Review Article

Self-reported sleep duration and cognitive performance in older adults: a systematic review and meta-analysis

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ABSTRACT

Sleep is important for optimal cognitive functioning across the lifespan. Among older adults (≥55 years), self-reported short and long sleep durations have been repeatedly, albeit inconsistently, reported to elevate the risk for poor cognitive function. This meta-analytic review quantitatively summarizes the risk for poorer cognitive function among short and long sleepers in older adults. Eligible publications were searched online and manually. A total of 35 independent samples (N = 97,264) from 11 cross-sectional and seven prospective cohort studies were included. Pooled odds ratios (OR) with 95% confidence intervals (CI) were derived using random-effects models. Self-reported short and long sleep increased the odds for poor cognitive function by 1.40 (CI = 1.27–1.56) and 1.58 times (CI = 1.43–1.74), respectively. Effect sizes varied across studies and may have been moderated by both study type (cross-sectional and prospective) and cognitive domain assessed. For cross-sectional studies, extreme sleep durations were significantly associated with poorer multiple-domain performance, executive functions, verbal memory, and working memory capacity. Prospective cohort studies revealed the significant long-term impact of short and long sleep on multiple-domain performance only. These findings establish self-reported extreme sleep duration as a risk factor for cognitive aging.

1. Introduction

Rapid population aging is of rising concern in many developed and developing nations in part because neurodegenerative diseases increase with age and impose heavy socio-economic burdens. While some lifestyle factors, such as physical exercise, have been identified as moderators of age-related brain and cognitive aging [1], the contribution of sleep is less clear. Previous research has revealed adequate sleep to be vital for optimal cognitive function across the lifespan [2–7]. Although the association between sleep and cognitive function is likely to be bi-directional, it has been suggested that alterations in sleep duration might occur prior to the appearance of cognitive symptoms in Alzheimer's Disease (AD) [8]. In fact, almost half of older adults report at least one sleep problem [9],

and there is growing concern that sleep complaints and disturbances might have negative effects on cognition [10]. While many studies on older adults show evidence for the negative impact of self-reported short [11–25] and long [11–13,16,17,20,22,23,26–30] sleep on cognitive function, others have failed to find relationships between sleep and everyday functioning in this age group [19,31].

In an attempt to resolve these heterogeneous findings, the present study adopted meta-analytic procedures to review and quantify the risk of self-reported short and long sleep for poor cognitive function in older adults. In addition, risk for poor cognitive function was treated separately for cross-sectional and prospective studies in order to estimate the association between extreme sleep durations and current as well as future cognitive functioning. Since studies vary widely in the cognitive tasks used, we grouped tasks into five types, namely, those assessing multiple cognitive domains which provide a general measure of cognitive function (such as the Mini-Mental State Examination, MMSE), executive functions, verbal memory, working memory capacity, and speed of processing. This allowed us to examine whether the impact of self-reported sleep duration varied across study types (cross-sectional vs prospective cohort) and cognitive domains. We also evaluated whether age and gender might account for between-study heterogeneity.

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2. Methods

2.1. Literature search

This meta-analysis was performed using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines. We conducted computer and manual searches to locate studies that examined the associations between self-reported sleep duration and cognitive performance of older adults. We searched three electronic databases, PUBMED, MEDLINE, and PsycINFO, for relevant articles published between 1990 and mid-June 2014 using combinations of one of the sleep-related keywords ('sleep' and 'sleep duration') and one of the cognition-related keywords ('cognition', 'cognitive performance', 'cognitive function', 'cognitive decline', 'mild cognitive impairment', 'dementia', and 'Alzheimer's Disease'). We considered only full-length articles that were written in English. A manual search was conducted on seven journals that were likely to publish relevant studies. These journals were "Sleep", "Journal of Sleep Research", "Journal of Clinical Sleep Medicine", "Sleep Medicine", "Alzheimer Disease and Associated Disorders", "International Journal of Geriatric Psychiatry", and "Journal of American Geriatric Psychiatry". We also examined the reference lists of relevant articles and review papers to identify other studies not found by the electronic and manual searches.

2.2. Inclusion and exclusion criteria

Studies needed to fulfill the following criteria: (1) original article; (2) either a cross-sectional study or a prospective cohort study with sleep duration assessed at baseline and cognitive performance/ status assessed at least one year later; (3) assessment of sleep duration in hours with self-reported measures; (4) objective assessment of cognitive performance/status; (5) sleep duration as an exposure variable and cognitive performance/status as a criterion variable; (6) report of descriptive or inferential statistics that could be converted to odds ratios (OR) and 95% confidence intervals (CI); (7) participants aged 55 years and above; and (8) participants with no sign of dementia at baseline.

We did not include cross-sectional studies that compared sleep duration between cognitively intact persons, individuals with mild cognitive impairment (MCI), AD, and dementia because differences in sleep in cognitively impaired and normal persons could be a consequence of clinical conditions. However, we did include studies which investigated whether sleep duration predicted incident AD [22] and dementia [11]. We also excluded studies which examined cognitive impairment associated with sleep disorders because of the potential co-morbidity with medical conditions, such as mood disorders [32].

A few studies only partially met the inclusion criteria. For example, the minimum age in some studies was below 55 years. Also, in some studies, sleep duration was indicated by a subscale score of a questionnaire, eg, the Pittsburgh Sleep Quality Index, or the outcome variable was the change in cognitive performance from baseline to follow-up. For these studies, we asked the authors for data or findings which met the inclusion criteria. In the end, there were five studies among which the minimum age was 39, and they were retained in our data set (Table 1). Note that subsequent analyses revealed no influence of the minimum age of the sample on the effect sizes of self-reported short and long sleep (refer to Sections 3.2.1 and 3.3.1 for more details).

Tworoger et al. [21] and Devore et al. [12] both reported findings from the Nurses' Healthy Study. We used the former for quantifying the cross-sectional associations between sleep duration and cognitive function; we used the latter for quantifying the impact of sleep duration at baseline on cognitive function in the future. Meta-analysis requires independence of effect sizes. In the analyses where both the cross-sectional and the prospective cohort studies were considered, we included Devore et al. [12] rather than Tworoger et al. [21] for a more balanced sample number of the two types of studies. Note that prospective cohort studies are less frequent than cross-sectional studies. Similarly, for articles that reported both cross-sectional and longitudinal associations between sleep duration and cognitive function [12,15,19], we only included the effect size representing the contribution of sleep duration at baseline on cognition years later.

Two studies [16,17] used data from the Health 2000 Survey. We included only the study that used more comprehensive cognitive assessment [16]. Keage et al. [15] reported the risk for cognitive impairment for short and long sleepers at the 2- and the 10-year follow-ups. We included the OR at the 10-year follow-up only.

2.3. Data extraction

Data were extracted independently by two trained technicians, and differences were resolved by discussion with J.C.L. Data extracted included the first author's surname, year of publication, country of origin and name of the cohort studied, study type (cross-sectional or prospective cohort), baseline year, duration of follow-up (0 for cross-sectional studies), sample size, age at baseline (mean and range), gender, reference sleep duration category, shortest sleep duration category, longest sleep duration category, the cognitive tasks used, the relevant descriptive or inferential statistics for the sleep duration groups, and covariates adjusted in the statistical analysis. For studies that did not report OR, we converted the descriptive or inferential statistics to OR using standard formulas [33]. For example, for studies that used continuous measures for cognitive performance, we first converted the descriptive statistics of the reference, short-, and long-sleep-duration groups into Cohen's d and then OR [33].

2.4. Definition of 'short' and 'long' sleep durations

While reference sleep durations ranged from 5 to 9 h across studies, 7 h, 8 h, and 7–8 h were most commonly used (Table 1). For studies that used multiple short-sleep-duration groups, we selected the most extreme group for quantifying the effects of short sleep [34,35], the mode being 5 h or less (Table 1). The same applied to long sleep, with the most common category being 9 h or more (Table 1).

2.5. Cognitive domains

The cognitive tasks used differed across studies (Table 1). To classify these tasks into distinct cognitive domains, we categorized tasks according to two handbooks on cognitive neuroscience – Neuropsychological Assessment [36] and Cognitive Neuroscience: The Biology of the Mind [37]. We assumed diagnoses of AD and dementia to imply the existence of impairment in multiple cognitive domains. To allow reliable estimates of effect sizes, a minimum of four independent samples (k) were required for each cognitive domain [38]. With these considerations, we derived the pooled OR of self-reported short and long sleep for poor performance in five types of cognitive tasks: (1) multiple cognitive domains; (2) executive functions; (3) verbal memory; (4) working memory capacity; and (5) speed of processing (refer to Table S1 for the tasks in each domain). One limitation of this approach was that separating studies into cross-sectional and prospective studies could cause k to drop below four. When this occurred, findings should be best treated as preliminary.

Table 1
Description of the studies included in the meta-analysis.

