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Original Article

Long sleep duration is associated with lower cognitive function among middle-age adults – the Doetinchem Cohort Study

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ABSTRACT

Objectives: In older adults, both short and long sleep duration are associated with lower cognitive function, suggesting an inverted U-shaped association between sleep duration and cognitive outcomes. This study examined whether sleep duration is associated with (changes in) cognitive function in a middle-aged population.

Methods: In the Doetinchem Cohort Study, the cognitive function of 2970 men and women aged 41–75 years at baseline (1995–2007) was examined 2–3 times, with 5-year time intervals. Global cognitive function and the domains memory, information processing speed, and cognitive flexibility were assessed. In multivariable linear regression models, (change in) self-reported sleep duration was studied in association with the level and change in cognitive function. In a subsample of the population ($n = 2587$), the association of sleep duration and feeling rested with cognitive function was studied.

Results: Sleep duration of 9 h and more was statistically significantly associated with lower global cognitive function ($p < 0.01$), memory ($p = 0.02$), and flexibility ($p = 0.03$), compared to a sleep duration of 7 or 8 h. Among adults feeling frequently not well rested, both short and long sleep duration were associated with a lower speed of cognitive function. An inverted U-shaped association between sleep duration and cognitive function was observed for speed, flexibility, and global cognitive function. Sleep duration was not associated with change in cognitive function.

Conclusions: Middle-age adults with long sleep duration had a lower cognitive function.

1. Introduction

The number of people with dementia will steadily increase over the next 25 years [1]. Most epidemiological studies focus on older adults (65+), however, a diagnosis of dementia is usually preceded by a long-lasting decline in cognitive function [2]. Therefore, identification of risk factors affecting the age-related decline in cognitive function at middle age is important in order to prevent or delay the development of dementia.

Sleep is critical for optimal cognitive function and with ageing sleeping patterns change [3]. There is a growing interest in the relationship between sleep duration and cognitive function. In a recent experimental study among middle-aged men, sleep deprivation increased the number of amyloid plaques (a key protein in Alzheimer disease), whereas unrestricted sleep diminished the number of plaques [4].

Epidemiological studies among older adults showed that both short and long sleepers have worse cognitive function [5–8] and greater cognitive decline compared to adults sleeping 7 or 8 h per night [9,10]. Recently, a review of Yaffe and colleagues suggested a potential inverted U-shaped association between sleep duration and cognitive outcomes [11]. Prospective studies in middle-aged adults (mean age ≤65) are however scarce. Yaffe et al. showed that short sleep duration was significantly associated with white matter quality in midlife, though cognitive performance did not differ between adults with short and moderate sleep duration [12]. Ramos et al. recently observed inverted U-shaped associations with neurocognitive function in a cross-sectional study among middle-

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aged Hispanic/Latino adults in the US, with worse scores among those with longer sleep duration [13]. Ferrie et al. showed that changes in sleep duration (from moderate sleep duration to both short and long sleep duration) were associated with poorer cognitive function [14]. These findings may support an inverted U-shaped relationship between sleep duration and cognitive outcomes. Lo et al. reported that self-reported short sleep duration only was associated with greater decline in general cognitive performance in the subsequent two years [15]. Yet, the few studies on the relationship between sleep duration and cognitive function in middle-aged adults are different in their objectives and whether an inverted U-shaped association at middle-age can be supported is unknown.

Besides sleep duration, sleep quality is assumed to affect cognitive function [11,16]. The need for number of hours sleep may differ between individuals, and it could well be that both short and long sleep duration may be adequate for those with good sleep quality. Therefore, it is important to consider sleep duration and sleep quality in relation to cognitive function and cognitive decline in middle-age men and women, in order to help preventing cognitive decline.

Based on a middle-aged to old age population with a 10-year follow-up for cognitive function, this study examined the association between (1) sleep duration and cognitive function (2), sleep duration and change in cognitive function and (3) changes in sleep duration and cognitive function. Since we had no validated measure of sleep quality, we explored the combined associations of (4) sleep duration and feeling rested with cognitive function in a subsample of our population.

2. Methods

2.1. Dataset

The Doetinchem Cohort Study (DCS) is an ongoing study that started in 1987–1991 among 12,405 men and women aged 20–59 years [17]. From 1987 to 1991, each year an age and sex-stratified random sample from the municipal registers was invited to participate (initial response rate 62%). Due to extension of the protocol, with similar budget, not all participants could be re-invited. Instead, a random sample of in total 7769 of the respondents at baseline was invited for re-examination. The response rates for all follow-up measurements varied between 75% and 80%, resulting in 6113, 4916, 4520, and 4017 participants for rounds 2 (1993–97), 3 (1998–2002), 4 (2003–07), and 5 (2008–12), respectively. As presented in Fig. 1, between 1995 and 2007 3730 respondents aged 41–75 years, participated in cognitive testing for the first time. Five years later 2865 respondents were cognitively tested, and 2278 respondents were tested again after 10-years of follow-up. The first cognitive measurement of each respondent was used as baseline and all respondents with at least two stroke free measurements were included in this study (n = 2970 respondents).

The study was approved by the external Medical Ethics Committee of the Netherlands Organization of Applied Scientific Research Institute and the University of Utrecht according to the guidelines of the Helsinki Declaration. All participants gave written informed consent. Details on the DCS are described elsewhere [17,18].

