Sleep Medicine 16 (2015) 850–855

Contents lists available at ScienceDirect

Sleep Medicine

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

Original Article

Associations of the 24-h activity rhythm and sleep with cognition: a population-based study of middle-aged and elderly persons

Annemarie I. Luik [a], Lisette A. Zuurbier [a], Albert Hofman [a], Eus J.W. Van Someren [b,c], M. Arfan Ikram [a,d,e], Henning Tiemeier [a,f,g,*]

[a] Department of Epidemiology, Erasmus University Medical Center, Rotterdam, The Netherlands
[b] Department of Sleep and Cognition, Netherlands Institute for Neuroscience, an Institute of the Netherlands Royal Academy of Arts and Sciences, Amsterdam, The Netherlands
[c] Departments of Integrative Neurophysiology and Medical Psychology, Center for Neurogenomics and Cognitive Research, Neuroscience Campus Amsterdam, VU University and Medical Center, Amsterdam, The Netherlands
[d] Department of Neurology, Erasmus University Medical Center, Rotterdam, The Netherlands
[e] Department of Radiology, Erasmus University Medical Center, Rotterdam, The Netherlands
[f] Department of Child and Adolescent Psychiatry, Erasmus University Medical Center, Rotterdam, The Netherlands
[g] Department of Psychiatry, Erasmus University Medical Center, Rotterdam, The Netherlands

ARTICLE INFO

Article history:
Received 5 January 2015
Received in revised form 19 March 2015
Accepted 23 March 2015
Available online 15 April 2015

Keywords:
Circadian rhythm
Activity rhythm
Sleep
Cognition
Aging

ABSTRACT

Background: Cognitive functioning changes with age, sleep, and the circadian rhythm. We investigated whether these factors are independently associated with different cognitive domains assessed in middle-aged and elderly persons.
Methods: In 1723 middle-aged and elderly persons (age 62 ± 9.4 years, mean ± standard deviation, SD) of the Rotterdam Study, we collected actigraphy recordings of on average 138 h. Actigraphy was used to quantify 24-h rhythms by calculating the stability of the rhythm over days and the fragmentation of the rhythm. Sleep parameters including total sleep time, sleep-onset latency, and wake after sleep onset were also estimated from actigraphy. Cognitive functioning was assessed with the word learning test (WLT), word fluency test (WFT), letter digit substitution task (LDST), and Stroop color word test (Stroop).
Results: Persons with less stable 24-h rhythms performed worse on the LDST ($B = 0.42$ per SD increase, $p = 0.004$) and the Stroop interference trial ($B = -1.04$ per SD increase, $p = 0.003$) after full adjustment. Similarly, persons with more fragmented rhythms performed worse on the LDST ($B = -0.47$ per SD increase, $p = 0.002$) and the Stroop ($B = 1.47$ per SD increase, $p < 0.001$). By contrast, longer observed sleep-onset latencies were related to worse performance on the WLT delayed recall ($B = -0.19$ per SD increase, $p = 0.027$) and the WFT ($B = -0.45$ per SD increase, $p = 0.007$).
Conclusions: Disturbances of sleep and the 24-h activity rhythm were independently related to cognition; while persons with longer sleep-onset latencies had worse performance on memory and verbal tasks, persons with 24-h rhythm disturbances performed less on executive functioning and perceptual speed tasks.

1. Introduction

Disturbed sleep and disturbed circadian rhythms can exacerbate cognitive impairment. Recent population-based studies have shown compelling evidence for an association of sleep and cognitive functioning in the elderly. Self-rated sleep characteristics have been associated with worse cognitive functioning in population-based samples [1,2]. Moreover, the association of sleep and cognition has also been assessed objectively by means of actigraphy in large population-based studies. Shorter total sleep time, longer sleep-onset latencies, more wake after sleep onset, and lower sleep efficiency have been related to worse cognitive performance in elderly persons [3,4].

Circadian rhythms have also been related to cognition. The fragmentation of the circadian rhythm is suggested to be particularly important for cognitive performance. For example, a fragmented 24-h activity rhythm was significantly related to impaired mental speed and impaired executive functioning in 144 home-dwelling middle-aged and elderly persons [5]. In a larger sample of very old persons, fragmentation of the activity rhythm was associated with diminished performance on multiple cognitive tasks [6]. Moreover, changes in the activity rhythm have been associated with an increased odds of developing mild cognitive impairment and dementia [7]. However,

* Corresponding author. Department of Epidemiology, Erasmus University Medical Center, P.O. Box 2040, 3000 CA Rotterdam, The Netherlands. Tel.: +31 10 4043489; fax: +31 107044657.
E-mail address: h.tiemeier@erasmusmc.nl (H. Tiemeier).

http://dx.doi.org/10.1016/j.sleep.2015.03.012
1389-9457/

it is not clear if the associations of 24-h activity rhythm disturbances with cognition can be explained by the association of sleep with cognition, as circadian rhythms are intrinsically related to sleep [8].