First author	Publication year	Country	Cohort	Study type	Baseline year	Follow-up (year)	Sample size	Baseline mean age (range)	Gender	Quality score	Sleep duration (h) Ref.	Short sleep	Long sleep	Cognitive task	Adjusted variables[a]
Auyeung [26]	2013	Hong Kong	MrOs and MsOs (Hong Kong)	Cross-sectional	2002–2004	0	2918	73.9 (≥65)	Male, female	14	7–7.9	<4	≥10	Mini-Mental State Examination	1, 4, 20, 21, 31
Benito-Leon [11]	2009	Spain	NEDICES	Prospective	1994–1995	3.2	3286	73.2 (≥65)	Male, female	18	7	≤5	≥9	Dementia, Alzheimer's Disease, non-Alzheimer's Disease type dementia	1, 2, 4, 9, 11, 12, 14, 25, 29
Devore [12]	2014	USA	Nurses' Health Study	Prospective	1986	6	13052	61.1 (56–66)	Female	16	7	≤5	≥9	Telephone interview for cognitive status, East Boston Memory Test, Digit Span Backwards Test	1, 4, 7–9, 11, 12
Faubel [27]	2009	Spain	–	Cross-sectional	2001	0	3210	71.6 (≥60)	Male, female	16	7	≤5	≥11	Mini-Examen Cognoscitivo	1, 4, 6
Ferrie [13]	2011	UK	Whitehall II	Cross-sectional	1997–1999	0	5425	(45–69)	Male, female	14	7	≤5	≥9	Mini-Mental State Examination, free recall test, Alice Heim 4-I, Mill Hill Vocabulary Test, phonemic fluency task, semantic fluency task	1, 2, 4–6, 8–12, 15, 16, 18, 24
Gildner [14]	2014	China, Ghana, India, Mexico, Russia, South Africa	Study on Global Ageing and Adult Health	Cross-sectional	2007–2010	0	30,200	66.76 (≥50)	Male, female	15	6.6–7.5	<5.5	≥8.5	Immediate verbal recall, delayed verbal recall, digit span forward, digit span backward, verbal fluency	1, 4
Keage [15]	2012	UK	MRC Cognitive Function and Aging	Prospective	1991–1993	10	1503	(65–94)	Male, female	16	>6.5 to <8.5	≤6.5	≥8.5	Mini-Mental State Examination	1, 4, 7–9, 11, 12
Kronholm [16]	2009	Finland	Health 2000 Survey	Cross-sectional	2000–2001	0	2232	(≥55)	Male, female	16	7–8	<6	>9	Verbal fluency task, delayed recall test	1, 4, 8–12, 14, 19, 22, 23, 32–35
Lambiase [28]	2014	USA	Healthy Women Study	Cross-sectional	2010–2011	0	121	73.3 (68–77)	Female	13	7	≤5	≥9	Modified Mini-Mental State Examination, Digit Symbol Substitution Test, Trail Making Test A and B, categorical fluency task, alphabetic fluency task	—
Lo [18]	2014	Singapore	Singapore-Longitudinal Aging Brain Study	Prospective	2009–2011	2.1	66	67.4 (58–83)	Male, female	16	≥6.5	<6.5	–	Symbol Digit Modalities Test, Symbol Search Task, Trail Making Test A and B, Category verbal fluency test, design fluency test, digit span test, spatial span test, verbal paired associates test, Rey Auditory Verbal Learning Test, visual reproduction test, visual paired associates test	—

Table 1 (*continued*)

First author	Publication year	Country	Cohort	Study type	Baseline year	Follow-up (year)	Sample size	Baseline mean age (range)	Gender	Quality score	Sleep duration (h)			Cognitive task	Adjusted variables[a]
											Ref.	Short sleep	Long sleep		
Loerbroks [19]	2010	Germany	HeiDE	Prospective		1.0	689	72.3 (≥70)	Male, female	13	7	≤6	≥9	Telephone interview for cognitive status, East Boston Memory Test [1], fluency task, digit span backwards test	1, 4, 8, 9
Potvin [20]	2012	Canada	Survey on Elders' Health	Prospective	2005–2006	1	1,664	73.5 (65–96)	Male, female	19	>5 to <9	≤5	≥9	Mini-Mental State Examination	1, 4, 12
Ramos [29]	2013	USA	Northern Manhattan Study	Cross-sectional	2006	0	927	75 (≥45)	Male, female	15	≥6 to ≤8.9	<6	≥9	Mini-Mental State Examination	1–4, 9, 13, 14, 19, 20, 26, 27
Saint Martin [31]	2012	France	Prognostic Indicator of Cardiovascular and Cerebrovascular Events Trial	Cross-sectional	2001–2003	0	272	74.8 (≥71)	Male, female	15	≥7 to <8	≤5	≥8	Mini-Mental State Examination, Free and Cued Selective Reminding Test, Benton Visual Retention Test, Trial Making Test A, Trial Making Test B, Stroop Test, categorical fluency task, alphabetic fluency task, WAIS-III Similarities Test	1, 2, 4
Schmutte [30]	2007	USA	Bronx Aging Study	Cross sectional	1980–1983	0	222	79.4 (75–85)	Male, female	15	7–8	≤5	9–10	Months backward, digit span test, information, vocabulary, similarities, selective reminding, digit symbol, block design, object assembly, Purdue pegboard	1, 4, 8, 9, 11, 14, 21, 23, 30
Tworoger [21]	2006	USA	Nurses' Health Study	Cross-sectional	2000	0	1,844	74.1 (70–81)	Male, female	15	7	≤5	≥9	Telephone Interview for Cognitive Status, East Boston Memory Test, Category fluency task, digit span backwards test	—
Virta [22]	2013	Finland	Finnish Twin Cohort	Prospective	1975–1981	22.1	1,323	52.3 (≥39)	Male, female	18	≥7 to ≤8	<7	>8	Alzheimer's Disease	1, 2, 4, 12, 28
Xu [23]	2011	China	Guangzhou Bio-bank	Cross-sectional	2003–2008	0	28,670	62.0 (50–85)	Male, female	15	7	≤4	≥10	Delayed word recall test	1, 2, 4–6, 8–12, 16–18, 24

[a] 1 = age; 2 = sex; 3 = race; 4 = education; 5 = employment; 6 = occupation; 7 = shift work history; 8 = smoking; 9 = alcohol intake; 10 = caffeine intake; 11 = physical activity; 12 = body mass index; 13 = diabetes; 14 = hypertension; 15 = high cholesterol; 16 = systolic blood pressure; 17 = high-density lipoprotein and low-density lipoprotein; 18 = fasting plasma glucose; 19 = medications; 20 = depression; 21 = hypnotic use; 22 = anxiolytic medication; 23 = mental health status; 24 = self-rated health; 25 = life satisfaction; 26 = medical insurance; 27 = risk for sleep-disordered breathing; 28 = cognition at baseline; 29 = apolipoprotein; 30 = living status; 31 = medical comorbidities; 32 = night-time awakening; 33 = number of social ties; 34 = head of family's work status; 35 = number of chronic diseases.

2.6. Study quality assessment

The quality of the studies included in the meta-analyses was assessed using a modified version of the Downs & Black Quality Index score system [39]. The original scale was developed for assessing the quality of both randomized and non-randomized studies. Thus, some of the items were not applicable to the current meta-analyses (Table S2). The modified scale has five subscales covering reporting, external validity, bias, confounding, and power, and has a maximum score of 16 for cross-sectional studies and 19 for prospective cohort studies. All the studies were of satisfactory quality (score for cross-sectional studies: 13–16; prospective studies: 13–19; Table 1).

2.7. Statistical analyses

Random-effects meta-analyses were performed using Comprehensive Meta-Analysis Version 2.2 (Biostat, Englewood, NJ). The effect size reported here was OR. Since a 'pure' cognitive task rarely exists, cognitive tasks categorized into different domains may still recruit similar cognitive processes, eg, attention, and their measures may be correlated. Thus, for studies which used multiple cognitive measures, we performed intra-study meta-analyses [40,41] to combine all the ORs to form an independent effect size of the *overall* impact of self-reported short or long sleep on cognitive performance. For studies that used multiple tasks for the same cognitive domain, we meta-analyzed the results to generate an independent effect size for this domain. For those studies that used multiple statistical models, results from the most restricted model, ie, the largest number of covariates, were used to provide an estimate of the unique contribution of sleep to cognitive functions.