2.2. Cognitive tests

The neuropsychological test battery included four tests: the 15 Words Verbal Learning Test, the Stroop Colour-Word Test, the Word Fluency test, and the Letter Digit Substitution Test. These tests have a continuous score without a maximum, except the Verbal Learning Test (but only two participants in the study population reached the maximum score over the 10-year study period). It measures global cognitive function (all cognitive tests combined) and specific cognitive domains, i.e. memory function (Verbal Learning Test), information processing speed (Stroop Colour-Word Test and Letter Digit Substitution Test), and cognitive flexibility (i.e. higher order information processing; Stroop Colour-Word Test). For each cognitive domain (memory function, information processing speed, cognitive flexibility, and global cognitive function), a standardised z-score was computed at baseline and follow-up, based on the means and standard deviations of the total population at baseline. The cognitive tests have been described in more detail elsewhere [19]. The tests are sensitive to age, including the middle-age range, and have been used in several other large-scale studies on cognitive function [20–22].

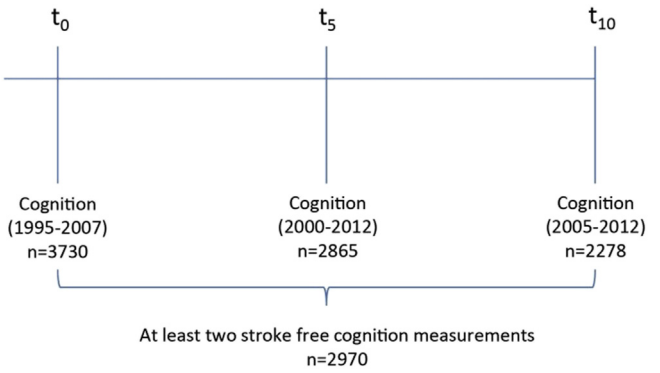

Fig. 1. Timeline of the cognitive tests including the number of respondents used for the statistical analyses. Sleep duration was measured at t0, t5, and t10; feeling rested was only measured during the most recent DCS examination round (2008–2012), referring to t5 or t10.

2.3. Sleep

Information on sleep duration was obtained by a self-administered questionnaire. The average sleep duration was assessed by asking "How many hours of sleep do you usually get per 24-h period?" with answer categories "5 h or less", "6 h", "7 h", "8 h", and "9 h or more." The reference group was defined as 7 or 8 h of sleep per 24-h period. Short sleep duration was defined as 6 h or less and long sleep duration as 9 h or more. This was in accordance with the consensus recommendations of The American Academy of Sleep Medicine [23].

Feeling rested was assessed in the fifth examination round (2008–2012) by asking "do you ever feel not well rested after a usual night?" with answer categories "Never", "Rarely", "Frequently", or "Always". This is a non-validated question used as proxy for sleep quality [24]. Feeling well rested was defined by the categories never and rarely, feeling not well rested was defined by the categories frequently and always.

2.4. Other measures

Information on sociodemographic characteristics (age, gender, educational level, job status, living alone), lifestyle factors (smoking, physical activity, diet, and alcohol consumption), biological risk factors (body mass index (BMI), waist circumference, blood pressure, cholesterol, diabetes, oestrogen use, apoe4), and quality of life (vitality and mental health) was collected using standardized questionnaires and physical examinations at baseline and follow-up. Educational level was assessed as the highest level reached

and classified into five categories: 1) primary school, 2) lower vocational education, 3) intermediate secondary education, 4) intermediate vocational or higher secondary education, and 5) higher vocational education or university. Living alone was defined as living without partner, children, parents, or other adults. Job status was defined as having a paid job or not (including housewives or men, disabled, unemployed, and retired individuals).

Smoking status was categorized as never smoker, ex-smoker, or current smoker. Alcohol consumption was measured as the number of glasses of alcoholic beverages per day.

A validated self-administered semi-quantitative food-frequency questionnaire was used to assess the habitual consumption of 178 food items during the previous year. This food-frequency questionnaire was developed for the European Prospective Investigation into Cancer and Nutrition (EPIC) and assessed during the years 1993–2007 [25]. Coffee, tea, vegetable and fruit, fatty fish consumption, and total energy intake per day were derived from the food-frequency questionnaire. Coffee and tea consumption were defined as the number of cups per day and for coffee consumption only caffeinated coffee was considered. Fatty fish, vegetable and fruit were expressed in grams per day. Physical activity level was assessed by the use of the validated EPIC questionnaire on physical activity and categorized in four categories according to the Cambridge Physical Activity Index: inactive, moderately inactive, moderately active, and active [26,27].

Height, weight, waist circumference, and blood pressure (two times) were measured by trained paramedics, and non-fasting blood samples were obtained [17]. Body mass index was determined as weight (kg) divided by height squared (m^2). Total and HDL cholesterol were measured from blood samples using standardized enzymatic methods. Hypercholesterolaemia was defined as ≥6.5 mmol/l or the use of cholesterol lowering medication. Low levels of HDL cholesterol were defined as <1.03 mmol/l (for men) and <1.29 mmol/l (for women). Random plasma glucose level was determined with the hexokinase method [28]. Diabetes was self-reported or a random plasma glucose of 11.1 mmol/l or more [29]. Apolipoprotein (APOE) E4 alleles were determined based on two single-nucleotide polymorphisms (SNP's): rs429358 and rs7412, using KASP™ (LGC Genomics, Hoddesdon, UK), and categorized as no APOE E4 or one or two APOE E4 alleles. For women only, use of oestrogen was defined as current use of oestrogen or other female hormones.

