International Psychogeriatrics: page 1 of 11 © International Psychogeriatric Association 2023
doi:10.1017/S1041610223000911

Effects of age on the relationship between sleep quality and cognitive performance: Findings from the Human Connectome Project-Aging cohort‡

Daniel E. Cohen,[1] Hyun Kim,[1,2] Alina Levine,[3] Davangere P. Devanand,[1,2,4] Seonjoo Lee,[3,5] and Terry E. Goldberg[1,2,6]

[1]*Division of Geriatric Psychiatry, New York State Psychiatric Institute, New York, NY, USA*
[2]*Department of Psychiatry, Columbia University Irving Medical Center, New York, NY, USA*
[3]*Division of Mental Health Data Science, New York State Psychiatric Institute, New York, NY, USA*
[4]*Department of Neurology, Columbia University Irving Medical Center, New York, NY, USA*
[5]*Department of Biostatistics, Mailman School of Public Health, Columbia University, New York, NY, USA*
[6]*Department of Anesthesiology, Columbia University Irving Medical Center, New York, NY, USA*

ABSTRACT

Background: The association between sleep quality and cognition is widely established, but the role of aging in this relationship is largely unknown.

Objective: To examine how age impacts the sleep–cognition relationship and determine whether there are sensitive ranges when the relationship between sleep and cognition is modified. This investigation could help identify individuals at risk for sleep-related cognitive impairment.

Subjects: Sample included 711 individuals (ages 36.00–89.83, 59.66 ± 14.91, 55.7 % female) from the Human Connectome Project-Aging (HCP-A).

Methods: The association between sleep quality (Pittsburgh Sleep Quality Index, PSQI) and cognition (Crystallized Cognition Composite and Fluid Cognition Composite from the NIH Toolbox, the Trail Making Test, TMT, and the Rey Auditory Verbal Learning Test, RAVLT) was measured using linear regression models, with sex, race, use of sleep medication, hypertension, and years of education as covariates. The interaction between sleep and age on cognition was tested using the moderation analysis, with age as both continuous linear and nonlinear (quadratic) terms.

Results: There was a significant interaction term between the PSQI and nonlinear age term (age^2) on TMT-B ($p = 0.02$) and NIH Toolbox crystallized cognition ($p = 0.02$), indicating that poor sleep quality was associated with worse performance on these measures (sensitive age ranges 50–75 years for TMT-B and 66–70 years for crystallized cognition).

Conclusions: The sleep–cognition relationship may be modified by age. Individuals in the middle age to early older adulthood age band may be most vulnerable to sleep-related cognitive impairment.

Keywords: cognitive assessment, sleep, risk factors, aging

Introduction

Age-related cognitive declines are prevalent in both pathological and nonpathological aging (Dzierzewski *et al.*, 2018; Keller, 2006; Li *et al.*, 2004) and are difficult to reverse after declines begin. For instance, pharmaceutical trials have shown limited ability to improve cognitive outcomes in patients with Alzheimer's disease (Alexander *et al.*, 2021; Doody *et al.*, 2014). Thus, researchers are increasing attention to lifestyle modifications that may ameliorate age-related cognitive decline (Shatenstein *et al.*, 2015) and Alzheimer's disease progression (Bhatti *et al.*, 2019). Sleep is a variable in older adults' cognitive functioning that may be modifiable through treatment (Taylor and

Correspondence should be addressed to: Hyun Kim, Division of Geriatric Psychiatry, New York State Psychiatric Institute, New York, NY, USA. Email: monhykim@bu.edu. Received 18 Oct 2022; revision requested 15 Jan 2023; revised version received 10 Oct 2023; accepted 10 Oct 2023.
Data used in preparation of this article were obtained for the Human Connectome Project Aging (HCP-A) database (https://www.humanconnectome.org/). As such, the investigators within the HCP-A contributed to the design and implementation of HCP-A and/or provided data but did not participate in the writing of this report. A complete listing of HCP-A investigators can be found at: https://www.humanconnectome.org/study/hcp-lifespan-aging
Daniel E. Cohen and Hyun Kim have equal contribution to authorship.
‡This article was originally published with errors in the abstract which led to information being misconstrued. The errors have been rectified and the article updated. A correction notice has been published.

Pruiksma, 2014), given its association with various types of memory, including memory consolidation and retrieval (Bonnet, 2005; Nadel *et al.*, 2012; Plihal and Born, 1997; Scullin and Bliwise, 2015); therefore, improving sleep presents a potential avenue to enhance cognition (Dzierzewski *et al.*, 2018).

Given changes in sleep architecture (e.g. reduced slow-wave sleep) and reductions in sleep need as individuals age (Hirshkowitz *et al.*, 2015), it is hypothesized that sleep's influence on cognition may vary depending on age (Wilckens *et al.*, 2014). Cognitive functioning also changes with advancing age; therefore, it is postulated that the cognitive impacts of various lifestyle and clinical factors also differ by age group.

Previous studies that compared the effects of sleep disturbance (e.g. sleep deprivation and poor self-reported sleep quality) in different age groups (e.g. 20–25 vs. 50–60; 50–64 vs. 65 +) have found worse performance in the older adult group across multiple domains of cognitive function, such as word detection (distinguishing words from nonwords), word memory, processing speed, psychomotor vigilance task, executive functions (EFs), and verbal fluency (Miller *et al.*, 2014; Webb, 1985) (Bartolacci *et al.*, 2020; Kim *et al.*, 2013), even though older adults reported lower levels of subjective level of sleepiness in some of these studies (Bartolacci *et al.*, 2020; Kim *et al.*, 2013).

On this note, it is postulated that more cognitively demanding tasks of executive functioning governed by the frontal network system, such as inhibitory control (Harrison and Horne, 1998; Wilckens *et al.*, 2014) and decision-making (Harrison and Horne, 1998, 1999; Muzur *et al.*, 2002), are particularly vulnerable to poor sleep. Sleep deprivation literatures also noted that sleep-related EF deficits remain, even though vigilance may be resilient via mechanisms such as stimulant use (Killgore, 2010). The frontal network, including the fronto-striatal systems, is implicated in age-related changes in attention and EF (Buckner, 2004; Hedden and Gabrieli, 2004; Pace *et al.*, 2011), and the combination of the aging process and sleep disturbance may lead older adults with sleep disturbance to be particularly susceptible to impairment in EF tasks.

Nonetheless, some studies have indicated no age effect or less sleep-related susceptibility in older adults, further contributing to the unclear understanding in this area. For instance, research has shown sleep may be less beneficial in older adults compared to younger adults in terms of improving memory performance, particularly declarative memory and slow-wave sleep-dependent memory consolidation (Scullin and Bliwise, 2015; Spencer *et al.*, 2007; Stickgold, 2005). In other studies, psychomotor vigilance was less impacted by sleep disturbance in older adults (Bliese *et al.*, 2006; Stenuit and Kerkhofs, 2005), indicating that the effect of age on the sleep–cognition relationship may be dependent on the cognitive domain that is being examined.