Previous research shows that the effects of circadian rhythm and sleep may differ per cognitive domain. Population-based studies on rhythm disturbances mostly demonstrate effects on non-memory tasks [5,6]. Disturbed sleep has been related to all cognitive domains [3,4,9], but the relation between disturbed sleep and memory was mainly demonstrated in smaller populations. Experimental studies suggest that objectively measured sleep disturbance is also related to impaired memory, in particular to problems in memory consolidation [9]. The association between sleep and memory has hardly been tested in population-based studies.

Recent population-based studies of sleep, circadian rhythm, and cognition have focused mostly on elderly populations with mean ages above 70 years. Although the effect of sleep on cognition has shown to be independent of age in most studies [3,4,6], it is unclear whether these associations can already be observed in middle age. Possibly, the aging process creates a vulnerability to the impact of sleep and circadian rhythm disturbances on cognitive performance. Detecting if these associations are present in middle-aged and elderly persons could broaden the treatment choices for cognitive problems in this population. Activity rhythms and sleep are behaviors amenable to change and a possible target for intervention in patients with cognitive problems. Differential associations can indicate that manipulation of both circadian rhythms and sleep could be valuable for the treatment of selected cognitive problems.

In this population-based study of middle-aged and elderly persons, we assessed circadian rhythms and sleep with actigraphy and cognitive functioning with multiple cognitive tests. This allowed us to test whether (1) the 24-h activity rhythm is associated with cognitive functioning independently of sleep, (2) whether the associations of sleep and the 24-h activity rhythm are distinct per cognitive domain, and (3) whether the effects are specific to old age.

2. Material and methods

2.1. Study population

This study was conducted within the Rotterdam Study, a population-based cohort of middle-aged and elderly inhabitants of Rotterdam, the Netherlands. The study began in 1990 by inviting inhabitants of the district of Ommoord aged 55 years and over. In 2000, the study population was extended with a second cohort of inhabitants aged 55 and over. In 2006, a new cohort with inhabitants aged 45 and over was added. A more detailed description of the study can be found elsewhere [10]. The study is in accordance with the guideline proposed in the World Medical Association Declaration of Helsinki and approved by the Medical Ethics Committee of the Erasmus University Rotterdam. Written informed consent was obtained from all participants.

From December 2004 until April 2007, 2632 consecutive persons were invited to participate in the actigraphy study; 2063 (78%) agreed. Women (60.5% vs. 53.4%, $p = 0.003$) and older-aged persons (mean age 67.5 vs. 62.3 years, $p < 0.001$) were more likely to refuse participation in the actigraphy study. The recordings of 340 participants (16%) were excluded, of which 329 participants' recordings either did not consist of four consecutive days and nights or had technical problems, and 11 participants had no information on cognitive functioning. Recordings of 1723 participants were suitable for further analyses.

2.2. Assessment of the 24-h activity rhythm and sleep

All participants were asked to wear an actigraph around the nondominant wrist (Actiwatch model AW4, Cambridge Technology Ltd) continuously for seven consecutive days and nights, and to remove it only while bathing. Actigraphs were measured in 30-s epochs. To prevent a time-of-day effect, 24-h periods with more than three continuous hours missing were excluded from the analyses [11]. Recordings had a mean duration of 138 h (standard deviation, SD: 14 h).

Activity rhythms were quantified using nonparametric indicators [11,12]. This allowed us to describe the rhythm without making strong assumptions about the shape of the rhythm [13]. We calculated the interdaily stability and the intradaily variability to assess the 24-h activity rhythm. The interdaily stability indicates the stability of the rhythm, that is, the extent to which the profiles of individual days resemble each other, and it is calculated as the ratio between the variance of the average 24-h pattern around the mean and the overall variance. The intradaily variability quantifies the fragmentation of the rhythm, and it is calculated as the ratio of the mean squares of the difference between consecutive hours (first derivative) and the mean squares around the grand mean (overall variance). More frequent alterations between an active and an inactive state lead to a higher intradaily variability.

We also used the actigraphy recordings to calculate total sleep time, sleep-onset latency, and wake after sleep onset with a validated algorithm [14]. Although sleep is best assessed with polysomnography, actigraphy is considered a reliable alternative to estimate sleep characteristics [15]. The procedure used to calculate these measures has been described in more detail elsewhere [11].