The mental health and vitality scales of the Dutch version of the SF-36 evaluate feelings of depression and nervousness, and feelings of energy and fatigue [30]. The validity and reliability of the SF-36 have been established [31,32]. Scores on both scales range from 0 to 100 in which higher scores represent better (mental) health.

2.5. Statistical analyses

Multivariable generalized estimated equations (GEE) were used to examine [1] the association of sleep duration with cognitive function in two different models. The exchangeable working correlation structure was applied since correlations between cognitive measurements over follow-up were considered relatively stable and QIC was lowest over all cognitive domains [33]. The first model included the sociodemographic characteristics sex, age, age squared, educational level, job status, and living alone, and lifestyle characteristics: smoking status, alcohol consumption, physical activity. Dietary characteristics (coffee, tea, vegetable and fruit, fatty fish, and total energy intake) did not confound the association between sleep duration and cognitive function, and were therefore not included in the models. The second model included additional adjustment for biological risk factors: systolic blood pressure, waist circumference, low HDL cholesterol, use of oestrogen, APOE E4 allele; and health-related quality of life: mental health and vitality scales. For diabetes and BMI, no confounding effects (defined as a change of >10 percent of the Beta coefficient for sleep duration [34,35]) were shown and therefore these variables were not included in the final models. To test whether the association between sleep duration and cognitive function was different for men and women, additional analyses were performed including an interaction term of sleep duration and sex. Linear and quadratic trends between sleep duration (based on all five categories) and cognitive function were tested in the GEE model including all follow-up measurements. In order to report effect sizes in age-equivalents, the Beta coefficients for sleep duration categories were divided by the Beta coefficient for age (in years).

The association between (2) sleep duration and change in cognitive function was tested by including an interaction term between sleep duration and age. Interactions were considered significant at $p < 0.10$. For analyses of the association of (3) changes in sleep duration over a 5-year period with cognitive function, changes in sleep duration were categorized as previously [14,36]. Two categories of change in sleep duration were expected to have a beneficial effect on cognitive function: 'increase from 5 or 6 h' and 'decrease from 9 h or more'; and two categories were expected to have a detrimental effect on cognitive function 'decrease from 6, 7, or 8 h' and 'increases from 7 or 8 h'.

Finally, the association of (4) sleep duration and feeling rested with cognitive function was explored in cross-sectional models including a subsample of respondents with data on feeling rested ($n = 2587$). These models were also adjusted for the number of cognitive tests performed during follow-up. Interaction between sleep duration and feeling rested was tested and analyses were stratified for feeling rested when significant interactions were observed.

All analyses were performed using SAS statistical software (version 9.3; SAS Institute Inc., Cary, NC, USA).

3. Results

At baseline, long sleepers (≥9 h) were slightly older, had more frequently no paid job, were more often physically inactive, and had more often hypertension compared to adults with less than 9 h sleep (Table 1). Both short and long sleepers had lower cognitive function domain scores at baseline, reported more frequently feeling not well rested, and reported lower scores for vitality compared to those with moderate sleep.

3.1. Sleep duration and cognitive function

Long sleepers had significantly lower cognitive function scores for memory (z–score Beta: −0.09 (95% confidence interval: −0.16–0.01)), flexibility (−0.07 (−0.14–0.01)), and global cognitive function (−0.06 (−0.11–0.02)), compared to adults with a moderate sleep duration and adjusted for sociodemographic and lifestyle characteristics (Table 2). Expressed in age equivalents and compared to adults with moderate sleep duration, the effect of being a long sleeper was statistically equivalent to being 3–4 years older for memory and global cognitive function and 2–3 years older for the domain of flexibility. After additional adjustment for biological risk factors, vitality, and mental health, long sleepers scored lower on memory and global cognitive function (−0.08 (−0.15–0.01) and −0.06 (−0.11–0.02) respectively), compared to a moderate sleep duration. Linear trends were found between sleep duration and memory function (model 2: $p < 0.05$) and between sleep duration and global cognitive functioning (model 1 and 2:

Table 1
Baseline characteristics of the study population (totals and stratified according to sleep duration), the Doetinchem Cohort Study.