While the cognitive tasks used varied across studies, a majority used the MMSE or variants of it (Table S1). The MMSE includes tests of executive functions and verbal memory. As tasks may share similar cognitive processes resulting in correlated measures of performance, two main meta-analyses were performed to compute the effect size for the overall impact of self-reported short and long sleep on cognitive function. Between-study heterogeneity in effect sizes was indexed by Q statistic and I^2 value. A significant Q value indicates that the effect sizes are heterogeneous. I^2 ranges between 0 and 100%, with 25%, 50%, and 75%, respectively, indicating low, moderate, and high levels of heterogeneity [42]. We assessed the possibility of publication bias using three techniques. We generated funnel plots for the effects of self-reported short and long sleep separately. In a funnel plot, the effect sizes (log OR in our case) of all studies are plotted against their standard errors. If there is no publication bias, the plot will be funnel shaped, since studies with larger samples will show less variability in effect sizes, while those with smaller samples will have more variable effect sizes [43,44]. We used Egger's test of intercept [45] and the 'trim and fill' method [43,46] to, respectively, quantify and identify funnel plot asymmetry.

Four moderator analyses were performed to determine whether specific features of a study or the cognitive domain assessed affected the effect sizes of short and long sleep. First, we performed meta-regression using the random-effects model (methods of moments) to determine whether the minimum age of the samples moderated the associations between sleep duration and cognitive function. Mean age was not used since this information was missing for five of the 35 samples. Second, we used meta-regression to examine the effects of gender by using the percentage of male participants in each sample. In these meta-regressions, the estimated slope indicates the change in log OR for every one-point increase in minimum age or percentage of male participants. Third, we derived effect sizes of self-reported short and long sleep separately for the cross-sectional and the prospective cohort studies. This allowed us to quantify the cross-sectional associations of short and long sleep with cognitive function, as well as the long-term impact of extreme sleep durations. Finally, to investigate whether certain cognitive domains were more sensitive to the effects of extreme sleep durations, we quantified the effect sizes of short and long sleep on performance in tasks assessing multiple cognitive domains, executive functions, verbal memory, working memory capacity, and speed of processing. This was done for all the cross-sectional and the prospective cohort studies both separately and combined.

3. Results

3.1. Characteristics of included studies

Eighteen studies met all the selection criteria (Fig. 1). Of these, 11 were cross-sectional, and seven used a prospective cohort design (Table 1). Some studies reported statistics separately for males and females, and one reported data from six countries, resulting in a total of 35 independent samples (26 cross-sectional and nine prospective). Overall, the meta-analysis included 97,624 individuals from 14 countries (five studies from the USA, three from China, two each from the UK, Spain, and Finland, and one each from France, Ghana, India, Mexico, Russia, South Africa, Germany, Singapore, and Canada). For the prospective cohort studies, mean follow-up duration ranged from 1 to 22 years.

3.2. Self-reported short sleep and cognitive function

3.2.1. Overall short sleep effect

ORs of self-reported short sleep for poor overall cognitive function from 35 samples (18 studies; N = 97,624) are illustrated in Fig. 2a. The odds for poor cognitive function were 1.40-times higher among short sleepers than normal sleepers (OR = 1.40, 95% CI = 1.27–1.56; Table 2). There was no evidence for publication bias (Fig. 3a; Egger's test: p = 0.71). The 'trim and fill' method suggested no missing study. There was significant heterogeneity in effect sizes across studies (Q = 55.82, p = 0.01, I^2 = 39.09%). Moderator analyses showed that neither age (slope = 0.00; p = 0.91) nor gender (slope = 0.00; p = 0.49) affected the overall effect size of short sleep.

3.2.2. Overall short sleep effect: by study type

Study type alone did not account for the between-study heterogeneity. In the subgroup analyses where we quantified the effect size of self-reported short sleep on performance for cross-sectional and prospective cohort studies separately (Table 2), cross-sectional studies showed 1.42-times higher odds for poor cognitive function for short relative to normal sleepers (OR = 1.42, 95% CI = 1.28–1.59). Prospective cohort studies also revealed that short sleep posed 1.45-times higher odds for poor cognitive function later in life (OR = 1.45, 95% CI = 1.13–1.87). Thus, the cross-sectional associations and the long-term impact of self-reported short sleep on cognitive performance were similar.

Among the prospective cohort studies, the follow-up duration ranged from 1 to 22 years, allowing us to explore whether this factor affected the effect size of short sleep duration. The OR from studies with shorter follow-up periods (<6 years; k = 6) was 1.60 (95% CI = 1.14–2.24), while the OR from studies with longer follow-up period (≥6 years; k = 3) was 1.38 (95% CI = 0.91–2.07). The latter association just missed statistical significance; however, this finding should be treated as preliminary given that the determination of effect size was based on only three independent samples.

3.2.3. Short sleep effect: by cognitive domain

The effect sizes of self-reported short sleep appeared to vary across cognitive domains (Table 2). Short sleep was significantly associated with poorer performance in multiple-domain tasks (OR = 1.28, 95% CI = 1.07–1.53). Since we assumed that impairment
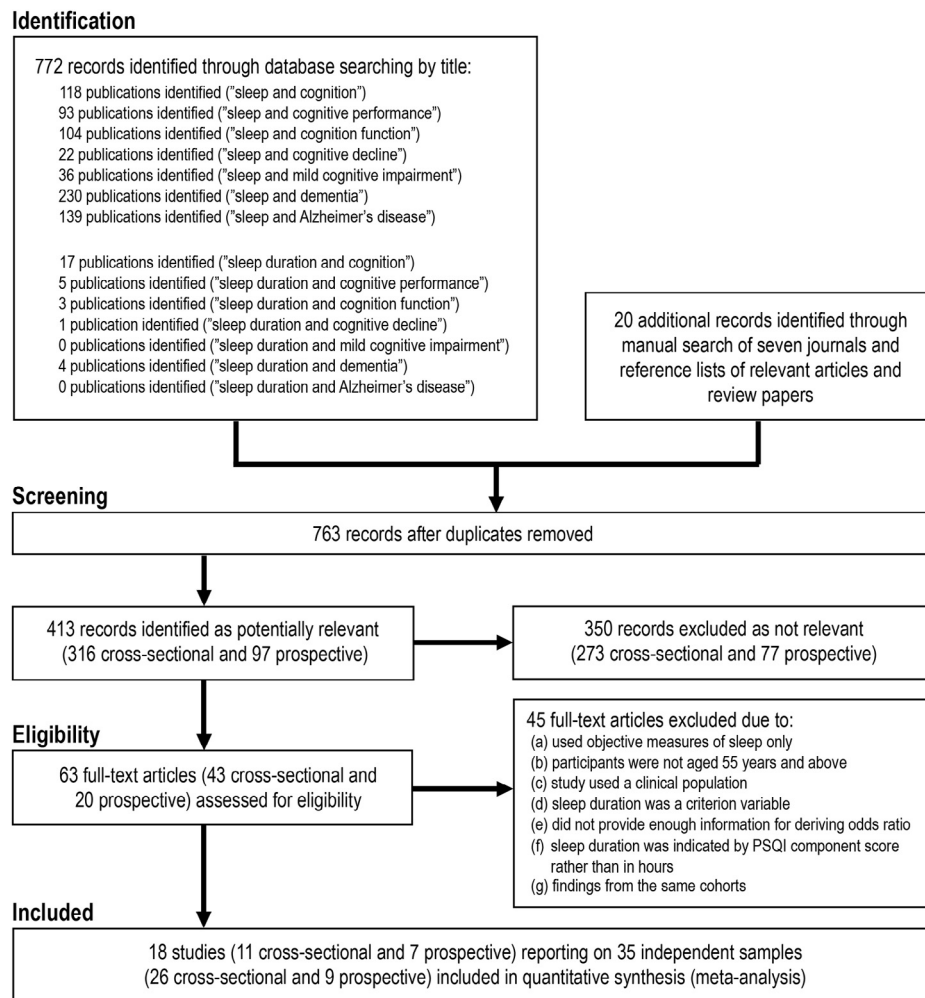
Identification

772 records identified through database searching by title:

   118 publications identified ("sleep and cognition")
   93 publications identified ("sleep and cognitive performance")
   104 publications identified ("sleep and cognition function")
   22 publications identified ("sleep and cognitive decline")
   36 publications identified ("sleep and mild cognitive impairment")
   230 publications identified ("sleep and dementia")
   139 publications identified ("sleep and Alzheimer's disease")

   17 publications identified ("sleep duration and cognition")
   5 publications identified ("sleep duration and cognitive performance")
   3 publications identified ("sleep duration and cognition function")
   1 publication identified ("sleep duration and cognitive decline")
   0 publications identified ("sleep duration and mild cognitive impairment")
   4 publications identified ("sleep duration and dementia")
   0 publications identified ("sleep duration and Alzheimer's disease")

20 additional records identified through manual search of seven journals and reference lists of relevant articles and review papers

Screening

763 records after duplicates removed

413 records identified as potentially relevant (316 cross-sectional and 97 prospective)

350 records excluded as not relevant (273 cross-sectional and 77 prospective)

Eligibility

63 full-text articles (43 cross-sectional and 20 prospective) assessed for eligibility

45 full-text articles excluded due to:
  (a) used objective measures of sleep only
  (b) participants were not aged 55 years and above
  (c) study used a clinical population
  (d) sleep duration was a criterion variable
  (e) did not provide enough information for deriving odds ratio
  (f) sleep duration was indicated by PSQI component score rather than in hours
  (g) findings from the same cohorts

Included

18 studies (11 cross-sectional and 7 prospective) reporting on 35 independent samples (26 cross-sectional and 9 prospective) included in quantitative synthesis (meta-analysis)

Fig. 1. Flow chart indicating the results of the systematic literature search with inclusion and exclusion of studies. PSQI, Pittsburgh Sleep Quality Index.

in multiple cognitive domains was associated with AD and dementia, to determine whether these clinical conditions might have inflated the risk for poor performance in this domain, we also calculated a pooled OR excluding the two relevant studies [11,22]. This OR was of a similar magnitude and remained statistically significant (OR = 1.24, 95% CI = 1.02–1.50).