In addition, previous studies were limited by their use of age as a categorical concept (by age groups, e.g. young, middle-aged, and older adults), which may have underestimated the changes that happen within each age group due to lower statistical power (Altman and Royston, 2006). Examining age as a continuous variable may help to understand the relationship between sleep and cognition along with the broad continuum of the aging process and allow for the identification of specific age ranges during which the change in the relationship between sleep and cognition occurs. This is especially important in brain aging research, given that age-related changes in brain structures and networks may affect sleep quality, cognition, and the interaction between these two variables (Hukkelhoven *et al.*, 2003; Scullin and Bliwise, 2015; Yagi *et al.*, 2020).

In this study, we examined the associations of age with the relationship between sleep quality and cognitive performance within an age-diverse adult sample using the Human Connectome Project-Aging (HCP-A) data. We hypothesized that there will be a significant age × sleep quality interaction in various cognitive domains, particularly in demanding executive functioning tasks, fluid cognition, and episodic memory. Specifically, we examined sleep's interaction with age, with age as both a linear and nonlinear (quadratic) term, which allows us to identify the "sensitive age ranges" outside of traditionally defined age groups, where the relationship between sleep quality and cognitive performance is modified. We hypothesized that ages in midlife to older adulthood (ages 50–70 years) would be particularly vulnerable to sleep-related cognitive changes, given that significant changes in both sleep architecture and age-related neurodegenerative processes begin in midlife and continue with the aging process (Holanda and de Almondes, 2016). We also examined different cognitive domains included in the HCP-A study, such as executive function, episodic memory, and fluid and crystallized cognition that are part of the NIH Toolbox (TB) Cognition Battery (Weintraub *et al.*, 2013). Of note, it may be important to specify which specific EF tasks are implicated in sleep disturbance because EF tasks more broadly have shown mixed associations with sleep disturbance (Killgore, 2010). Therefore, we added the Trail Making Test (TMT), a measure of set-shifting abilities, given that sleep has a crucial role in tasks that require the ability to quickly change behaviors and adapt flexibly to modifying conditions (Couyoumdjian *et al.*, 2010).

https://doi.org/10.1017/S1041610223000911 Published online by Cambridge University Press

Methods

Participants

Data analyses were performed using the most recent HCP-A dataset release (available at https://www.humanconnectome.org/). A detailed description of the dataset has been previously published (Bookheimer *et al.*, 2019). Briefly, the HCP-A participants were recruited to represent the current US population, with regard to age, gender, race, ethnicity, and socioeconomic metrics. Participants were recruited from four sites (Washington University St Louis, University of Minnesota, Massachusetts General Hospital, and University of California, Los Angeles), and all sites strived for a balance of participants with low, middle, and high socioeconomic status. Participants were recruited through advertisements and flyers, active senior centers, places of worship, public lectures and workshops on aging, and senior living centers.

Participant eligibility was determined through phone screens to identify exclusionary health conditions. For instance, individuals diagnosed and treated for major psychiatric disorders (e.g. schizophrenia, bipolar disorder, and severe depression) or neurological disorders (e.g. stroke, brain tumors, and Parkinson's disease), scoring <30 on the Telephone Interview for Cognitive Status modified (TICS-M) (for participants aged 60–80 years) (de Jager *et al.*, 2003), not passing critical orientation items (day of the week, date, season, age, and phone number) of the TICS-M for participants over 80 years, and scoring below age-bracket thresholds (<20 for ages 36–79 years, <18 for ages >79 years) for the Montreal Cognitive Assessment (MoCA) were excluded (Nasreddine *et al.*, 2005). For the current study, we used a dataset of 725 individuals from HCP-A who completed neuropsychological tests and had self-reported sleep data. A flow chart of sample selection is presented in Supplemental Figure 1.

Measures

The Pittsburgh Sleep Quality Index (PSQI) (Buysse *et al.*, 1989) is a self-rated measure of sleep quality and disturbances over the past month. The PSQI contains 19 items, which produce a total score and 7 component scores: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance, use of sleeping medication, and daytime dysfunction. Each component score is rated on a 0–3 scale, with higher scores representing poorer sleep, and adds up to a 0–21 total score. The PSQI total score has acceptable internal homogeneity, consistency, and validity (Buysse *et al.*, 1989).

The NIH Toolbox (TB) Cognition Battery (Weintraub *et al.*, 2013) consists of seven measures assessing subdomains of executive function, episodic memory, language, processing speed, working memory, and attention. Composite measures have been developed using factor analytic methods (Akshoomoff *et al.*, 2013) to represent overall cognition and/or certain categories of abilities that change across the lifespan. The Crystallized Cognition Composite score includes the Oral Reading Recognition Test and the Picture Vocabulary Test, and the Fluid Cognition Composite score includes the Dimensional Change Card Sort Test (cognitive flexibility), the List Sorting Working Memory Test, the Picture Sequence Memory Test (episodic memory), the Pattern Comparison Processing Speed Test, and the Flanker Inhibitory Control and Attention Test. Higher scores on the NIH TB Cognition Battery reflect better performance. The NIH TB Cognition Battery demonstrated strong test–retest reliabilities and adequate convergent and discriminant validities (Weintraub *et al.*, 2013). Full descriptions of the tasks are provided in Weintraub *et al.*, 2013. For the analysis, the uncorrected standard scores were used to model with age.

While the NIH Toolbox has the advantage of compiling crystallized and fluid cognition broadly, its construct validity with standard executive function measures is limited, and it does not encompass some key executive functions such as cognitive set-shifting abilities or learning and recall that may be impacted by sleep (Ott *et al.*, 2022; Scott *et al.*, 2019). Therefore, we added the following individual neuropsychological tests included in the HCP-A dataset to supplement our cognitive outcome measures.

The Trail Making Test (TMT) A and B (Army Individual Test Battery, 1944; Reitan and Wolfson, 1985) consists of two tests of processing speed and working memory. In TMT-A, an individual draws lines connecting 25 circled numbers that are spread out on a sheet of paper, and in TMT-B the person does a similar task but alternates between numbers and letters (Tombaugh, 2004). Accordingly, TMT-B has been shown to measure cognitive set shifting (Olivera-Souza *et al.*, 2000). In both TMT-A and TMT-B, higher scores reflect poorer performance. The TMT has strong interrater reliability (Strauss *et al.*, 2006) and construct validity (Sanchez-Cubillo *et al.*, 2009).