Subjective sleep quality was assessed daily with a sleep diary that was kept during the week of actigraphy. Perceived sleep quality indicates the average of three questions about sleep quality (range 0–7).

2.3. Assessment of cognitive functions

Cognitive function was assessed with a neuropsychological test battery consisting of a 15-word learning test (WLT, based on the Rey recall of words) [16], a categorical word fluency test (WFT, animal categories) [17], the letter digit substitution task (LDST, range 0–125) [18], the Stroop color word test (Stroop) [19], and the Mini Mental State Exam (MMSE, range 0–30) [20]. The WLT consisted of three immediate recall trials (range 0–45 words) and a delayed recall trial after 10 min (range 15 words). The LDST is a substitution test that consists of a key with letter–digit pairs, followed by a list of only letters. Participants have to write down the appropriate digits underneath the randomized letters as quickly as possible in 1 min. The examinations were performed by the same research team and in identical order for all participants.

We constructed a compound score for global cognition, which has been described in more detail elsewhere [21]. The global cognition score is a summary measure of the *Z*-scores of all assessed cognitive tests, except the MMSE. All Stroop trials are included in the compound score; the *Z*-scores of the Stroop are inverted in this compound score to ensure that a higher score reflects a better performance on all tasks.

2.4. Assessment of covariates

A priori, we selected the following potential confounders based on the previous literature [6,11]: sex, age, employment status, education, smoking, body mass index (BMI), depressive symptoms, activities of daily living (ADL), myocardial infarction (MI), stroke, diabetes mellitus (DM), possible apnea, and time of cognitive testing. All confounders were routinely collected in the Rotterdam Study. During a home interview, all participants were asked about their employment status, their education (low indicating primary education level, middle indicating vocational training to medium-level

secondary education, and high indicating high-level vocational training to university level), current smoking, depressive symptoms, and ADL. Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression (CES-D) scale [22] (range 0–60). ADL was assessed with the Stanford Health Assessment Questionnaire [23] (range 0–3). Height and weight were measured without shoes and heavy clothing during a center visit to calculate the BMI (kg/m^2). MI, stroke, and DM were determined during the center visit and medical records. Possible apnea was assessed with two questions from the Pittsburgh Sleep Quality Index [24]. We considered apnea possible when participants reported (1) loud snoring at least two nights per week and at least occasional respiratory pauses or (2) respiratory pauses during sleep with a frequency of at least one to two nights per week [25]. Time of cognitive testing was assessed to prevent a time-of-day effect on cognitive functioning.

2.5. Statistical analyses

We assessed the associations of the 24-h activity rhythm and sleep with cognitive functioning using linear regression analyses. We studied the associations of the 24-h activity rhythm and sleep with global cognitive functioning (averaged *Z*-scores), the WLT immediate recall (number of words over three trials), the WLT delayed recall (number of words), WFT (number of named animals), LDST (number of correct items), and the inference trial of the Stroop (time in seconds). Of the sleep variables, total sleep time was also tested in a quadratic model to test a possible U-shaped relation of total sleep time with cognitive function. Associations were tested in two successive models. The first model was adjusted for sex, age, employment status, education, BMI, smoking, depressive symptoms, ADL, MI, stroke, DM, possible apnea, and time of testing. The second model was also mutually adjusted to test if the effects of indicators of the 24-h activity rhythm and sleep were independent. Potential determinants were only tested in the second model if an association between the sleep or activity rhythm parameter and the respective cognitive task had been observed in the first step. Analyses were repeated excluding participants with a MMSE score <26 [20], to assess whether effects could be explained by severe cognitive impairment only. To assess whether the effects of the 24-h activity rhythm and sleep differed by age, we assessed the interaction terms of age with activity rhythm and sleep parameters quantitatively. Because these interaction analyses were exploratory, we used a more stringent cutoff for significance ($p < 0.001$) to correct for multiple testing. To facilitate the interpretation of possible interactions, we will illustrate interactions observed between continuous variables by categorizing these variables. All analyses were performed using IBM SPSS Statistics, version 21 (IBM Corp., Somers, NY, USA).

As the number of missing values per confounder never exceeded 5%, the missing values in quantitative predictors were replaced by the median. A separate missing category was used for qualitative predictors. All 24-h activity rhythm and sleep indicators and cognitive test scores were Winsorized at four SDs from the mean. To obtain normally distributed values, interdaily stability, intradaily variability, sleep-onset latency, wake after sleep onset, and subjective sleep quality were transformed using a Box–Cox transformation [26,27]. All activity rhythms and sleep parameters were standardized to facilitate interpretation.