Other than performance in multiple-domain tasks, we also found significant associations between short sleep duration and poor executive function, verbal memory, and working memory capacity, with ORs ranging from 1.33 to 1.35 (Table 2). However, no significant association was found for speed of processing. This is most likely due to the smaller number of studies ($k = 6$) investigating the contribution of sleep duration to this cognitive domain as the OR for speed of processing was of similar magnitude to the other domains.

3.2.4. Short sleep effect: by cognitive domain and study type

The associations between self-reported short sleep and performance on various cognitive domains were still observed when we considered cross-sectional studies only (Table 2). Self-reported short sleep was associated with higher odds for deficits in multiple-domain tasks, executive functions, verbal memory, and working memory capacity, with ORs ranging from 1.30 to 1.38. A significant association was not present for speed of processing.

In prospective cohort studies, self-reported short sleepers showed elevated risk for poor performance only in multiple-domain tasks (OR = 1.44, 95% CI = 1.02–2.04). No significant association was found

in other domains (Table 2), and this was likely due to the small number of prospective cohort studies which assessed performance in these cognitive domains ($k = 2$–4).
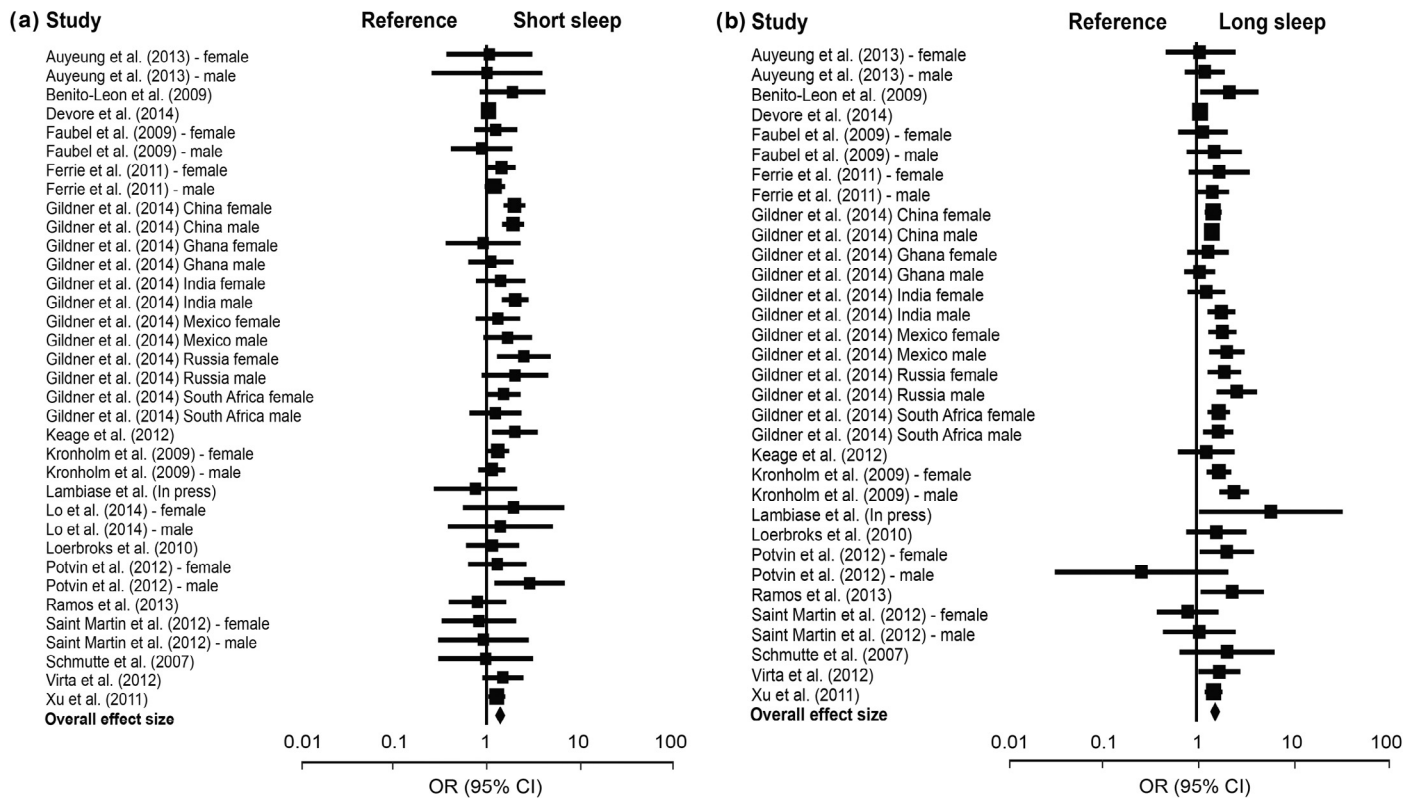
3.3. Self-reported long sleep and cognitive function

3.3.1. Overall long sleep effect

ORs of self-reported long sleep for poor overall cognitive function from 33 samples (17 studies; $N = 97,558$) are shown in Fig. 2b. Long sleep was associated with 1.58-times higher odds for poor cognitive function (OR = 1.58, 95% CI = 1.43–1.74; Table 2). Although the 'trim and fill' method identified that one study on the right side of the funnel plot should be placed on the left side in order to achieve symmetry (adjusted OR = 1.50, 95% CI = 1.41–1.60), the Egger's test was not significant (Fig. 3b; Egger's test: $p = 0.18$). Therefore, we concluded that there was no strong evidence for publication bias. Effect sizes across studies were heterogeneous ($Q = 61.62$, $p = 0.001$, $I^2 = 48.07\%$). However, neither age (slope = –0.01; $p = 0.26$) nor gender (slope = 0.00; $p = 0.41$) appeared to moderate the relationship between self-reported long sleep and poor cognitive performance.

3.3.2. Overall long sleep effect: by study type

Study type alone could not explain the heterogeneity in the effect sizes of self-reported long sleep across studies. The odds for poor cognitive function among long sleepers were both significant from the cross-sectional (OR = 1.61, 95% CI = 1.48–1.76) and the prospective

Fig. 2. Forest plots showing all studies relating self-reported (a) short and (b) long sleep to poor cognitive function as compared to a reference group. Results are expressed as odds ratios (OR) and 95% confidence intervals (CI). Higher ORs indicate greater risks for poor cognitive performance relative to the reference group.

cohort studies (OR = 1.47, 95% CI = 1.08–2.00). This suggested similarity in the cross-sectional associations and the long-term impact of self-reported long sleep on cognitive performance.

To explore whether the follow-up durations in prospective cohort studies influenced the effect size of long sleep duration, we derived pooled ORs separately for studies with shorter (<6 years: $k = 4$) and longer (≥6 years: $k = 3$) follow-up. Long sleep duration appeared to

have stronger impact on cognitive performance in studies with shorter follow-up (OR = 1.81, 95% CI = 1.14–2.86 vs OR = 1.25, 95% CI = 0.93–1.67). However, it is worth noting that only three independent samples contributed to the pooled ORs for longer follow-up; thus, this association and the apparent difference in findings due to different follow-up durations should be interpreted with caution.

Table 2
Odds ratios (95% confidence interval) of self-reported short and long sleep for poor cognitive performance.