The Rey Auditory Verbal Learning Test (RAVLT) (Rey, 1964) is a test of verbal episodic memory where participants are asked to learn 15 words across 5 learning trials (Ivnick *et al.*, 1990). The tester reads List A before each recall trial, and then the tester reads a separate list, List B, and asks

https://doi.org/10.1017/S1041610223000911 Published online by Cambridge University Press

the subject to freely recall the words. In trial 6, the tester then asks the participant to recall the words from List A. The HCP-A employs an alternate RAVLT administration, which does not include the additional 20-min delayed recall in the standard RAVLT (Bookheimer *et al.*, 2019). This abbreviated version reduces the length of the testing battery, which may otherwise be overly burdensome for older participants, and is supported by findings that short-term delayed recall is equivalent to long-term delayed recall in identifying amnestic mild cognitive impairment and other neurological dysfunctions (Bookheimer *et al.*, 2019; Schoenberg *et al.*, 2006; Zhao *et al.*, 2012). Higher scores on the RAVLT reflect better performance. The RAVLT has shown adequate test–retest reliability, internal consistency, and divergent and convergent validity (de Sousa Magalhães *et al.*, 2012).

Statistical analyses

Residual diagnoses were performed to test for normality and homoscedasticity of cognitive outcomes. Multicollinearity was examined using the variance inflation factor (VIF). For our analyses, one individual with a TMT-A score <1 s was removed and two individuals with a TMT-B score <20 s were removed. In addition, TMT-B was truncated at 300 s, so three individuals' scores were lowered to 300. The following numbers of individuals had cognitive outcomes for each of the measures indicated: TMT-A: 705, TMT-B: 706, NIH TB Fluid Cognition: 608, NIH TB Crystallized Cognition: 607, and RAVLT: 694.

Descriptive analysis was used to profile the characteristics of the participants (Table 1) using mean, standard deviation, and range for continuous variables and frequency and percentage for discrete variables. For the primary analysis, we tested the association of PSQI and age moderation using linear regression models. Since previous studies reported the quadratic association of age (Hukkelhoven *et al.*, 2003), we added the quadratic term of age (age^2). Age moderation was tested by adding age × PSQI and age^2 × PSQI interaction terms. For the models with significant age × PSQI or age^2 × PSQI interactions, we performed *post hoc* contrast analyses to identify age ranges with significant PSQI associations. All models included sex, race, education, hypertension, and sleep medication as covariates (Knutson *et al.*, 2009; Lee *et al.*, 2022), and age was centered on the mean age (59.66 years).

Since our models are hypothesis-driven and primarily aim to evaluate age moderation to examine the consistency of the existing literature, we reported regression coefficients (B) with their 95% confidence intervals and standardized regression coefficients (β) to inform future studies. We also performed multiple comparison corrections using the False Discovery Rate corrections. Additionally, we reran the models without quadratic age terms to test the robustness of the interactive association. When defining the sensitive period at which the association between sleep quality and cognitive performance is most strongly presented, we determined the areas of significance by inspecting when the confidence intervals for the PSQI beta coefficient stopped including zero. We also conducted analyses to examine whether there are other higher-order polynomial terms of age (e.g. cubic and quartic terms) that interact with sleep and found that the quadratic model performed the best for all cognitive outcomes based on the Bayesian information criterion (BIC) (e.g. For crystallized cognition, BIC for quadratic was the smallest [4508.10]

Table 1. Demographics of the study sample

	Total ($N = 711$)
Age (mean, range ± SD)	59.66 (36.00 – 89.83 ± 14.91)
Sex (*n*, %)	
Male	315 (44.3%)
Female	396 (55.7%)
Race	
Asian	52 (7.3%)
Black or African American	100 (14.1%)
More than one race	30 (4.2%)
Unknown or not reported	16 (2.3%)
White	513 (72.2%)
Education (y) (mean ± SD)	17.51 ± 2.19
Employment (*n*, %)	442 (68.7%)
Annual family income per person ($, mean ± SD)	45,935.47 ± 45,831.23
PSQI total (mean ± SD)	4.59 ± 2.67
PSQI ≥ 5 ("poor sleep") (*n*,%)	323 (45.4%)
No sleep meds or < once week	611 (85.9%)
Sleep meds ≥ once a week	100 (14.0%)
NIH Fluid Cog Comp (mean ± SD)	99.37 ± 12.34
NIH Cryst Cog Comp (mean ± SD)	110.97 ± 9.20
TMT-A (mean ± SD)	29.91 ± 11.76
TMT-B (mean ± SD)	74.29 ± 40.97
RAVLT SD TC (mean ± SD)	60.08 ± 14.09
RAVLT SD LB TC (mean ± SD)	5.15 ± 1.90
RAVLT Trials 1-5 SD TC (mean ± SD)	45.54 ± 10.32

SD, standard deviation; PSQI, Pittsburgh Sleep Quality Index; RAVLT SD TC, Rey Auditory Verbal Learning Test Short Delay Total Correct; TMT-A, Trails Making Test A; TMT-B, Trails Making Test B; RAVLT LB TC, Rey Auditory Verbal Learning Test Short Delay List B Total Correct; RAVLT Trials 1-5 SD TC, Rey Auditory Verbal Learning Test Short Delay Trials 1-5 Total Correct. Uncorrected scores were used for composite scores from the NIH Toolbox.

https://doi.org/10.1017/S1041610223000911 Published online by Cambridge University Press

followed by cubic [4511.80] and qartic [4523.88]. Similar patterns were evident for other cognitive outcomes). All analyses were performed using R 4 .1.2, and p values <0.05 were considered to indicate statistical significance.

Results

Demographic characteristics

Demographic characteristics of the study sample are presented in Table 1. The mean age of the study sample ($N = 711$) was 59.66 (SD = 14.91), and 55.7% were females. The sample consisted of predominately White (72.2%) participants. The mean years of education in the sample was 17.51 years (SD = 2.19).

The association between sleep quality and cognitive performance

The associations between sleep, age, and cognitive performance are presented in Table 2, with the main associations of PSQI and age presented in Model 1 and their interactive terms presented in Model 2. In Model 1, higher PSQI scores (i.e. poorer sleep) were associated with worse performance on TMT-B (β = 0.09; Std. CI = 0.02 – 0.17; $p = 0.02$), but not with other cognitive outcomes (Ps ≥ 0.42) after adjusting for race, sex, hypertension, use of sleep medication, and years of education (Table 2. Model 1). In Model 2, higher PSQI scores were associated with poorer performance on TMT-B (β = 0.09; Std. CI = 0.02 – 0.17; $p = 0.001$) and crystallized cognition tasks (β = – 0.03; 95% CI = – 0.11 to 0.05; $p = 0.03$), but not TMT-A, fluid cognition tasks, or RAVLT short-term delayed total recall (Table 2. Model 2).

The association between age and cognitive performance

In Model 1, higher age was associated with poorer performance on all cognitive measures (linear term, $p < 0.001$) except for crystallized cognition tasks (Table 2. Model 1). When the nonlinear (quadratic) term for age was examined, age^2 was only associated with TMT-A (β = 0.15; Std. CI = 0.08 – 0.22; $p < 0.001$) and TMT-B (β = 0.13; Std. CI = 0.06 – 0.19; $p < 0.001$) (Table 2. Model 1).