	All (n = 2970)	Sleep duration (hours per 24-h period)		
		≤6 (n = 551)	7–8 (n = 2203)	≥9 (n = 196)
Sociodemographic characteristics				
Age in years	55.2 (6.9)	55.0 (6.7)	55.0 (6.9)	57.7 (7.6)
Gender, % women	51.1	52.6	52.0	50.0
Educational level, % low educated[a]	30.5	34.9	29.2	32.1
Living alone, %	8.4	11.1	7.4	11.8
Work status, % with paid job	55.7	58.0	57.2	30.1
Cognitive function domain scores (z-scores)				
Memory function n = 2959	0.00 (0.94)	−0.05 (0.70)	0.03 (0.94)	−0.20 (1.08)
Speed of cognitive processes n = 2954	0.00 (0.84)	−0.06 (0.88)	0.04 (0.82)	−0.28 (0.95)
Cognitive flexibility n = 2958	0.00 (1.00)	−0.08 (1.07)	0.05 (0.97)	−0.31 (1.05)
Global cognitive function n = 2940	0.00 (0.73)	−0.04 (0.83)	0.04 (0.73)	−0.24 (0.81)
Lifestyle				
Smoking, %	22.2	21.3	22.3	21.0
Physical activity, % inactive[b]	25.2	25.6	24.2	32.7
Alcohol consumption (glasses/day)	0.9 (0.0–2.0)	0.9 (0.0–2.0)	0.9 (0.0–2.0)	0.9 (0.0–1.9)
Coffee consumption (cups/day)	4.0 (2.0–5.9)	4.0 (2.0–6.0)	4.0 (2.0–5.2)	3.0 (1.0–5.0)
Tea consumption (cups/day)	1.2 (0.3–2.6)	0.9 (0.2–2.2)	1.4 (0.3–2.7)	1.4 (0.3–2.6)
Biological risk factors				
Systolic blood pressure (mmHg)	130.4 (17.7)	131.4 (17.5)	129.8 (17.5)	134.8 (20.6)
Hypertension, %	35.2	38.8	33.7	41.8
Total cholesterol (mmol/l)	5.84 (1.01)	5.94 (1.01)	5.82 (1.01)	5.81 (1.01)
HDL cholesterol (mmol/l)				
Men	1.22 (0.32)	1.22 (0.32)	1.22 (0.32)	1.19 (0.31)
Women	1.54 (0.39)	1.57 (0.41)	1.54 (0.38)	1.49 (0.43)
Waist circumference (cm)				
Men	99.0 (9.3)	100.4 (9.8)	98.4 (8.9)	102.2 (10.5)
Women	89.6 (11.0)	90.7 (11.4)	89.4 (10.9)	90.6 (11.3)
Body mass index (kg/m^2)	26.4 (3.8)	26.8 (4.0)	26.2 (3.8)	26.9 (4.3)
Oestrogen use (%)	18.4	19.6	18.3	14.4
Apoe4 (%)	28.6	28.1	29.0	26.1
Quality of life				
Vitality (0–100)	67.6 (17.1)	63.3 (19.1)	69.4 (15.8)	60.2 (20.1)
Mental health (0–100)	77.1 (15.0)	72.5 (17.9)	78.5 (13.8)	74.5 (16.0)
Sleep				
Feeling not well rested, %	10.9	19.2	8.4	16.2

Values are %, mean (SD) or median (interquartile range).
[a] Primary school or lower vocational education as highest attained level.
[b] Being classified as inactive or moderately inactive according the Cambridge Physical Activity Index [26].

Table 2
Beta coefficients and 95% confidence intervals of the association of sleep duration with cognitive function.

		Sleep duration			P trend[a]	
		≤6 h	7–8 h	≥9 h	Linear	Quadratic
Memory	Model 1 (Obs = 7815)	0.02 (−0.03 0.06)	REF	−0.09 (−0.16–0.01)	0.13	0.59
	Model 2 (Obs = 7543)	0.03 (−0.02 0.07)	REF	−0.08 (−0.15–0.01)	0.04	0.79
Speed	Model 1 (Obs = 7783)	−0.00 (−0.03 0.03)	REF	−0.04 (−0.10 0.01)	0.47	0.04
	Model 2 (Obs = 7513)	0.00 (−0.03 0.03)	REF	−0.03 (−0.09 0.02)	0.23	0.12
Flexibility	Model 1 (Obs = 7787)	0.02 (−0.03 0.07)	REF	−0.07 (−0.14–0.01)	0.15	0.03
	Model 2 (Obs = 7517)	0.03 (−0.02 0.08)	REF	−0.06 (−0.12 0.01)	0.09	0.23
Global cognitive function	Model 1 (Obs = 7755)	0.02 (−0.01 0.04)	REF	−0.06 (−0.11–0.02)	0.01	0.03
	Model 2 (Obs = 7486)	0.02 (−0.00 0.05)	REF	−0.06 (−0.11–0.02)	<0.01	0.10

Model 1: analyses adjusted for sex, age, age squared, educational level, living alone, work status, smoking, alcohol use, and physical activity.
Model 2: analyses adjusted for variables of model 1 and additionally for systolic blood pressure, waist circumference, low HDL cholesterol, oestrogen use, apoe4, and the quality of life scales vitality and mental health.
REF = reference category.
[a] Linear and quadratic trends between sleep duration (based on all five categories) and cognitive function were tested for all models.

$p < 0.05$), whereas quadratic trends were found between sleep duration and speed, flexibility and global cognitive function (model 1 only: $p < 0.05$) (Table 2). No significant interactions were found between sleep duration and sex.

Analyses for our second objective showed no significant associations between sleep duration and change in cognitive function ($p > 0.05$ for all four cognitive domains). Within the scope of our third objective, none of the categories of changes in sleep duration was significantly associated with cognitive function ($p > 0.10$).