	Cross-sectional and prospective combined			Cross-sectional			Prospective		
	k	OR	95% CI		k	OR	95%		k	OR	95% CI	
Overall[a]												
Short sleep	35	**1.40**	1.27	1.56	27	**1.42**	1.28	1.59	9	**1.45**	1.13	1.87
Long sleep	33	**1.58**	1.43	1.74	27	**1.61**	1.48	1.76	7	**1.47**	1.08	2.00
Multiple cognitive domains[a]												
Short sleep	19	**1.28**	1.07	1.53	11	**1.30**	1.05	1.59	9	**1.44**	1.02	2.04
Long sleep	17	**1.42**	1.13	1.78	11	1.36	0.98	1.89	7	**1.43**	1.04	1.97
Executive functions												
Short sleep	22	**1.33**	1.22	1.46	20	**1.33**	1.21	1.47	2	1.69	0.69	4.11
Long sleep	20	**1.47**	1.29	1.68	20	**1.47**	1.29	1.68	–	–	–	–
Verbal memory[a]												
Short sleep	23	**1.33**	1.19	1.49	20	**1.38**	1.25	1.53	4	1.00	0.86	1.16
Long sleep	21	**1.47**	1.31	1.66	20	**1.49**	1.33	1.67	2	1.28	0.76	2.13
Working memory capacity												
Short sleep	15	**1.35**	1.15	1.59	13	**1.38**	1.17	1.62	2	0.78	0.32	1.88
Long sleep	13	**1.34**	1.22	1.47	13	**1.34**	1.22	1.47	–	–	–	–
Speed of processing												
Short sleep	6	1.36	0.88	2.12	4	1.31	0.79	2.19	2	1.53	0.63	3.72
Long sleep	4	1.69	0.90	3.17	4	1.69	0.90	3.17	–	–	–	–

k, number of independent samples; OR, odds ratio; CI, confidence intervals.

[a] For these cognitive domains, data from Tworoger et al. [21] and Devore et al. [12], who studied the same cohort, were respectively included in the meta-analyses of cross-sectional and prospective cohort studies. For the combined analyses, to ensure independence of effect sizes across studies, only data from Devore et al. [12] was included since prospective cohort studies were under-represented.

Odds ratios in bold were statistically significant at $p < 0.05$.

a Short sleep
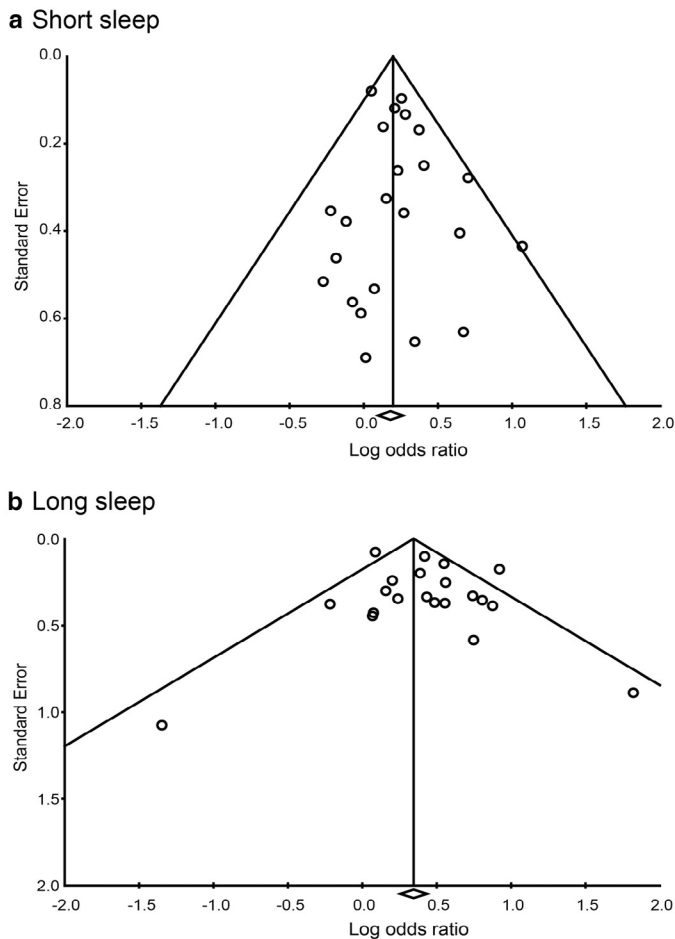
b Long sleep

Fig. 3. Funnel plots for meta-analyses of self-reported (a) short and (b) long sleep and poor cognitive function.

3.3.3. Long sleep effect: by cognitive domain

Cognitive domain seemed to contribute to the heterogeneity in the effect sizes of long sleep on cognitive performance. Subgroup analyses revealed that long sleep increased the odds for poor multiple-domain performance by 1.42-times (95% CI = 1.13–1.78), and this OR was of a similar magnitude even after studies linking long sleep with incident AD and dementia were removed (OR = 1.35, 95% CI = 1.06–1.73).

We also found significant associations between long sleep and poor executive function, verbal memory, and working memory capacity, with ORs ranging between 1.34 and 1.47 (Table 2). In contrast, long sleep did not significantly affect the odds for slower processing speed (Table 2), although the OR appeared to be greatest among all the domains studied (OR = 1.69, 95% CI = 0.90–3.17). This was likely a result of the small number of independent samples ($k = 4$) available for analysis.

3.3.4. Long sleep effect: by cognitive domain and study type

The effects of self-reported long sleep also seemed to vary across cognitive domains when we performed subgroup analyses separately for the two types of studies. For cross-sectional studies, self-reported long sleep was associated with poorer executive function, verbal memory, and working memory capacity, with ORs ranging from 1.34 to 1.49 (Table 2). Long sleep did not affect the odds for slower processing speed (Table 2). The association between long sleep and poor multiple-domain performance in cross-sectional studies was marginally non-significant (OR = 1.36, 95% CI = 0.98-1.89), but was similar in magnitude to the significant OR reported

in prospective cohort studies (OR = 1.43, 95% CI = 1.04–1.97). Note that no prospective cohort study has reported the impact of self-reported long sleep on executive functions, working memory capacity, or speed of processing, and only two samples investigated the long-term impact of long sleep on verbal memory.

4. Discussion

The present study quantitatively reviews the last decade of data on the association between self-reported short and long sleep on cognitive performance among older adults. Overall, self-reported short and long sleep elevated the odds for poor cognitive function by 1.40-times and 1.58-times, respectively. These effect sizes are considered in the small range by convention [47]. Although it has been previously shown that age and gender might affect sleep duration [48–50], the findings from this meta-analysis revealed minimal influence of these demographic factors on the association between sleep duration and cognitive function. Extreme sleep durations had broad impact across multiple cognitive domains including executive function, verbal memory, and working memory capacity. Although speed of processing appeared spared, this result is likely a result of the paucity of studies specifically addressing this domain. Most of these significant associations remained significant when only cross-sectional studies were considered. The long-term impact of self-reported short and long sleep on overall cognitive performance was significant, but was limited to multiple-domain performance probably due to the small number of prospective cohort studies investigating the long-term contribution of extreme sleep durations to specific cognitive domains.

4.1. Potential explanations for the association between sleep duration and cognitive function

The biological mechanisms underlying the association between extreme sleep durations and poorer cognitive function in older adults remain unclear. However, progress has been made in uncovering putative pathways.

4.1.1. Effects of short sleep on the brain

Short sleep has negative effects on brain morphometry, activation, and physiology. In community-dwelling older adults, short sleep has been associated with a higher rate of ventricular expansion and faster decline in global cognitive score [18]. Poor sleep quality has been associated with higher rates of cortical atrophy in frontal, temporal, and parietal lobes [51]. Relative to short sleepers, older adults who slept for 8 h evidenced greater parahippocampal and inferior frontal activation during a verbal encoding task for optimal performance [52].

Recently, sleep has also been found to be important for the clearance of beta-amyloid from the brain [53]. This clearance can be attenuated following acute total sleep deprivation [53,54]. These experimental findings were buttressed by an epidemiological study that reported a cross-sectional association between self-reported short sleep duration and greater amyloid burden in community-dwelling older adults [55]. Amyloid deposition in brain regions that control sleep could in principle aggravate disruption of sleep, setting up a vicious cycle [8]. Indeed, using a *Drosophila* model of AD, a recent study demonstrated that accumulation of beta-amyloid results in reduced and fragmented sleep, and sleep deprivation for one week increases beta-amyloid burden, suggesting a bi-directional relationship between sleep and cognition [56]. However, the long-term effects of chronic short sleep on amyloid accumulation in humans remain to be clarified.

4.1.2. Effects of short and long sleep via systemic inflammation

Several cohort studies on older adults have linked chronic, low grade inflammation evidenced by elevated levels of inflammatory markers, such as interleukin-6 (IL-6) and C-reactive protein (CRP), with negative effects on brain structure [57], as well as increased risk for vascular dementia and AD [58]. However, one large study did not find an association between inflammatory markers and cognitive decline [59]. Elevated levels of IL-6 and CRP have been found in sleep-deprived individuals [60,61], as well as long sleepers [62], suggesting a possible link between short and long sleep, increased inflammation, and impaired cognition. However, a recent longitudinal study that recruited relatively healthy older adults did not find any significant associations between high-sensitivity CRP, and sleep duration, brain volumes or performance in five cognitive domains [18].