Age moderation on the association between sleep quality on cognitive performance

In Model 2, there was a significant interaction term between the PSQI and age (linear) on crystallized cognition (β = – 0.09; Std. CI = – 0.16 to – 0.02; $p = 0.01$) (Table 2. Model 2). TMT-A, TMT-B, fluid cognition, and RAVLT short-term delayed recall were not significantly associated with the interaction of age (linear) and sleep. The interaction between the nonlinear age term (age^2) and PSQI was significantly associated with crystallized cognition (β = 0.08; Std. CI = 0.01 – 0.15; $p = 0.02$) and TMT-B (β = – 0.08; Std. CI = – 0.15 to – 0.02; $p = 0.02$) (Table 2. Model 2), and these findings remained significant after the false discovery rate correction.

Finally, when the estimates of PSQI's association with cognitive performance (y-axis) were visualized with age (x-axis) for TMT-B and crystallized cognition (Figures 1 and 2, along with 95% confidence intervals), the sensitive age ranges were determined to be ages 50–75 years for TMT-B and ages 66–70 years for crystallized cognition, indicating that poorer sleep quality and worse cognitive performance were most strongly associated in these age ranges.

Discussion

The present study examined the relationship between sleep quality, age, and cognition. We first examined the association between sleep quality and cognitive performance and found that worse sleep quality was significantly associated with poorer performance on a measure of cognitive set shifting and speed (TMT-B). Furthermore, we tested the hypothesis that age would significantly modify the relationship between sleep quality and cognitive performance, using age as both linear and nonlinear quadratic terms. Our results showed that there was a significant interaction between the quadratic age term and sleep quality in cognitive set shifting and crystallized cognition. These findings suggest that worse sleep quality begins to negatively affect set-shifting abilities at the age of 50 years, with this effect peaking around the age of 62 years, and crystallized cognition may be most associated with sleep quality for individuals between 66 and 70 years. There was also a significant interaction between the linear age term and sleep quality on crystallized cognition. These findings suggest that age could modify the association between sleep quality and cognitive performance and that there are more sensitive age ranges, namely midlife and early late-life, for when sleep-related cognitive changes are evident.

Identification of these sensitive age ranges suggests that individuals in younger ages (e.g. under 50 years) may be able to preserve cognitive performance in certain domains even in the presence of sleep disturbance. In contrast, older individuals (e.g. aged >50 years for Trails B) may experience a more salient negative impact from sleep disturbance. This finding is somewhat consistent with a previous study that demonstrated the preservation

https://doi.org/10.1017/S1041610223000911 Published online by Cambridge University Press

Table 2. Regression of sleep quality and age on cognition

	Model 1 (Main associations)					Model 2 (With interaction terms)					
Cognitive Measures	B	CI	β	Std. CI	P	B	CI	β	Std. CI	P	Cohen's f^2
Trail Making Test-A											
PSQI	0.11	− 0.23 − 0.46	0.03	− 0.05 − 0.10	0.52	0.27	− 0.20 − 0.73	0.02	− 0.05 − 0.10	0.26	
Age (Linear)	0.33	0.27 − 0.39	0.42	0.35 − 0.49	**<0.001**	0.26	0.15 − 0.37	0.42	0.35 − 0.49	**<0.001**	
Age^2 (Quadratic)	0.01	0.01 − 0.01	0.15	0.08 − 0.22	**<0.001**	0.01	0.004 − 0.019	0.15	0.08 − 0.21	**0.003**	
PSQI * Age (Linear)						0.02	− 0.01 − 0.04	0.06	− 0.02 − 0.13	0.12	0.003
PSQI * Age^2 (Quadratic)						− 0.001	− 0.002 − 0.001	− 0.03	− 0.10 − 0.03	0.32	0.001
Trail Making Test-B											
PSQI	1.453	0.26 −2.60	0.09	0.02 − 0.17	**0.02**	2.74	1.15 − 4.33	0.09	0.02 − 0.17	**0.001**	
Age (Linear)	1.04	0.84 −1.23	0.38	0.31 − 0.45	**<0.001**	0.85	0.47 −1.22	0.38	0.31 − 0.45	**<0.001**	
Age^2 (Quadratic)	0.02	0.01 − 0.04	0.13	0.06 − 0.19	**<0.001**	0.05	0.03 −0.08	0.13	0.06 − 0.19	**<0.001**	
PSQI * Age (Linear)						0.04	− 0.03 − 0.12	0.04	− 0.03 − 0.11	0.23	0.002
PSQI * Age^2 (Quadratic)						− 0.01	− 0.011 − − 0.001	− 0.08	− 0.15 − − 0.02	**0.02**	0.008
Crystallized Cognition											
PSQI	− 0.12	− 0.39 − 0.16	− 0.03	− 0.11 − 0.05	0.42	− 0.41	− 0.78 − − 0.04	− 0.03	− 0.11 − 0.05	**0.03**	
Age (Linear)	0.03	− 0.13 − 0.08	0.05	− 0.02 − 0.12	0.16	0.13	0.04 − 0.22	0.04	− 0.03 − 0.11	**0.005**	
Age^2 (Quadratic)	0	− 0.003 − 0.003	0.001	− 0.07 − 0.07	0.97	− 0.01	− 0.0122 − 0.0004	0.01	− 0.06 − 0.08	0.07	
PSQI * Age (Linear)						− 0.02	− 0.04 − − 0.01	− 0.09	− 0.16 − − 0.02	**0.01**	0.01
PSQI * Age^2 (Quadratic)						0.001	0.0002 − 0.0026	0.08	0.01 − 0.15	**0.02**	0.009
Fluid Cognition											
PSQI	− 0.12	− 0.45 − 0.22	− 0.03	− 0.10 − 0.05	0.50	− 0.04	− 0.48 − 0.41	− 0.02	− 0.10 − 0.05	0.87	
Age (Linear)	− 0.54	− 0.60 − − 0.49	− 0.63	− 0.69 − − 0.57	**<0.001**	− 0.51	− 0.61 − − 0.40	− 0.63	− 0.69 − 0.56	**<0.001**	
Age^2 (Quadratic)	− 0.001	− 0.005 − 0.002	− 0.02	− 0.08 − 0.04	0.44	0.001	− 0.01 − 0.01	− 0.02	− 0.08 − 0.04	0.87	
PSQI * Age (Linear)						− 0.01	− 0.03 − 0.01	− 0.03	− 0.09 − 0.04	0.42	0.001
PSQI * Age^2 (Quadratic)						0	− 0.002 − 0.001	− 0.02	− 0.08 − 0.04	0.56	0.001
RAVLT Short Delay Total Recall											
PSQI	0.05	− 0.24 − 0.35	0.01	− 0.06 − 0.09	0.72	− 0.05	− 0.45 − 0.35	0.01	0.06 − 0.09	0.80	
Age (Linear)	− 0.30	− 0.33 − − 0.24	− 0.42	− 0.49 − − 0.35	**<0.001**	− 0.24	− 0.34 − 0.15	− 0.42	− 0.49 − 0.35	**<0.001**	
Age^2 (Quadratic)	− 0.002	− 0.01 − 0.001	− 0.05	− 0.12 − 0.02	0.14	− 0.005	− 0.011 − 0.002	− 0.05	− 0.11 − 0.02	0.16	
PSQI * Age (Linear)						− 0.01	− 0.03 − 0.01	− 0.04	− 0.11 − 0.03	0.31	0.001
PSQI * Age^2 (Quadratic)						0	− 0.0007 − 0.0017	0.03	− 0.04 − 0.09	0.43	0.005