3.2. Feeling rested and sleep duration and cognitive function

Cross-sectional analyses in a subsample of the study population (n = 2587) showed that sleep duration or feeling rested were not associated with memory and global cognitive function (Fig. 2, upper figures). Feeling rested itself was not statistically significantly associated with cognitive function. Significant interactions between sleep duration and feeling rested were observed for speed ($p < 0.01$) and flexibility ($p < 0.10$). Among adults frequently feeling

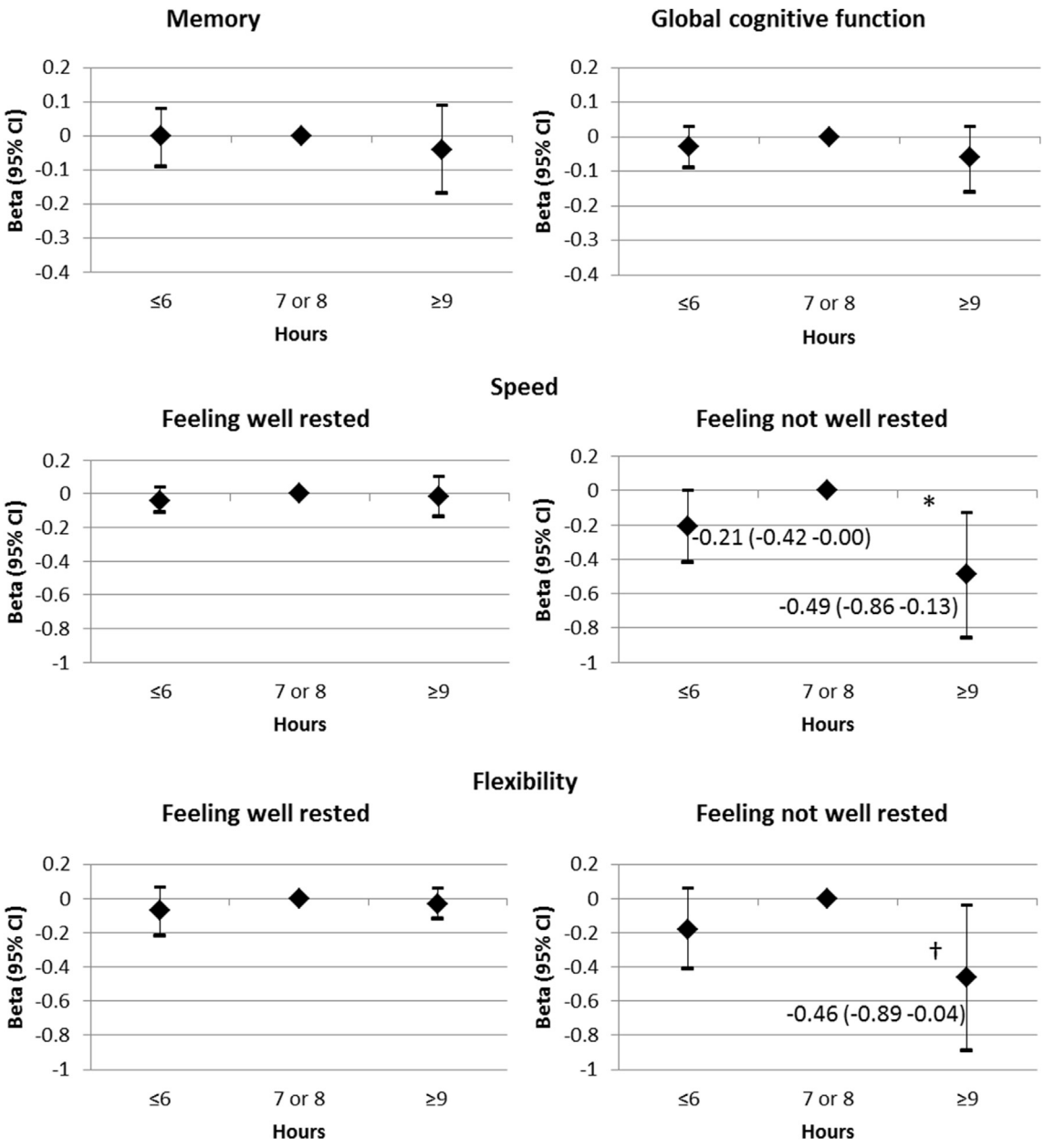

Fig. 2. Beta coefficients and 95% confidence intervals of memory and global cognitive function (upper figures), speed (middle figures), and flexibility (lower figures) by sleep duration and feeling rested. All coefficients are adjusted for sex, age, educational level, living alone, work status, smoking, alcohol use, physical activity, number of cognitive measurements, and feeling rested (for global cognitive function and memory only). For significant Beta coefficients the exact value of Beta coefficients and 95% confidence intervals were reported. *A quadratic trend between sleep duration and speed was observed for persons frequently feeling not well rested ($p < 0.01$). †A quadratic trend between sleep duration and flexibility was observed for persons frequently feeling not well rested ($p = 0.03$).

not well rested, both short and long sleepers had lower scores for speed (−0.21 (−0.42–0.00) and −0.49 (−0.86–0.13), respectively) and long sleepers had lower scores for flexibility (−0.46 (−0.89–0.04)) compared to adults with moderate sleep duration. Quadratic trends between sleep duration and speed ($p < 0.01$) and flexibility ($p = 0.03$) were confirmed (Fig. 2, middle and lower figures) in these cross-sectional models.