4.1.3. Medical comorbidities associated with extreme sleep durations

Cardiometabolic disease and depression associated with extreme sleep durations might have adverse effects on cognitive function. Both short and long sleep have been found to adversely affect cardiometabolic health [34,63], which can in turn have negative effects on brain aging and cognition [1,64]. Insomnia or hypersomnia are prominent symptoms in major depressive disorder [65] which can by itself give rise to cognitive impairment [66]. In addition, long-standing depression elevates the risk for later dementia via multiple mechanisms including hippocampal atrophy, amyloid deposition, increased inflammation, and elevated risk of vascular disease [67].

4.1.4. Overlapping neural correlates for decreasing sleep and performance with age

With increasing age, sleep becomes fragmented and this has been attributed to the interaction between attenuated homeostatic sleep drive and weaker circadian sleep-promoting signals in the early morning [68]. Circadian wake-promoting signals in the afternoon and evening also become weaker, leading older adults to fall asleep more readily during the wake maintenance zone, and to report higher levels of sleepiness in the late afternoon and evening than their younger counterparts [69]. Such fragmentation in rest–activity rhythm has been associated with slower processing speed, poorer memory, and poorer executive function [70]. Furthermore, sleep fragmentation elevates the risk of incident AD and the rate of cognitive decline in older adults [71].

The locus coeruleus is important for the regulation of arousal [72,73] and there is evidence for its contribution to cognitive performance [74,75], the latter possibly related to the neuronal projection from the locus coeruleus to the prefrontal cortex (PFC; [73]). A recent animal study showed that sleep deprivation can result in neuronal loss in the locus coeruleus [76], which may lead to negative cognitive consequences. This is a candidate mechanism explaining how self-reported short sleep might lead to poorer cognitive function in older adults.

The high prevalence of sleep problems among individuals with MCI [77], AD, and other dementias [78], sundowning (ie, increased confusion and restlessness in the evening) among patients with AD [79], and the high conversion rates of patients with REM sleep behavior disorder to various forms of dementia [80,81] all suggest that common brain areas may underlie disrupted sleep–wake regulation and neurodegenerative diseases [10,82].

4.2. Broad effects of sleep duration on cognitive performance

We showed here that self-reported extreme sleep durations had significant associations with poorer multiple-domain performance, executive functions, verbal memory, and working memory capacity. The significant association with multiple-domain performance was likely due to the effects of sleep duration on the sub-domains assessed in these tasks. Most of the studies included in this meta-analysis used the MMSE or its variant to measure multiple-domain performance (Table S1). The broad-based effect on multiple cognitive functions is consistent with the multi-regional [51] or non-localized [18] associations between poor sleep quality or shorter sleep duration and faster brain aging in older adults.

Although the hippocampus, which supports declarative memory is vulnerable to multiple insults [1], our meta-analysis on sleep duration and cognition in older adults did not uncover a specific predilection to memory impairment. The small number of studies examining speed of processing may not have provided sufficient information as to whether self-reported short and long sleep contributes to slower processing speed, a cognitive domain that shows strong age-related decline [83].

It has been argued that because sleep loss invokes functional deficits in working memory and executive functions that are supported by the PFC [84], this part of the brain might be particularly sensitive to sleep loss [85]. While the results of the present meta-analysis support contribution of extreme sleep durations to degradation of these cognitive domains, the effect is not disproportionate to verbal memory.

4.3. Limitations and future studies

Our meta-analysis has several limitations. First, sleep duration was based on self-report. Most epidemiological studies evaluated sleep with subjective measures possibly because of the low cost and ease of administration. However, it is still not clear what leads someone to declare not sleeping 7–8 h when prompted with a question as simple as "how many hours of sleep do you get each night?" [86]. To further complicate the situation, response to this simple question may not even reflect the actual amount of sleep as discrepancies between subjective and objective measures of sleep exist [87]. Reasons for self-reported short sleep duration include, but are not limited to, lower sleep need, busy work schedule, sleep disorders, and medical conditions. Self-reported long sleep duration may indicate health problems. For example, patients with major depressive disorder tend to either over-estimate or underestimate the amount of sleep [88]. Despite these limitations of self-reported sleep duration, the present data may provide some insights into the interactions between sleep and cognition in older adults.

Second, we focused on the association between self-reported sleep duration and cognitive performance, although a number of studies have also found poor self-reported sleep quality and sleep complaints to be associated with poor cognitive function in older adults [14,20,22,23,25,26,30,31,89–97]. Only a handful of studies have examined the contribution of sleep macrostructure to older adults' cognitive function. More stage 1 sleep [98] and less rapid eye movement (REM) sleep [98,99] are associated with poorer cognitive function. In addition, we and others have shown that less slow wave sleep (SWS) is associated with impaired sleep-dependent memory consolidation [100] and more frequent false memory recollection [101]. The contribution of sleep microstructure to older adults' cognitive function is also not well characterized. Some recent evidence has suggested an association of lower spindle and slow wave density with poorer performance in executive functions, attention, and verbal memory [99].

Third, studies varied widely in the question probing sleep duration, making it impossible to unify the operational definition of sleep duration. While most studies assessed average or habitual sleep duration without specifying the time window this was observed for References 11–13, 15, 16, 19, 21–23, 26, 27, and 30; others specified the previous night [28], two nights [14], four weeks [29], or one month [18,20,31]. Moreover, some studies measured nocturnal sleep duration only [13–15,18–20,26,28–31], while others assessed sleep

duration per day or in a 24-h period and thus, included daytime naps [11,12,17,21–23,27]. Findings regarding the effects of daytime napping on cognitive performance in older adults are heterogeneous. Cross-sectional studies have shown that both frequent and long naps are associated with higher risks for poor cognitive function [23,102]. In contrast, in a prospective cohort study where cognitive performance was tracked over time, older adults who napped at baseline had lower risk for cognitive decline at the 2- and the 10-year follow-up visits [15]. The equivocal nature of these results remains to be explained, but may be partly due to differences in the reasons for taking a nap across individuals. While for older adults with disrupted nocturnal sleep, naps are needed to satisfy their sleep needs, others may doze off during the day because of health issues or lack of stimulation.

Other than the differences in how sleep duration was assessed, studies also varied considerably in their definition of old age, the confounding factors considered, the duration of follow-up (for prospective cohort studies), and the sleep duration categories used. For example, while most studies involving older adults screened out participants with signs of dementia, those including younger participants might not, and could have included participants with incipient cognitive impairment. However, findings from our meta-regression analyses did not reveal any significant contribution of the minimum age of the samples to the differences in effect sizes across studies. It is also worth noting that where possible, we used the statistical models that included the largest number of covariates for a better estimate of the unique contribution of self-reported sleep duration to cognitive function. This analytic strategy cannot benefit studies that did not record health variables. We also explored the possible influence of follow-up durations on the sleep–cognition associations in prospective cohort studies. It appears that extreme sleep durations do not contribute to cognitive function beyond six years of sleep measurement; however, these findings were from three studies only. To take into account of the diversity across studies in the sleep duration categories used, we selected the most extreme category for the quantification of effect size. While this might result in inflated effect sizes, setting arbitrary cutoffs for short and long sleep duration, eg, <6 or >9 h, would exclude studies that did not use such a categorization scheme, and might underestimate the impact of extreme sleep durations on cognition.

Finally, the number of independent samples from cross-sectional studies contributing to our meta-analysis was almost three-times more than that from prospective cohort studies (26 vs 9). Most of the prospective studies only used a general measure of cognition, eg, MMSE [15,20], or diagnosis of AD [22] or dementia [11]. In only three prospective studies was performance in specific cognitive domains assessed [12,18,19], limiting the possibility of quantifying the long-term impact of extreme sleep durations on specific domains. Future studies should adopt a prospective cohort design and use a more comprehensive cognitive test battery.

5. Conclusion

Both short and long sleep, as assessed by self-report, are associated with poorer cognitive performance in older adults. These findings suggest the possibility that having good sleep hygiene and establishing good sleep habits may reduce cognitive deficits associated with aging.

Conflict of interest

The authors declare that they have no conflicts of interest.
The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2015.08.021.

Appendix: Supplementary material

Supplementary data to this article can be found online at doi:10.1016/j.sleep.2015.08.021.