PSQI, Pittsburgh Sleep Quality Index; Crystalized Cognition, NIH-TB Crystalized Cognition Composite; Fluid Cognition, NIH-TB Fluid Cognition Composite.
Covariates: sex, race, use of sleep medication, and years of education.
*Higher scores on Trail Making Test-A, Trail Making Test-B, and PSQI indicate poorer cognitive performance/sleep. For all other metrics, a higher score indicates stronger cognitive performance.
NOTE: Separate regression models were conducted to examine the main effect of sleep ("Model 1") and the interactive effect of sleep and age on cognitive performance ("Model 2").

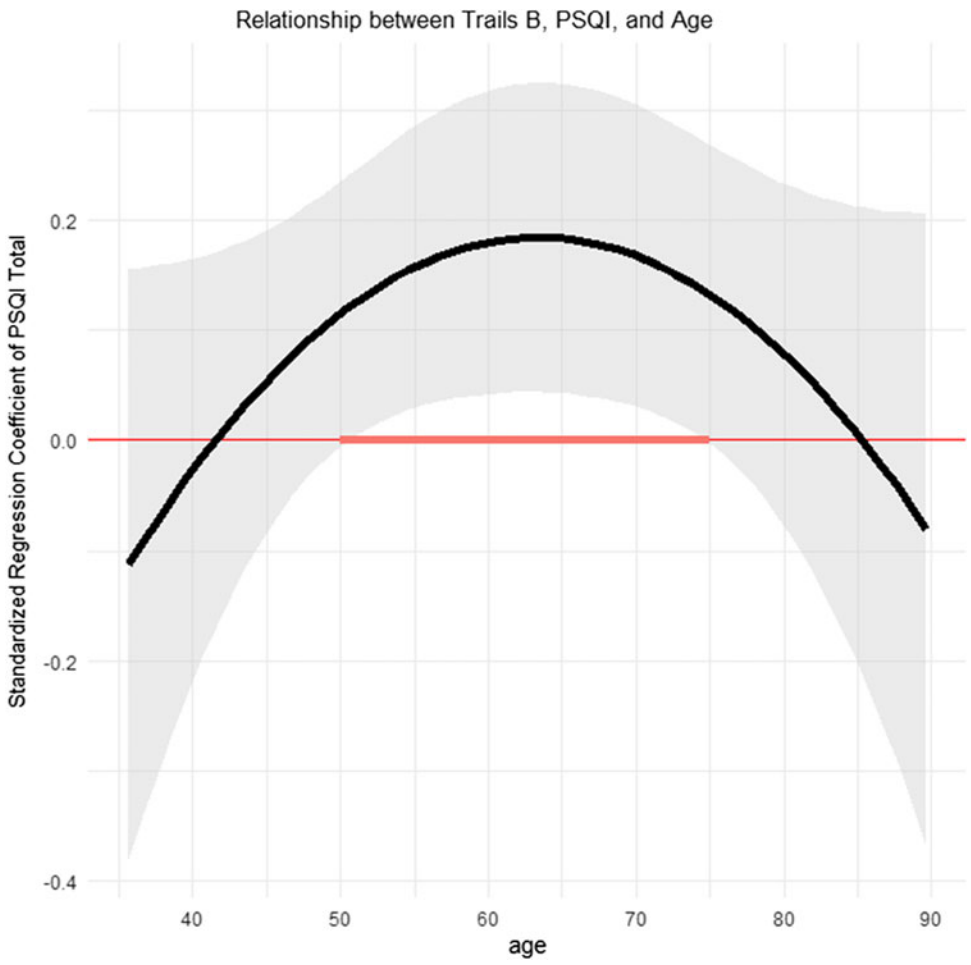

Figure 1. PSQI total interaction with age for TMT-B.

of multiple aspects of frontal network functioning, such as sustained attention, inhibition, and decision-making in sleep-restricted young adults (ages 18–35 years) (Schaedler *et al.*, 2018) and another study that indicated the impairment of similar cognitive domains in sleep-deprived middle-aged adults ranging from ages 50 to 60 years (Webb, 1985). Nevertheless, our findings contradicted other studies which suggested that cognition in older adults (e.g. ages 55–65 years) may be resilient to sleep deprivation (Bliese *et al.*, 2006; Stenuit and Kerkhofs, 2005). Our results also indicate that within older adulthood, sleep's association with cognitive performance becomes notably reduced in the oldest old group (mid-70s and older).

The sensitive age ranges of 50–75 years (Trails B) and 66–70 (Crystalized Cognition) may be supported by age-related changes in sleep and sleep need. As adults may need less sleep as they age, the association between sleep-related neurobiological mechanisms (e.g. slow-wave-dependent cognitive performance) and cognition in older adults may be weaker compared to young and middle-aged adults (Scullin and Bliwise, 2015). Our findings are in line with previous literature that showed sleep-related executive function impairments may begin as early as midlife (Wilckens *et al.*, 2014). Furthermore, these data are consistent with the literature on modifiable risk factors for age-related cognitive impairments that highlight the importance of risk management in midlife (Barnes and Yaffe, 2011; Nishtala *et al.*, 2014).

While sleep quality and the interaction between sleep quality and age were not associated with poorer performance on NIH Toolbox fluid cognition tests, an additional test of fluid cognition, TMT-B, demonstrated such an association. The TMT-B assays different executive functioning subdomains, such as cognitive set shifting, and was demonstrated to measure a separate construct than the NIH fluid cognition measures (Ott *et al.*, 2022; Scott *et al.*, 2019). To this point, TMT-B's association with the sleep quality and age interaction term was consistent with findings suggesting that performance on executive functioning tasks is sensitive to sleep deficits in early older adulthood (Wilckens *et al.*, 2014). Declines in executive cognitive control tasks may be especially impacted by sleep deprivation due to reliance on the prefrontal cortex functioning

https://doi.org/10.1017/S1041610223000911 Published online by Cambridge University Press

