered resting-state dynamic functional brain networks in major depressive disorder: findings from the REST-meta-MDD consortium. Neuroimage Clin 2020;26:102163. https://doi.org/10.1016/j.nicl.2020.102163.
[34] Littner M, Kushida CA, Anderson WM, Bailey D, Berry RB, Davila DG, et al. Practice parameters for the role of actigraphy in the study of sleep and circadian rhythms: an update for 2002. Sleep 2003;26(3):337–41. https://doi.org/10.1093/sleep/26.3.337.
[35] Carney CE, Buysse DJ, Ancoli-Israel S, Edinger JD, Krystal AD, Lichstein KL, et al. The consensus sleep diary: standardizing prospective sleep self-monitoring. Sleep 2012;35(2):287–302. https://doi.org/10.5665/sleep.1642.
[36] Cole RJ, Kripke DF, Gruen W, Mullaney DJ, Gillin JC. Automatic sleep/wake identification from wrist activity. Sleep 1992;15(5):461–9. https://doi.org/10.1093/sleep/15.5.461.
[37] Ancoli-Israel S, Martin JL, Blackwell T, Buenaver L, Liu L, Meltzer LJ, et al. The SBSM guide to actigraphy monitoring: clinical and research applications. Behav Sleep Med 2015;13(Suppl 1):S4–38. https://doi.org/10.1080/15402002.2015.1046356.
[38] Gardener SL, Sohrabi HR, Shen K-K, Rainey-Smith SR, Weinborn M, Bates KA, et al. Cerebral glucose metabolism is associated with verbal but not visual memory performance in community-dwelling older adults. J Alzheimer's Dis 2016;52(2):661–72. https://doi.org/10.3233/JAD-151084.
[39] André C, Laniepce A, Chételat G, Rauchs G. Brain changes associated with sleep disruption in cognitively unimpaired older adults: a short review of neuroimaging studies. Ageing Res Rev 2021;66:101252. https://doi.org/10.1016/j.arr.2020.101252.
[40] Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep Med 2001;2(4):297–307. https://doi.org/10.1016/s1389-9457(00)00065-4.
[41] Lovibond PF, Lovibond SH. The structure of negative emotional states: comparison of the depression anxiety stress scales (DASS) with the beck depression and anxiety inventories. Behav Res Ther 1995;33(3):335–43. https://doi.org/10.1016/0005-7967(94)00075-u.
[42] Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med 1999;131(7):485–91. https://doi.org/10.7326/0003-4819-131-7-199910050-00002.
[43] Ancoli-Israel S, Cole R, Alessi C, Chambers M, Moorcroft W, Pollak CP. The role of actigraphy in the study of sleep and circadian rhythms. Sleep 2003;26(3):342–92. https://doi.org/10.1093/sleep/26.3.342.
[44] Lee D. The convergent, discriminant, and nomological validity of the depression anxiety stress scales-21 (DASS-21). J Affect Disord 2019;259:136–42. https://doi.org/10.1016/j.jad.2019.06.036.
[45] Maich KH, Lachowski AM, Carney CE. Psychometric properties of the consensus sleep diary in those with insomnia disorder. Behav Sleep Med 2018;16(2):117–34. https://doi.org/10.1080/15402002.2016.1173556.
[46] Tan A, Yin JD, Tan LW, van Dam RM, Cheung YY, Lee C-H. Using the Berlin questionnaire to predict obstructive sleep apnea in the general population. J Clin Sleep Med 2017;13(3):427–32. https://doi.org/10.5664/jcsm.6496.
[47] R Core Team. (2023). *R: A Language and Environment for Statistical Computing*. In R Foundation for Statistical Computing. https://www.R-project.org/.
[48] Martin JL, Hakim AD. Wrist actigraphy. Chest 2011;139(6):1514–27. https://doi.org/10.1378/chest.10-1872.
[49] Winser MA, McBean AL, Montgomery-Downs HE. Minimum duration of actigraphy-defined nocturnal awakenings necessary for morning recall. Sleep Med 2013;14(7):688–91. https://doi.org/10.1016/j.sleep.2013.03.018.
[50] Venables W, Ripley B. Modern applied statistics with S. 4 ed. Springer; 2002.
[51] Althouse AD. Adjust for multiple comparisons? It's not that simple. Ann Thorac Surg 2016;101(5):1644–5. https://doi.org/10.1016/j.athoracsur.2015.11.024.
[52] Shapiro SS, Wilk MB. An Analysis of variance test for normality (complete samples). Biometrika 1965;52(3/4):591–611. https://doi.org/10.2307/2333709.