References

[1] Fotuhi M, Do D, Jack C. Modifiable factors that alter the size of the hippocampus with ageing. Nat Rev Neurol 2012;8:189–202.
[2] Carskadon MA. Sleep's effects on cognition and learning in adolescence. Prog Brain Res 2011;190:137–43.
[3] Lim J, Dinges DF. A meta-analysis of the impact of short-term sleep deprivation on cognitive variables. Psychol Bull 2010;136:375–89.
[4] O'Brien LM. The neurocognitive effects of sleep disruption in children and adolescents. Child Adolesc Psychiatr Clin N Am 2009;18:813–23.
[5] Pace-Schott EF, Spencer RM. Age-related changes in the cognitive function of sleep. Prog Brain Res 2011;191:75–89.
[6] Groeger JA, Stanley N, Deacon S, et al. Dissociating effects of global SWS disruption and healthy aging on waking performance and daytime sleepiness. Sleep 2014;37:1127–42.
[7] Lo JC, Groeger JA, Santhi N, et al. Effects of partial and acute total sleep deprivation on performance across cognitive domains, individuals and circadian phase. PLoS ONE 2012;7:e45987.
[8] Ju YE, Lucey BP, Holtzman DM. Sleep and Alzheimer disease pathology – a bidirectional relationship. Nat Rev Neurol 2014;10:115–19.
[9] Neikrug AB, Ancoli-Israel S. Sleep disorders in the older adult: a mini-review. Gerontology 2010;56:181–9.
[10] Yaffe K, Falvey CM, Hoang T. Connections between sleep and cognition in older adults. Lancet Neurol 2014;13:1017–28.
[11] Benito-Leon J, Bermejo-Pareja F, Vega S, et al. Total daily sleep duration and the risk of dementia: a prospective population-based study. Eur J Neurol 2009;16:990–7.
[12] Devore EE, Grodstein F, Duffy JF, et al. Sleep duration in midlife and later life in relation to cognition. J Am Geriatr Soc 2014;62:1073–81.
[13] Ferrie JE, Shipley MJ, Akbaraly TN, et al. Change in sleep duration and cognitive function: findings from the Whitehall II Study. Sleep 2011;34:565–73.
[14] Gildner TE, Liebert MA, Kowal P, et al. Associations between sleep duration, sleep quality, and cognitive test performance among older adults from six middle income countries: results from the Study on Global Ageing and Adult Health (SAGE). J Clin Sleep Med 2014;10:613–21.
[15] Keage HA, Banks S, Yang KL, et al. What sleep characteristics predict cognitive decline in the elderly? Sleep Med 2012;13:886–92.
[16] Kronholm E, Sallinen M, Suutama T, et al. Self-reported sleep duration and cognitive functioning in the general population. J Sleep Res 2009;18:436–46.
[17] Kronholm E, Sallinen M, Era P, et al. Psychomotor slowness is associated with self-reported sleep duration among the general population. J Sleep Res 2011;20:288–97.
[18] Lo JC, Loh KK, Zheng H, et al. Sleep duration and age-related changes in brain structure and cognitive performance. Sleep 2014;37:1171–8.
[19] Loerbroks A, Debling D, Amelang M, et al. Nocturnal sleep duration and cognitive impairment in a population-based study of older adults. Int J Geriatr Psychiatry 2010;25:100–9.
[20] Potvin O, Lorrain D, Forget H, et al. Sleep quality and 1-year incident cognitive impairment in community-dwelling older adults. Sleep 2012;35:491–9.
[21] Tworoger SS, Lee S, Schernhammer ES, et al. The association of self-reported sleep duration, difficulty sleeping, and snoring with cognitive function in older women. Alzheimer Dis Assoc Disord 2006;20:41–8.
[22] Virta JJ, Heikkila K, Perola M, et al. Midlife sleep characteristics associated with late life cognitive function. Sleep 2013;36:1533–41.
[23] Xu L, Jiang CQ, Lam TH, et al. Short or long sleep duration is associated with memory impairment in older Chinese: the Guangzhou Biobank Cohort Study. Sleep 2011;34:575–80.
[24] Ohayon MM, Vecchierini MF. Normative sleep data, cognitive function and daily living activities in older adults in the community. Sleep 2005;28:981–9.
[25] Blackwell T, Yaffe K, Laffan A, et al. Associations of objectively and subjectively measured sleep quality with subsequent cognitive decline in older community-dwelling men: the MrOS Sleep Study. Sleep 2014;37:655–63.
[26] Auyeung TW, Lee JS, Leung J, et al. Cognitive deficit is associated with phase advance of sleep-wake rhythm, daily napping, and prolonged sleep duration: a cross-sectional study in 2,947 community-dwelling older adults. Age (Dordr) 2013;35:479–86.
[27] Faubel R, Lopez-Garcia E, Guallar-Castillon P, et al. Usual sleep duration and cognitive function in older adults in Spain. J Sleep Res 2009;18:427–35.

[28] Lambiase MJ, Gabriel KP, Kuller LH, et al. Sleep and executive function in older women: the moderating effect of physical activity. J Gerontol A Biol Sci Med Sci 2014;69:1170–6.

[29] Ramos AR, Dong C, Elkind MS, et al. Association between sleep duration and the Mini-Mental Score: the Northern Manhattan Study. J Clin Sleep Med 2013;9:669–73.

[30] Schmutte T, Harris S, Levin R, et al. The relation between cognitive functioning and self-reported sleep complaints in nondemented older adults: results from the Bronx aging study. Behav Sleep Med 2007;5:39–56.

[31] Saint Martin M, Sforza E, Barthelemy JC, et al. Does subjective sleep affect cognitive function in healthy elderly subjects? The Proof cohort. Sleep Med 2012;13:1146–52.

[32] Alvaro PK, Roberts RM, Harris JK. A systematic review assessing bidirectionality between sleep disturbances, anxiety, and depression. Sleep 2013;36:1059–68.

[33] Borenstein M, Hedges LV, Higgins JPT, et al. Introduction to meta-analysis. Chichester, UK: John Wiley & Sons; 2009.

[34] Cappuccio FP, Cooper D, D'Elia L, et al. Sleep duration predicts cardiovascular outcomes: a systematic review and meta-analysis of prospective studies. Eur Heart J 2011;32:1484–92.

[35] Qin Y, Zhou Y, Zhang X, et al. Sleep duration and breast cancer risk: a meta-analysis of observational studies. Int J Cancer 2014;134:1166–73.

[36] Lezak MD. Neuropsychological assessment. 3rd ed. New York, Oxford: Oxford University Press; 1995.

[37] Gazzaniga MS, Ivry RB, Mangun GR. Cognitive neuroscience: the biology of the mind. New York, London: W.W. Norton; 1998.

[38] Astill RG, Van der Heijden KB, Van Ijzendoorn MH, et al. Sleep, cognition, and behavioral problems in school-age children: a century of research meta-analyzed. Psychol Bull 2012;138:1109–38.

[39] Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. J Epidemiol Community Health 1998;52:377–84.

[40] Cooper HM, Hedges LV, Valentine JC. The handbook of research synthesis and meta-analysis. 2nd ed. New York: Russell Sage Foundation; 2009.

[41] Mullen B. Advanced BASIC meta-analysis. Hillsdale, NJ: L. Erlbaum Associates; 1989.

[42] Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. Br Med J 2003;327:557–60.

[43] Duval S, Tweedie R. A nonparametric "trim and fill" method of accounting for publication bias in meta-analysis. J Am Stat Assoc 2000;95:89–98.

[44] Sutton AJ, Duval SJ, Tweedie RL, et al. Empirical assessment of effect of publication bias on meta-analyses. Br Med J 2000;320:1574–7.

[45] Egger M, Davey Smith G, Schneider M, et al. Bias in meta-analysis detected by a simple, graphical test. Br Med J 1997;315:629–34.

[46] Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics 2000;56:455–63.

[47] Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. Hillsdale, NJ: Lawrence Erlbaum Associates; 1988.

[48] Groeger JA, Zijlstra FR, Dijk DJ. Sleep quantity, sleep difficulties and their perceived consequences in a representative sample of some 2000 British adults. J Sleep Res 2004;13:359–71.

[49] Ohayon MM, Carskadon MA, Guilleminault C, et al. Meta-analysis of quantitative sleep parameters from childhood to old age in healthy individuals: developing normative sleep values across the human lifespan. Sleep 2004;27:1255–73.

[50] Basner M, Spaeth AM, Dinges DF. Sociodemographic characteristics and waking activities and their role in the timing and duration of sleep. Sleep 2014;37:1889–906.

[51] Sexton CE, Storsve AB, Walhovd KB, et al. Poor sleep quality is associated with increased cortical atrophy in community-dwelling adults. Neurology 2014;83:967–73.

[52] Jonelis MB, Drummond SP, Salamat JS, et al. Age-related influences of prior sleep on brain activation during verbal encoding. Front Neurol 2012;3:49.

[53] Ooms S, Overeem S, Besse K, et al. Effect of 1 night of total sleep deprivation on cerebrospinal fluid beta-amyloid 42 in healthy middle-aged men: a randomized clinical trial. JAMA Neurol 2014;71:971–7.

[54] Kang JE, Lim MM, Bateman RJ, et al. Amyloid-beta dynamics are regulated by orexin and the sleep-wake cycle. Science 2009;326:1005–7.

[55] Spira AP, Gamaldo AA, An Y, et al. Self-reported sleep and beta-amyloid deposition in community-dwelling older adults. JAMA Neurol 2013;70:1537–43.

[56] Tabuchi M, Lone SR, Liu S, et al. Sleep interacts with abeta to modulate intrinsic neuronal excitability. Curr Biol 2015;25:702–12.