3. Results

The mean age of participants was 62 years (SD: 9 years), 53% of which was female. Fifteen percent low education and 33% were still employed (see Table 1). Uncorrected correlations between activity rhythm indicators, sleep parameters, and cognition measures can be found in supplement Table S1.

Table 1
Population characteristics, $N = 1723$.

Demographic	
Female, %	53.5
Age (years)	62.23 ± 9.35
Employment, %	33.3
Education, %	
Low	15.2
Intermediate	63.4
High	19.6
Health indicators	
Stroke, %	2.5
Myocardial infarction, %	1.9
Diabetes mellitus, %	8.9
Depressive symptoms, score	5.46 ± 7.02
Activities of daily living, score	0.29 ± 0.42
Smoking, %	20.7
Body mass index (BMI), kg/m^2	27.86 ± 4.16
Possible apnea, %	29.1
Use of medication, %	22.4
Circadian rhythm	
Duration actigraphy recording, hours	137.63 ± 14.19
Interdaily stability, score	0.80 ± 0.10
Intradaily variability, score	0.42 ± 0.13
Objectively assessed sleep	
Sleep-onset latency, minutes	14.54 ± 12.35
Total sleep time, hours	6.38 ± 0.86
Wake after sleep onset, minutes	69.65 ± 26.26
Sleep quality	
Perceived sleep quality, score	5.54 ± 1.61
Cognition	
Global cognitive functioning, averaged *Z*-score	0.01 ± 0.74
Word learning test (WLT) immediate recall, number of correct words	22.55 ± 6.43
Word learning test (WLT) delayed recall, number of correct words	7.47 ± 2.88
Word fluency test (WFT) , number of correct words	22.50 ± 5.87
Letter digit substitution task (LDST), number of correct items	30.23 ± 6.75
Stroop color word test (Stroop) interference trial, seconds	47.40 ± 16.04

Values are stated as mean ± standard deviation or percentage.

First, we studied whether 24-h activity rhythms were associated with general cognitive functioning and domain specific tasks (see Table 2). A lower intradaily variability, that is, a less fragmented rhythm, was associated with better global cognitive functioning [$B = –0.05$ per SD increase, standard error (SE) = 0.02, $p = 0.003$], while the stability of the rhythm was not associated with global cognition ($B = 0.02$ per SD increase, SE = 0.02, $p = 0.24$) after adjustment for confounders. A more stable rhythm ($B = 0.42$ per SD increase, SE = 0.15, $p = 0.004$) and a less fragmented rhythm ($B = –0.47$ per SD increase, SE = 0.15, $p = 0.002$) were both associated with a higher number of correct items on the LDST. Further, a more stable rhythm ($B = –1.04$ per SD increase, SE = 0.35, $p = 0.003$) and lower fragmentation ($B = 1.47$ per SD increase, SE = 0.36, $p < 0.001$) were related to less time, thus better performance, on the Stroop interference trial. The stability and fragmentation of the rhythm were not associated with the immediate and delayed recall of the WLT and the WFT.

Second, we studied the association of sleep with global cognitive functioning and domain-specific tests (Table 2). Of the objectively measured sleep parameters, only a short sleep-onset latency was associated with better global cognition ($B = –0.05$ per SD increase, SE = 0.02, $p = 0.015$). Persons with a shorter sleep-onset latency also knew more words on the delayed recall of the WLT ($B = –0.19$ per SD increase, SE = 0.09, $p = 0.027$) and named more words on the WFT ($B = –0.45$ per SD increase, SE = 0.17, $p = 0.007$). No other associations of sleep with cognitive tests were found.

Third, we assessed perceived sleep quality in relation to cognitive functioning. A lower reported sleep quality was not related to global cognitive functioning or specific cognitive tasks.

Table 2
Associations of the 24-h activity rhythm and sleep with cognition. Linear regression models adjusted for sex, age, employment status, education, depressive symptoms, body mass index, activities of daily living, stroke, myocardial infarction, diabetes mellitus, possible apnea, and time of testing. All variables were tested in a linear model. SE, standard error.