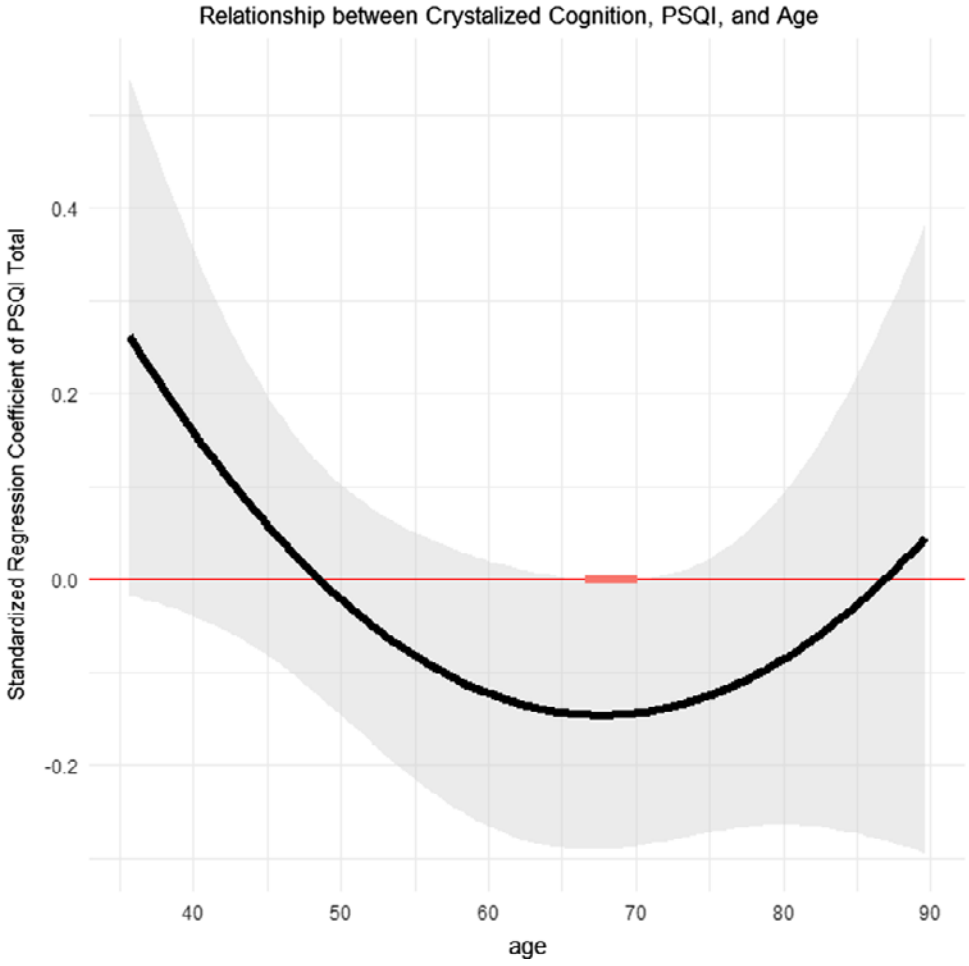

Figure 2. PSQI total interaction with age for crystallized cognition.

(Harrison and Horne, 1998, 1999; Muzur *et al.*, 2002; Wilckens *et al.*, 2014), which may become evident when performing everyday tasks (Rana *et al.*, 2018; Waters and Bucks, 2011)

Though crystallized cognition has been shown to remain stable (or improve) as individuals age (Dzierzewski *et al.*, 2018), as was the case in our study, the interaction between sleep quality and age (both linear and quadratic) was significantly associated with poorer crystallized cognition performance. This finding could be due to older adults experiencing difficulties with retrieval (Craik and Bialystok, 2006; Kurdziel *et al.*, 2017). For instance, word reading and recognition tasks that make up "crystallized cognition" in the current neuropsychological battery may depend on the information that was acquired throughout the lifespan but may also reflect the ability to retrieve previously learned information. As there are few studies conducted on sleep and crystallized cognition, further studies are needed to elucidate the relationship and mechanism between sleep and crystallized cognition in the brain aging process.

A strength of this paper is the use of age as a continuous variable (both as a linear and quadratic term), which may help clarify previous contradictory findings when comparing sleep and cognition between two distinct age groups. For instance, while we found that older individuals' cognition generally declines, poor sleep quality may be especially problematic for the maintenance of crystallized cognition and performance on cognitive set-shifting tasks during midlife and early late-life. Furthermore, examining quadratic age terms in sleep and cognition research is novel and allowed us to identify sensitive age ranges when sleep quality is most strongly associated with cognition. Finally, the current study includes multiple domains of cognitive functioning, which allows us to parse out the relationships between sleep quality with different cognitive domains. Our findings have important clinical implications in that they suggest that timely detection and intervention of sleep disturbance could benefit cognitive health, particularly in midlife to early older adulthood. Although prolonged use of pharmacological sleep treatments, such as benzodiazepines and non-benzodiazepine receptor agonists, are

https://doi.org/10.1017/S1041610223000911 Published online by Cambridge University Press

associated with poorer cognitive outcomes and adverse side effects (e.g. drowsiness and memory impairment) (Schroeck *et al.*, 2016), nonpharmacological treatments, such as cognitive-behavioral therapy for insomnia, could be effective without side effects and have superior long-term benefits compared with commonly prescribed sleep aids (Morin *et al.*, 1999).

A limitation of the paper is that it used a cross-sectional sample. Thus, we cannot make conclusions about the causal relationship between sleep, aging, and cognition. Another limitation of the paper is that we used a subjective rating of sleep quality (PSQI), which may capture sleep less accurately compared with polysomnography. Nonetheless, the PSQI is the most common measure of sleep quality, particularly in large-scale studies (Pilz *et al.*, 2018). The NIH Toolbox Fluid Cognition Composite is limited in the cognitive domains that it assesses and does not include a strong measure of memory and recall due to a lack of a delayed memory component. Similarly, it may have lower construct validity in domains such as attention, executive function, and processing speed and estimate different levels of performance compared to standard neuropsychological tests (Ott *et al.*, 2022; Scott *et al.*, 2019). To address some of these limitations, we additionally examined TMT-B, which assesses cognitive set shifting. It is also notable that the effect sizes for our findings are small; nonetheless, our sample is adequately powered to answer our research question, and heterogeneity and large unexplained variance in cognition are expected in large-scale, multisite studies as those in the HCP-A project.

Lastly, our sample consisted of predominantly White and highly educated participants (i.e. average years of education equivalent to a master's degree), which limits generalizability to a broader population.

Conclusion

In summary, findings from this study suggest the relationship between sleep quality and cognitive performance may be modified by age and related mechanisms. There may be a sensitive period, encompassing midlife to early late-life, that increases the risk of sleep-related cognitive performance decrements.

Conflict of interest

Daniel Cohen: Nothing to Disclose
Hyun Kim: Nothing to Disclose
Alina Levine: Nothing to Disclose
Davangere Devanand: *Grant support:* National Institute on Aging, Alzheimer's Association.
DSMB Chair: BioExcel Therapeutics.
Scientific Advisory Board member: Eisai, Biogen, Corium, Genentech, Acadia, Jazz
Pharmaceuticals, Tau Rx.
Seonjoo Lee: Nothing to Disclose
Terry Goldberg: *Grant support:* National Institute on Aging

Description of authors' roles

D. Cohen and H. Kim designed the study and oversaw the manuscript preparation. A. Levine conducted statistical analyses and assisted with manuscript preparation. D. Devanand assisted with manuscript preparation and revisions. S. Lee conducted statistical analyses and assisted with manuscript preparation. T. Goldberg assisted with study design, manuscript preparation, and revisions.