4. Discussion

In the present study, middle-aged adults with long sleep duration showed a poorer cognitive function for memory, flexibility and global cognitive function. The finding that long sleepers had a lower cognitive function was confirmed cross-sectionally among adults feeling not well rested. Both short and long sleepers had a lower speed of cognitive function and long sleepers also a lower flexibility compared to moderate sleepers. Support for an inverted U-shaped relationship between sleep duration and cognitive function among middle-aged adults was obtained for the domains of speed, flexibility, and global cognitive function. A linear relationship was shown for memory function and global cognitive function. Taking into account feeling rested, the inverted U-shaped relationship was only confirmed for speed and flexibility of cognitive function and among adults feeling not well rested. In our middle-aged

population, change in sleep duration over time was not associated with cognitive function, nor was sleep duration associated with change in cognitive function.

Prospective studies in older adults demonstrate a lower cognitive function and/or greater decline on various cognitive domains for both short and long sleep duration [5,6,8–10]. Therefore, recent reviews suggested a potential inverted U-shaped association between sleep duration and cognitive outcomes [11,37], with stronger evidence that long (rather than short) sleep durations are related to worse cognition [37]. Our findings are in line with this conclusion for long sleep duration. Furthermore, an inverted U-shaped relation between sleep duration and cognitive function was observed for the domains of speed, flexibility, and global cognitive function in our study. Also for middle-aged adults, Miller and colleagues showed that both short and long sleepers had lower cognitive functions (except for memory) [38]. Ferrie and colleagues showed that middle-age adults (45–69 years) who change their sleep duration from moderate to either short or long had a lower score on all cognitive domains, except for memory [14]. These findings are markedly different from ours, since we found no significant associations of changes in sleep duration with cognitive function. The assessment of sleep duration in the Ferrie study was similar to our study, therefore, inconsistent findings may relate to other aspects of the studies such as the cognitive tests applied, the number of follow-up measurements available, and the statistical model used. We found no evidence of a relationship between sleep duration and cognitive change over the 10-year follow-up period, other studies reported mixed findings [15,39]. Based on a small population, Lo et al. demonstrated that every hour decrease in sleep duration at baseline predicted a 0.67% greater annual decrease in global cognitive performance [15]. Recently Lutsey reported that sleep duration at midlife was not related to cognitive decline, except for short sleepers who had a larger decline in executive functioning and processing speed compared to those with moderate sleep duration [39]. A recent meta-analysis of observational epidemiological studies studied the relationship between sleep and the risk of cognitive decline in middle-aged and older adults. Half of the cohort studies included in this meta-analysis did not report a significant association in accordance with our results, however, pooling of results showed that longer durations of sleep increased the risk of cognitive decline, compared with average sleep duration [40]. Overall, this overview of epidemiological studies in middle-age adults shows that poor sleep characteristics affect cognitive function, but the particular relations between short and long sleep duration, poor sleep quality, and the various cognitive domains remain unclear.

Long sleep is known to be associated with depression, heart disease, and even mortality [3,41–43]. Adults with long sleep duration represent a specific group characterised by a higher prevalence of severe and chronic health problems. Our analyses showed that after adjustment for biological risk factors, mental health and vitality, associations between long sleep duration and the different domains of cognitive function were not statistical significant anymore. This suggests that long sleepers are a relatively unhealthy group within our study sample, which is supported by higher rates of hypertension. However, the association between long sleep duration and global cognitive function was not attenuated by adjustment for biological risk factors. Future studies on the relation between sleep and cognitive function should take into account underlying health status. Another issue is that the prevalence of sleep disturbances for persons with Alzheimer disease is high. Although dementia is (yet) uncommon in our middle-age population, reverse causation cannot be rejected. Cognitive decline and the development of sleep problems may occur concurrently [44]. However, we did not find an association between sleep and cognitive decline, which decreases the possibility of reverse causation.

Major strengths of the present study are the prospective design and the use of a sensitive cognitive test battery for this middle-age adult population. Although the participants were still relatively young and healthy when they entered the study, a clear decline in cognitive function, with a wide range, was detected. Since the Doetinchem Cohort Study has an extensive set of variables assessed during the measurements, we were able to adjust for a wide range of potential confounders.

Some limitations of this study need to be highlighted. First, both sleep duration and feeling rested were measured with a self-reported single survey item. The self-reported question on sleep duration did not consider a timeframe, distinguish between weekdays and weekends, or distinguish between naps and longer sleep periods. Sleep duration is shown to be overestimated by most adults and may actually represent time spent in bed rather than physiologic sleep duration [42,45,46]. However, insomnia is also a prevalent condition among adults and it is known that those people underestimate sleep duration [47]. By only using self-reported sleep duration in the present study, adults may be falsely categorized into sleep duration classes. Both reasons for misclassification may lead to bias towards null association and can be prevented when using more objective measurements of sleep duration in future studies. In our study, sleep quality was equated with feeling rested, although this may not necessarily measure all aspects of a sleep quality index. The measure of feeling well rested after a usual night lacks a specific time frame and is non-validated. Those feeling not well rested are likely to have poor sleep quality, even detecting people with micro-arousals or disturbances in sleep phases who might not even know they have poor sleep quality. Sleep quality, based on a question on rising rested, was previously shown to modify the relation between sleep duration and cardiovascular disease [48]. Hoevenaar et al. showed that short sleepers with poor sleep quality (and not short sleepers with good sleep quality) had a 63% higher risk of cardiovascular disease and a 79% higher risk of coronary heart disease incidence compared to normal sleepers with good sleep quality. However, the question on feeling well rested could also relate to excessive daytime sleepiness and excessive daytime fatigue, for which an independent relationship with cognitive decline has been shown [10,49]. Furthermore, the question on feeling rested was recently integrated in the study protocol of the Doetinchem Cohort Study and therefore available only for the last cognitive examination. Therefore, feeling rested was only considered in a cross-sectional analysis and future research should examine the impact of feeling rested longitudinally. Another limitation is that we could not adjust for potential confounders such as sleep apnoea, daytime sleepiness, major depression, and the use of sleep medication, since these data were not collected in the Doetinchem Cohort Study. Sleep medication affects sleep duration but there are also indications of adverse effects on cognitive function [50].