[53] Bonett DG, Calin-Jageman RJ. (2024). *statpsych: Statistical methods for psychologists*. In (Version 1.6.0) [R package]. Comprehensive R Archive Network (CRAN). https://CRAN.R-project.org/package=statpsych.
[54] Desikan RS, Ségonne F, Fischl B, Quinn BT, Dickerson BC, Blacker D, et al. An automated labeling system for subdividing the human cerebral cortex on MRI scans into gyral based regions of interest. Neuroimage 2006;31(3):968–80. https://doi.org/10.1016/j.neuroimage.2006.01.021.
[55] Fischl B, Salat DH, Busa E, Albert M, Dieterich M, Haselgrove C, et al. Whole brain segmentation: automated labeling of neuroanatomical structures in the human brain. Neuron 2002;33(3):341–55. https://doi.org/10.1016/s0896-6273(02)00569-x.

[56] Mevel K, Chételat G, Eustache F, Desgranges B. The default mode network in healthy aging and Alzheimer's disease. Int J Alzheimers Dis 2011;2011:535816. https://doi.org/10.4061/2011/535816.
[57] Marcus C, Mena E, Subramaniam RM. Brain PET in the diagnosis of Alzheimer's disease. Clin Nucl Med 2014;39(10):e413–26. https://doi.org/10.1097/RLU.0000000000000547.
[58] Mosconi L, Tsui W-H, De Santi S, Li J, Rusinek H, Convit A, et al. Reduced hippocampal metabolism in MCI and AD: automated FDG-PET image analysis. Neurology 2005;64(11):1860–7. https://doi.org/10.1212/01.WNL.0000163856.13524.08.
[59] Jessen NA, Munk ASF, Lundgaard I, Nedergaard M. The glymphatic system: a beginner's guide. Neurochem Res 2015;40(12):2583–99. https://doi.org/10.1007/s11064-015-1581-6.
[60] Christensen DS, Zachariae R, Amidi A, Wu LM. Sleep and allostatic load: a systematic review and meta-analysis. Sleep Med Rev 2022;64:101650. https://doi.org/10.1016/j.smrv.2022.101650.
[61] Clark AJ, Dich N, Lange T, Jennum P, Hansen AM, Lund R, et al. Impaired sleep and allostatic load: cross-sectional results from the Danish Copenhagen Aging and Midlife Biobank. Sleep Med 2014;15(12):1571–8. https://doi.org/10.1016/j.sleep.2014.07.013.
[62] Juster RP, McEwen BS, Lupien SJ. Allostatic load biomarkers of chronic stress and impact on health and cognition. Neurosci Biobehav Rev 2010;35(1):2–16. https://doi.org/10.1016/j.neubiorev.2009.10.002.
[63] Palagini L, Hertenstein E, Riemann D, Nissen C. Sleep, insomnia and mental health. J Sleep Res 2022;31(4):e13628.
[64] Draganich C, Erdal K. Placebo sleep affects cognitive functioning. J Exp Psychol Learn Mem Cogn 2014;40(3):857–64. https://doi.org/10.1037/a0035546.
[65] Gavriloff D, Sheaves B, Juss A, Espie CA, Miller CB, Kyle SD. Sham sleep feedback delivered via actigraphy biases daytime symptom reports in people with insomnia: implications for insomnia disorder and wearable devices. J Sleep Res 2018;27(6):e12726.
[66] Rahman SA, Rood D, Trent N, Solet J, Langer EJ, Lockley SW. Manipulating sleep duration perception changes cognitive performance - An exploratory analysis. J Psychosom Res 2020;132:109992. https://doi.org/10.1016/j.jpsychores.2020.109992.
[67] Jack Jr CR, Bennett DA, Blennow K, Carrillo MC, Dunn B, Haeberlein SB, et al. NIA-AA research framework: toward a biological definition of Alzheimer's disease. Alzheimers Dement 2018;14(4):535–62. https://doi.org/10.1016/j.jalz.2018.02.018.
[68] Marino M, Li Y, Rueschman MN, Winkelman JW, Ellenbogen JM, Solet JM, et al. Measuring sleep: accuracy, sensitivity, and specificity of wrist actigraphy compared to polysomnography. Sleep 2013;36(11):1747–55. https://doi.org/10.5665/sleep.3142.
[69] Kay DB, Dzierzewski JM, Rowe M, McCrae CS. Greater night-to-night variability in sleep discrepancy among older adults with a sleep complaint compared to noncomplaining older adults. Behav Sleep Med 2013;11(2):76–90.