Acknowledgements

The authors thank all Human Connectome Project-Aging participants. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. Dr Kim is supported by the National Institute on Aging (1K23AG080117-01). Dr Lee is supported by R01AG062578. Data and/or research tools used in the preparation of this manuscript were obtained from the National Institute of Mental Health (NIMH) Data Archive (NDA). NDA is a collaborative informatics system created by the National Institutes of Health to provide a national resource to support and accelerate research in mental health. Dataset identifier(s): 10.15154/1528398. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIH or of the Submitters submitting original data to NDA.

Supplementary material

The supplementary material for this article can be found at https://doi.org/10.1017/S1041610223000911.

References

Akshoomoff, N. *et al.* (2013). VIII. NIH Toolbox Cognition Battery (CB): composite scores of crystallized, fluid, and overall cognition. *Monographs of the Society for Research in Child Development*, 78, 119–132.

Alexander, G. C., Emerson, S. and Kesselheim, A. S. (2021). Evaluation of Aducanumab for Alzheimer disease: scientific evidence and regulatory review involving efficacy, safety, and futility. *JAMA*, 325, 1717–1718.

Altman, D. G. and Royston, P. (2006). The cost of dichotomising continuous variables. *BMJ*, 332, 1080.

Army Individual Test Battery, I. (1944). *Manual of Directions and Scoring*. Washington, DC: War Department, Adjunct General's Office.

Barnes, D. E. and Yaffe, K. (2011). The projected effect of risk factor reduction on Alzheimer's disease prevalence. *The Lancet Neurology*, 10, 819–828.

Bartolacci, C., Scarpelli, S., D'Atri, A., Gorgoni, M., Annarumma, L., Cloos, C., Giannini, A. M. and De Gennaro, L. (2020). The influence of sleep quality, vigilance, and sleepiness on driving-related cognitive abilities: a comparison between young and older adults. *Brain Sciences*, 10(6), 327.

Bhatti, G. K., Reddy, A. P., Reddy, P. H. and Bhatti, J. S. (2019). Lifestyle modifications and nutritional interventions in aging-associated cognitive decline and Alzheimer's disease. *Frontiers in Aging Neuroscience*, 11, 369.

Bliese, P. D., Wesensten, N. J. and Balkin, T. J. (2006). Age and individual variability in performance during sleep restriction. *Journal of Sleep Research*, 15, 376–385.

Bonnet, M. H. (2005). Acute Sleep Deprivation. In: M. H. Kryger (Eds.), *Principles and Practice of Sleep Medicine* (pp 51–66). Philadelphia, PA: W.B. Saunders Company.

Bookheimer, S. Y. *et al.* (2019). The lifespan human connectome project in aging: an overview. *Neuroimage*, 185, 335–348.

Buckner, R. L. (2004). Memory and executive function in aging and AD: multiple factors that cause decline and reserve factors that compensate. *Neuron*, 44, 195–208.

Buysse, D. J., Reynolds C. F., Monk, T. H., Berman, S. R. and Kupfer, D. J. (1989). The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Research*, 28, 193–213.

Couyoumdjian, A. *et al.* (2010). The effects of sleep and sleep deprivation on task-switching performance. *Journal of Sleep Research*, 19, 64–70.

Craik, F. I. and Bialystok, E. (2006). Planning and task management in older adults: cooking breakfast. *Memory & Cognition*, 34, 1236–1249.

de Jager, C. A., Budge, M. M. and Clarke, R. (2003). Utility of TICS-M for the assessment of cognitive function in older adults. *International Journal of Geriatric Psychiatry*, 18, 318–324.

de Sousa Magalhães, S., Mallow-Diniz, L. F. and Hamdan, A. C. (2012). Validity convergent and reliability test-tetest of the Rey Auditory Verbal Learning Test. *Clinical Neuropsychiatry*, 9, 129–137.

Doody, R. S. *et al.* (2014). Phase 3 trials of solanezumab for mild-to-moderate Alzheimer's disease. *New England Journal of Medicine*, 370, 311–321.

Dzierzewski, J. M., Dautovich, N. and Ravyts, S. (2018). Sleep and cognition in older adults. *Sleep Medicine Clinics*, 13, 93–106.

Harrison, Y. and Horne, J. A. (1998). Sleep loss impairs short and novel language tasks having a prefrontal focus. *Journal of Sleep Research*, 7, 95–100.

Harrison, Y. and Horne, J. A. (1999). One night of sleep loss impairs innovative thinking and flexible decision making. *Organizational Behavior and Human Decision Processes*, 78, 128–145.

Hedden, T. and Gabrieli, J. D. (2004). Insights into the ageing mind: a view from cognitive neuroscience. *Nature Reviews Neuroscience*, 5, 87–96.

Hirshkowitz, M. *et al.* (2015). National sleep foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health*, 1, 40–43.

Holanda, F. W. N. J. and de Almondes, K. M. (2016). Sleep and executive functions in older adults: a systematic review. *Dementia & Neuropsychologia*, 10, 185–197.

Hukkelhoven, C. W. *et al.* (2003). Patient age and outcome following severe traumatic brain injury: an analysis of 5600 patients. *Journal of Neurosurgery*, 99, 666–673.

Ivnick, R. J., Malec, J. F., Tangalos, E. G., Petersen, R. C., Kokmen, E. and Kurkland, L. T. (1990). The Auditory-Verbal Learning Test (AVLT): norms for ages 55 years and older. *Psychological Assessment: A Journal of Consulting and Clnical Psychology*, 2, 304–312.

Keller, J. N. (2006). Age-related neuropathology, cognitive decline, and Alzheimer's disease. *Ageing Research Reviews*, 5, 1–13.

Killgore, W. D. (2010). Effects of sleep deprivation on cognition. *Progress in Brain Research*, 185, 105–129.

Kim, H., Suh, S., Cho, E. R., Yang, H. C., Yun, C. H., Thomas, R. J., Lee, S. K. and Shin, C. (2013). Longitudinal course of insomnia: age-related differences in subjective sleepiness and vigilance performance in a population-based sample. *Journal of Psychosomatic Research*, 75(6), 532–538.

Knutson, K. L. *et al.* (2009). Association between sleep and blood pressure in midlife: the CARDIA sleep study. *Archives of Internal Medicine*, 169, 1055–1061.

Kurdziel, L. B. F., Mantua, J. and Spencer, R. M. C. (2017). Novel word learning in older adults: a role for sleep? *Brain and Language*, 167, 106–113.

Lee, S., Vigoureux, T. F., Hyer, K. and Small, B. J. (2022). Prevalent insomnia concerns and perceived need for sleep intervention among direct-care workers in long-term care. *Journal of Applied Gerontology*, 41, 274–284.