Another methodological issue is that participants in cohort studies usually have a relatively healthy profile and a certain drop-out of initial participants is inevitable. Despite the long follow-up period of our study, the drop-out rate was relatively low, approximately 20% at every 5-years of follow-up. Adults who participated at baseline only were on average 2-years older and scored 0.47 standardised points lower on global cognitive function and all cognitive domains compared to adults who participated at follow-up measurements as well. Drop-outs reported more often long sleep duration (6.6% vs. 10.9%). We do not think that multiple testing adjustment is necessary, since the study examined the specific association between sleep duration and cognitive function (in four different domains).

The present study provides varying support for an inverted U-shaped relationship between sleep duration and cognitive function in middle-aged adults: the form of the relationship between sleep duration and cognitive function differed per cognitive domain and depended on feeling rested. Long sleep duration was consistently associated with a poorer cognitive function in all cognitive domains, except for speed. Future studies should assess the role of sleep characteristics for cognitive decline at middle-age using objective assessments of sleep patterns and consider sleep quality.

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Conflicts of interest

None.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2017.07.029.

References

[1] Prince M, Knapp M, Guerchet M, et al. Dementia UK: update. 2nd ed. 2014.
[2] Singh-Manoux A, Kivimaki M, Glymour MM, et al. Timing of onset of cognitive decline: results from Whitehall II prospective cohort study. BMJ 2012;344:d7622.
[3] Ohayon MM, Vecchierini MF. Normative sleep data, cognitive function and daily living activities in older adults in the community. Sleep 2005;28(8):981–9.
[4] 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(8):971–7.
[5] 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(6):1073–81.
[6] Potvin O, Lorrain D, Forget H, et al. Sleep quality and 1-year incident cognitive impairment in community-dwelling older adults. Sleep 2012;35(4):491–9.
[7] 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: JCSM: Off Publ Am Acad Sleep Med 2013;9(7):669–73.
[8] 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(1):41–8.
[9] Benito-Leon J, Louis ED, Bermejo-Pareja F. Cognitive decline in short and long sleepers: a prospective population-based study (NEDICES). J Psychiatr Res 2013;47(12):1998–2003.
[10] Keage HA, Banks S, Yang KL, et al. What sleep characteristics predict cognitive decline in the elderly? Sleep Med 2012;13(7):886–92.
[11] Yaffe K, Falvey CM, Hoang T. Connections between sleep and cognition in older adults. Lancet Neurol 2014;13(10):1017–28.
[12] Yaffe K, Nasrallah I, Hoang TD, et al. Sleep duration and white matter quality in middle-aged adults. Sleep 2016;39(9):1743–7.
[13] Ramos AR, Tarraf W, Daviglus M, et al. Sleep duration and neurocognitive function in the Hispanic Community Health Study/Study of Latinos. Sleep 2016;39(10):1843–51.
[14] Ferrie JE, Shipley MJ, Akbaraly TN, et al. Change in sleep duration and cognitive function: findings from the Whitehall II Study. Sleep 2011;34(5):565–73.
[15] Lo JC, Loh KK, Zheng H, et al. Sleep duration and age-related changes in brain structure and cognitive performance. Sleep 2014;37(7):1171–8.
[16] Spira AP, Chen-Edinboro LP, Wu MN, et al. Impact of sleep on the risk of cognitive decline and dementia. Curr Opin Psychiatry 2014;27(6):478–83.
[17] Verschuren W, Blokstra A, Picavet H, et al. Cohort profile: the Doetinchem Cohort Study. Int J Epidemiol 2008;37:1236–41.
[18] Picavet HSJ, Blokstra A, Spijkerman AMW, et al. Cohort profile update: the Doetinchem Cohort Study 1987–2017: lifestyle, health and chronic diseases in a life course and ageing perspective. Int J Epidemiol 2017. https://doi.org/10.1093/ije/dyx103.
[19] Nooyens AC, Bueno-de-Mesquita HB, van Boxtel MP, et al. Fruit and vegetable intake and cognitive decline in middle-aged men and women: the Doetinchem Cohort Study. Br J Nutr 2011;106(5):752–61.
[20] Moller JT, Cluitmans P, Rasmussen LS, et al. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction. Lancet 1998;351(9106):857–61.
[21] Durga J, van Boxtel MP, Schouten EG, et al. Effect of 3-year folic acid supplementation on cognitive function in older adults in the FACIT trial: a randomised, double blind, controlled trial. Lancet 2007;369(9557):208–16.
[22] de Groot JC, de Leeuw FE, Oudkerk M, et al. Cerebral white matter lesions and cognitive function: the Rotterdam Scan Study. Ann Neurol 2000;47(2):145–51.