[57] Satizabal CL, Zhu YC, Mazoyer B, et al. Circulating IL-6 and CRP are associated with MRI findings in the elderly: the 3C-Dijon Study. Neurology 2012;78:720–7.

[58] Singh T, Newman AB. Inflammatory markers in population studies of aging. Ageing Res Rev 2011;10:319–29.

[59] Dik MG, Jonker C, Hack CE, et al. Serum inflammatory proteins and cognitive decline in older persons. Neurology 2005;64:1371–7.

[60] Mullington JM, Simpson NS, Meier-Ewert HK, et al. Sleep loss and inflammation. Best Pract Res Clin Endocrinol Metab 2010;24:775–84.

[61] van Leeuwen WM, Lehto M, Karisola P, et al. Sleep restriction increases the risk of developing cardiovascular diseases by augmenting proinflammatory responses through IL-17 and CRP. PLoS ONE 2009;4:e4589.

[62] Prather AA, Vogelzangs N, Penninx BW. Sleep duration, insomnia, and markers of systemic inflammation: results from the Netherlands Study of Depression and Anxiety (NESDA). J Psychiatr Res 2015;60:95–102.

[63] Knutson KL. Sleep duration and cardiometabolic risk: a review of the epidemiologic evidence. Best Pract Res Clin Endocrinol Metab 2010;24:731–43.

[64] Gorelick PB, Scuteri A, Black SE, et al. Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the American Heart Association/American Stroke Association. Stroke 2011;42:2672–713.

[65] American Psychiatric Association. Diagnostic and statistical manual of mental disorders. Fifth ed. Arlington, VA: American Psychiatric Association; 2013.

[66] Snyder HR. Major depressive disorder is associated with broad impairments on neuropsychological measures of executive function: a meta-analysis and review. Psychol Bull 2013;139:81–132.

[67] Byers AL, Yaffe K. Depression and risk of developing dementia. Nat Rev Neurol 2011;7:323–31.

[68] Dijk DJ, Duffy JF, Riel E, et al. Ageing and the circadian and homeostatic regulation of human sleep during forced desynchrony of rest, melatonin and temperature rhythms. J Physiol 1999;516(Pt 2):611–27.

[69] Munch M, Knoblauch V, Blatter K, et al. Age-related attenuation of the evening circadian arousal signal in humans. Neurobiol Aging 2005;26:1307–19.

[70] Oosterman JM, van Someren EJ, Vogels RL, et al. Fragmentation of the rest-activity rhythm correlates with age-related cognitive deficits. J Sleep Res 2009;18:129–35.

[71] Lim AS, Kowgier M, Yu L, et al. Sleep fragmentation and the risk of incident Alzheimer's disease and cognitive decline in older persons. Sleep 2013;36:1027–32.

[72] Carter ME, Yizhar O, Chikahisa S, et al. Tuning arousal with optogenetic modulation of locus coeruleus neurons. Nat Neurosci 2010;13:1526–33.

[73] Samuels ER, Szabadi E. Functional neuroanatomy of the noradrenergic locus coeruleus: its roles in the regulation of arousal and autonomic function part I: principles of functional organisation. Curr Neuropharmacol 2008;6:235–53.

[74] Schmidt C, Collette F, Leclercq Y, et al. Homeostatic sleep pressure and responses to sustained attention in the suprachiasmatic area. Science 2009;324:516–19.

[75] Usher M, Cohen JD, Servan-Schreiber D, et al. The role of locus coeruleus in the regulation of cognitive performance. Science 1999;283:549–54.

[76] Zhang J, Zhu Y, Zhan G, et al. Extended wakefulness: compromised metabolics in and degeneration of locus ceruleus neurons. J Neurosci 2014;34:4418–31.

[77] McKinnon A, Terpening Z, Hickie IB, et al. Prevalence and predictors of poor sleep quality in mild cognitive impairment. J Geriatr Psychiatry Neurol 2014;27:204–11.

[78] Bliwise DL. Sleep disorders in Alzheimer's disease and other dementias. Clin Cornerstone 2004;6(Suppl. 1A):S16–28.

[79] Bliwise DL, Watts RL, Watts N, et al. Disruptive nocturnal behavior in Parkinson's disease and Alzheimer's disease. J Geriatr Psychiatry Neurol 1995;8:107–10.

[80] Iranzo A, Tolosa E, Gelpi E, et al. Neurodegenerative disease status and post-mortem pathology in idiopathic rapid-eye-movement sleep behaviour disorder: an observational cohort study. Lancet Neurol 2013;12:443–53.

[81] Schenck CH, Boeve BF, Mahowald MW. Delayed emergence of a parkinsonian disorder or dementia in 81% of older men initially diagnosed with idiopathic rapid eye movement sleep behavior disorder: a 16-year update on a previously reported series. Sleep Med 2013;14:744–8.

[82] Zhong G, Naismith SL, Rogers NL, et al. Sleep-wake disturbances in common neurodegenerative diseases: a closer look at selected aspects of the neural circuitry. J Neurol Sci 2011;307:9–14.

[83] Park DC, Lautenschlager G, Hedden T, et al. Models of visuospatial and verbal memory across the adult life span. Psychol Aging 2002;17:299–320.

[84] Alvarez JA, Emory E. Executive function and the frontal lobes: a meta-analytic review. Neuropsychol Rev 2006;16:17–42.

[85] Harrison Y, Horne JA, Rothwell A. Prefrontal neuropsychological effects of sleep deprivation in young adults: a model for healthy aging? Sleep 2000;23:1067–73.

[86] Bliwise DL, Young TB. The parable of parabola: what the U-shaped curve can and cannot tell us about sleep. Sleep 2007;30:1614–15.

[87] O'Donnell D, Silva EJ, Munch M, et al. Comparison of subjective and objective assessments of sleep in healthy older subjects without sleep complaints. J Sleep Res 2009;18:254–63.

[88] Rotenberg VS, Indursky P, Kayumov L, et al. The relationship between subjective sleep estimation and objective sleep variables in depressed patients. Int J Psychophysiol 2000;37:291–7.

[89] Bastien CH, Fortier-Brochu E, Rioux I, et al. Cognitive performance and sleep quality in the elderly suffering from chronic insomnia: relationship between objective and subjective measures. J Psychosom Res 2003;54:39–49.

[90] Cricco M, Simonsick EM, Foley DJ. The impact of insomnia on cognitive functioning in older adults. J Am Geriatr Soc 2001;49:1185–9.

[91] Garcia S, Alosco ML, Spitznagel MB, et al. Poor sleep quality and reduced cognitive function in persons with heart failure. Int J Cardiol 2012;156:248–9.

[92] Haimov I, Hanuka E, Horowitz Y. Chronic insomnia and cognitive functioning among older adults. Behav Sleep Med 2008;6:32–54.

[93] Huang CQ, Dong BR, Zhou Y. Association between sleep quality and cognitive impairment among Chinese nonagenarians/centenarians. J Clin Neurophysiol 2012;29:250–5.

[94] Jelicic M, Bosma H, Ponds RW, et al. Subjective sleep problems in later life as predictors of cognitive decline. Report from the Maastricht Ageing Study (MAAS). Int J Geriatr Psychiatry 2002;17:73–7.
[95] Nebes RD, Buysse DJ, Halligan EM, et al. Self-reported sleep quality predicts poor cognitive performance in healthy older adults. J Gerontol B Psychol Sci Soc Sci 2009;64:180–7.
[96] Regestein QR, Friebely J, Shifren JL, et al. Self-reported sleep in postmenopausal women. Menopause 2004;11:198–207.
[97] Yue J, Huang C, Wu H, et al. Association of sleep quality and dementia among long-lived Chinese older adults. Age (Dordr) 2013;35:1423–32.
[98] Blackwell T, Yaffe K, Ancoli-Israel S, et al. Associations between sleep architecture and sleep-disordered breathing and cognition in older community-dwelling men: the Osteoporotic Fractures in Men Sleep Study. J Am Geriatr Soc 2011;59:2217–25.

[99] Lafortune M, Gagnon JF, Martin N, et al. Sleep spindles and rapid eye movement sleep as predictors of next morning cognitive performance in healthy middle-aged and older participants. J Sleep Res 2014;23:159–67.
[100] Mander BA, Rao V, Lu B, et al. Prefrontal atrophy, disrupted NREM slow waves and impaired hippocampal-dependent memory in aging. Nat Neurosci 2013;16:357–64.
[101] Lo JC, Sim SK, Chee MW. Sleep reduces false memory in healthy older adults. Sleep 2014;37:665–71.
[102] Blackwell T, Yaffe K, Ancoli-Israel S, et al. Poor sleep is associated with impaired cognitive function in older women: the study of osteoporotic fractures. J Gerontol A Biol Sci Med Sci 2006;61:405–10.