Li, S. C., Huxhold, O. and Schmiedek, F. (2004). Aging and attenuated processing robustness. Evidence from cognitive and sensorimotor functioning. *Gerontology*, 50, 28–34.

Miller, M. A., Wright, H., Ji, C. and Cappuccio, F. P. (2014). Cross-sectional study of sleep quantity and quality and amnestic and non-amnestic cognitive function in an ageing population: the English Longitudinal Study of Ageing (ELSA). *PLoS One*, 9, e100991.

Morin, C. M., Colecchi, C., Stone, J., Sood, R. and Brink, D. (1999). Behavioral and pharmacological therapies for late-life insomnia: a randomized controlled trial. *JAMA*, 281, 991–999.

Muzur, A., Pace-Schott, E. F. and Hobson, J. A. (2002). The prefrontal cortex in sleep. *Trends in Cognitive Sciences*, 6, 475–481.

Nadel, L., Hupbach, A., Gomez, R. and Newman-Smith, K. (2012). Memory formation, consolidation and transformation. *Neuroscience & Biobehavioral Reviews*, 36, 1640–1645.

https://doi.org/10.1017/S1041610223000911 Published online by Cambridge University Press

Nasreddine, Z. S. *et al.* (2005). The Montreal Cognitive Assessment, MoCA: a brief screening tool for mild cognitive impairment. *Journal of the American Geriatrics Society*, 53, 695–699.

Nishtala, A. *et al.* (2014). Midlife cardiovascular risk impacts executive function: Framingham offspring study. *Alzheimer Disease & Associated Disorders*, 28, 16–22.

Olivera-Souza, R. D. *et al.* (2000). Trail making and cognitive set-shifting. *Arquivos de Neuro-Psiquiatria*, 58, 826–829.

Ott, L. R. *et al.* (2022). Construct validity of the NIH toolbox cognitive domains: a comparison with conventional neuropsychological assessments. *Neuropsychology*, 36, 468–481.

Pace, V., Treloar, A. and Scott, S. (2011). *Dementia: From Advanced Disease to Bereavement*. Oxford Specialist Handbooks.

Pilz, L. K., Keller, L. K., Lenssen, D. and Roenneberg, T. (2018). Time to rethink sleep quality: PSQI scores reflect sleep quality on workdays. *Sleep*, 41(5).

Plihal, W. and Born, J. (1997). Effects of early and late nocturnal sleep on declarative and procedural memory. *Journal of Cognitive Neuroscience*, 9, 534–547.

Rana, B. K. *et al.* (2018). Association of sleep quality on memory-related executive functions in middle age. *Journal of the International Neuropsychological Society*, 24, 67–76.

Reitan, R. M. and Wolfson, D. (1985). *The Halstead-Reitan Neuropsychological Test Battery: Theory and Clinical Interpretation*. Tucson, Ariz: Neuropsychology Press.

Rey, A. (1964). *L' examen clinique en psychologie (The Clinical Psychological Examination)*. Paris: Presses Universitaires de France.

Sanchez-Cubillo, I. *et al.* (2009). Construct validity of the Trail Making Test: role of task-switching, working memory, inhibition/interference control, and visuomotor abilities. *Journal of the International Neuropsychological Society*, 15, 438–450.

Schaedler, T., Santos, J. S., Vincenzi, R. A., Pereira, S. I. R. and Louzada, F. M. (2018). Executive functioning is preserved in healthy young adults under acute sleep restriction. *Sleep Science*, 11, 152–159.

Schoenberg, M. R., Dawson, K. A., Duff, K., Patton, D., Scott, J. G. and Adams, R. L. (2006). Test performance and classification statistics for the Rey Auditory Verbal Learning Test in selected clinical samples. *Archives of Clinical Neuropsychology*, 21, 693–703.

Schroeck, J. L. *et al.* (2016). Review of safety and efficacy of sleep medicines in older adults. *Clinical Therapeutics*, 38, 2340–2372.

Scott, E. P., Sorrell, A. and Benitez, A. (2019). Psychometric properties of the NIH toolbox cognition battery in healthy older adults: reliability, validity, and agreement with standard neuropsychological tests. *Journal of the International Neuropsychological Society*, 25, 857–867.

Scullin, M. K. and Bliwise, D. L. (2015). Sleep, cognition, and normal aging: integrating a half century of multidisciplinary research. *Perspectives on Psychological Science*, 10, 97–137.

Shatenstein, B., Barberger-Gateau, P. and Mecocci, P. (2015). Prevention of age-related cognitive decline: which strategies, when, and for whom? *Journal of Alzheimer's Disease*, 48, 35–53.

Spencer, R. M., Gouw, A. M. and Ivry, R. B. (2007). Age-related decline of sleep-dependent consolidation. *Learning & Memory*, 14, 480–484.

Stenuit, P. and Kerkhofs, M. (2005). Age modulates the effects of sleep restriction in women. *Sleep*, 28, 1283–1288.

Stickgold, R. (2005). Sleep-dependent memory consolidation. *Nature*, 437, 1272–1278.

Strauss, E., Sherman, E. M. S. and Spreen, O. (2006). *A Compendium of Neuropsychological Tests : Administration, Norms, and Commentary*. Oxford: Oxford University Press.

Taylor, D. J. and Pruiksma, K. E. (2014). Cognitive and behavioural therapy for insomnia (CBT-I) in psychiatric populations: a systematic review. *International Review of Psychiatry*, 26, 205–213.

Tombaugh, T. N. (2004). Trail Making Test A and B: normative data stratified by age and education. *Archives of Clinical Neuropsychology*, 19, 203–214.

Waters, F. and Bucks, R. S. (2011). Neuropsychological effects of sleep loss: implication for neuropsychologists. *Journal of the International Neuropsychological Society*, 17, 571–586.

Webb, W. B. (1985). A further analysis of age and sleep deprivation effects. *Psychophysiology*, 22, 156–161.

Weintraub, S. *et al.* (2013). Cognition assessment using the NIH Toolbox. *Neurology*, 80, S54–64.

Wilckens, K. A., Woo, S. G., Kirk, A. R., Erickson, K. I. and Wheeler, M. E. (2014). Role of sleep continuity and total sleep time in executive function across the adult lifespan. *Psychology and Aging*, 29, 658–665.

Yagi, A., Nouchi, R., Murayama, K., Sakaki, M. and Kawashima, R. (2020). The role of cognitive control in age-related changes in well-being. *Frontiers in Aging Neuroscience*, 12, 198.

Zhao, Q., Lv, Y., Zhou, Y., Hong, Z. and Guo, Q. (2012). Short-term delayed recall of auditory verbal learning test is equivalent to long-term delayed recall for identifying amnestic mild cognitive impairment. *PLoS One*, 7, e51157.

https://doi.org/10.1017/S1041610223000911 Published online by Cambridge University Press