[23] Watson NF, Badr MS, Belenky G, et al. Recommended amount of sleep for a healthy adult: a joint consensus statement of the American Academy of Sleep Medicine and Sleep Research Society. Sleep 2015;38(6):843–4.
[24] Harvey AG, Stinson K, Whitaker KL, et al. The subjective meaning of sleep quality: a comparison of individuals with and without insomnia. Sleep 2008;31(3):383–93.
[25] Ocke MC, Bueno-de-Mesquita HB, Goddijn HE, et al. The Dutch EPIC food frequency questionnaire. I. Description of the questionnaire, and relative validity and reproducibility for food groups. Int J Epidemiol 1997;26(Suppl. 1):S37–48.
[26] Pols MA, Peeters PH, Ocke MC, et al. Estimation of reproducibility and relative validity of the questions included in the EPIC Physical Activity Questionnaire. Int J Epidemiol 1997;26(Suppl. 1):S181–9.
[27] Wareham NJ, Jakes RW, Rennie KL, et al. Validity and repeatability of a simple index derived from the short physical activity questionnaire used in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. Public Health Nutr 2003;6(4):407–13.
[28] Tietz NW, editor. Clinical guide to laboratory tests. Philadelphia: WB Saunders; 1995.
[29] World Health Organisation. Definition and diagnosis of diabetes mellitus and intermediate hyperglycemia: report of a WHO/IDF consultation. Geneva. 2006.
[30] van der Zee KI, Sanderman R. Het Meten van Gezondheidstoestand Met de RAND-36: een Handleiding. Groningen, The Netherlands: Noordelijk Centrum voor Gezondheidsvraagstukken; 1993 [in Dutch].
[31] Ware JE, Snow KK, Kosinski M, et al. SF-36 health survey manual and interpretation guide. Boston, MA: New England Medical Center, The Health Institute; 1993.
[32] Ware Jr JE, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30(6):473–83.
[33] Cui J. QIC program and model selection in GEE analyses. Stata J 2007;7(2):209–20.
[34] Mickey RM, Greenland S. The impact of confounder selection criteria on effect estimation. Am J Epidemiol 1989;129(1):125–37.
[35] Maldonado G, Greenland S. Simulation study of confounder-selection strategies. Am J Epidemiol 1993;138(11):923–36.
[36] Ferrie JE, Shipley MJ, Cappuccio FP, et al. A prospective study of change in sleep duration: associations with mortality in the Whitehall II cohort. Sleep 2007;30(12):1659–66.
[37] Devore EE, Grodstein F, Schernhammer ES. Sleep duration in relation to cognitive function among older adults: a systematic review of observational studies. Neuroepidemiology 2016;46(1):57–78.
[38] Miller MA, Wright H, Ji C, et al. 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 2014;9(6), e100991.
[39] Lutsey PL, Bengtson LG, Punjabi NM, et al. Obstructive sleep apnea and 15-year cognitive decline: the Atherosclerosis Risk in Communities (ARIC) study. Sleep 2016;39(2):309–16.
[40] Kim HB, Myung SK, Lee SM, et al., Korean Meta-Analysis Study G. Longer duration of sleep and risk of cognitive decline: a meta-analysis of observational studies. Neuroepidemiology 2016;47(3–4):171–80.
[41] Grandner MA, Drummond SP. Who are the long sleepers? Towards an understanding of the mortality relationship. Sleep Med Rev 2007;11(5):341–60.
[42] Kline CE, Zielinski MR, Devlin TM, et al. Self-reported long sleep in older adults is closely related to objective time in bed. Sleep Biol Rhythms 2010;8(1):42–51.
[43] Stamatakis KA, Punjabi NM. Long sleep duration: a risk to health or a marker of risk? Sleep Med Rev 2007;11(5):337–9.
[44] Bedrosian TA, Nelson RJ. Pro: Alzheimer's disease and circadian dysfunction: chicken or egg? Alzheimers Res Ther 2012;4(4):25.

[45] Lauderdale DS, Knutson KL, Yan LL, et al. Self-reported and measured sleep duration: how similar are they? Epidemiology 2008;19(6):838–45.
[46] Silva GE, Goodwin JL, Sherrill DL, et al. Relationship between reported and measured sleep times: the sleep heart health study (SHHS). J Clin Sleep Med: JCSM: Off Publ Am Acad Sleep Med 2007;3(6):622–30.
[47] Harvey AG, Tang NK. (Mis)perception of sleep in insomnia: a puzzle and a resolution. Psychol Bull 2012;138(1):77–101.
[48] Hoevenaar-Blom MP, Spijkerman AM, Kromhout D, et al. Sleep duration and sleep quality in relation to 12-year cardiovascular disease incidence: the MORGEN study. Sleep 2011;34(11):1487–92.
[49] Carvalho DZ, St Louis EK, Boeve BF, et al. Excessive daytime sleepiness and fatigue may indicate accelerated brain aging in cognitively normal late middle-aged and older adults. Sleep Med 2017;32:236–43.
[50] Billioti de Gage S, Begaud B, Bazin F, et al. Benzodiazepine use and risk of dementia: prospective population based study. BMJ 2012;345, e6231.