	Global cognition (N = 1482)		Word learning test (WLT) Immediate recall (N = 1554)		Word learning test (WLT) Delayed recall (N = 1548)		Word fluency test (WFT) (N = 1704)		Letter digit substitution task (LDST) (N = 1682)		Stroop Color Word Test (Stroop) Interference trial (N = 1549)	
	B (SE)	*P*	*B* (SE)	*P*	*B* (SE)	*P*	*B* (SE)	*P*	*B* (SE)	*P*	*B* (SE)	*P*
Circadian rhythm												
Interdaily stability	0.02 (0.02)	0.24	–0.11 (0.15)	0.49	0.00 (0.07)	0.95	0.15 (0.14)	0.28	**0.42 (0.15)**	**0.004**	**–1.04 (0.35)**	**0.003**
Intradaily variability	**–0.05 (0.02)**	**0.003**	–0.17 (0.16)	0.28	–0.12 (0.07)	0.096	–0.19 (0.14)	0.18	**–0.47 (0.15)**	**0.002**	**1.47 (0.36)**	**<0.001**
Sleep												
Sleep–onset latency	**–0.05 (0.02)**	**0.015**	–0.31 (0.19)	0.10	**–0.19 (0.09)**	**0.027**	**–0.45 (0.17)**	**0.007**	–0.27 (0.18)	0.13	0.28 (0.43)	0.51
Wake after sleep onset	–0.02 (0.02)	0.26	–0.14 (0.15)	0.35	–0.09 (0.07)	0.20	–0.21 (0.13)	0.11	–0.07 (0.14)	0.63	0.55 (0.34)	0.10
Total sleep time	0.01 (0.02)	0.75	–0.11 (0.16)	0.47	0.00 (0.07)	0.96	–0.07 (0.14)	0.62	0.16 (0.15)	0.28	0.00 (0.35)	0.99
Sleep quality												
Perceived sleep quality	–0.03 (0.02)	0.064	–0.19 (0.16)	0.24	–0.14 (0.07)	0.064	–0.07 (0.14)	0.63	–0.23 (0.16)	0.14	0.36 (0.37)	0.32

The results for the associations of the activity rhythm, sleep, and sleep quality did not change largely when persons with MMSE <26 were excluded (n = 138) from the analyses (results available upon request).

To test the independence of the effects of the 24-h activity rhythm and sleep, the associations of the activity rhythm and sleep with global cognition, LDST score, and performance on the Stroop interference trial were assessed in a mutually adjusted model, as these outcomes were associated with multiple activity rhythm and sleep indicators. The association of intradaily variability (B = –0.05 per SD increase, SE = 0.02, p = 0.011) with global cognition remained significant after mutual adjustment, as well as the association of intradaily variability with performance on the Stroop interference task (B = 1.32 per SD increase, SE = 0.43, p = 0.002). Of the sleep variables, only the association of sleep-onset latency with global cognition remained significant (B = –0.06 per SD increase, SE = 0.02, p = 0.013). None of the other associations of the 24-h activity rhythm and sleep with cognitive tests remained significant.

Lastly, we performed exploratory analysis to assess whether the effects of the 24-h activity rhythm and sleep were modified by age; three interaction terms met the stringent limit of $p < 0.001$. Age

Fig. 1. Illustration of the continuous tested interaction of intradaily variability (IV) and age for the Stroop interference trial, and the interaction of sleep-onset latency (SOL) and age for the Stroop interference trial and the letter digit substitution task (LDST). Bars present means per group, and error bars depict standard deviations of the group mean.

modified the association of intradaily variability with performance on the Stroop interference trial ($p < 0.001$). In addition, age modified the association between sleep-onset latency and LDST score ($p < 0.001$) and the association between sleep-onset latency and time spent for the Stroop interference trial ($p < 0.001$). Sleep-onset latency and age were categorized to illustrate the quantitative interaction in Fig. 1. A more fragmented rhythm was more strongly associated with worse performance on the Stoop interference trial in older ages. Similarly, longer sleep-onset latency was more strongly associated with worse performance on the LDST and the Stroop interference trial in older-aged persons compared to middle-aged persons.

4. Discussion

In our population-based study, both aspects of the 24-h activity rhythm and sleep were related to global cognitive functioning. More specifically, disturbances in the 24-h activity rhythm were mostly related to tasks that draw on perceptual speed and executive functioning, while an increased sleep-onset latency was related to tasks that are associated with memory performance and verbal abilities.

Fragmentation of both the activity rhythm and sleep-onset latency affected global cognition. Yet, these effects of the fragmentation of the rhythm and sleep-onset latency on global cognition were independent from each other. Activity rhythm and sleep parameters were also only modestly correlated in our sample. This suggests that disturbances of circadian rhythms and disturbances of sleep affect cognitive functioning relatively independently; the small decreases in effect size after mutual adjustment suggested only limited shared variance. The effects of circadian rhythm on cognition have previously been suggested to be independent of sleep in studies in which the human circadian rhythm was desynchronized [28]. Circadian control of pathways, synchronization of local clocks, and neurogenesis have been named as possible mechanisms through which circadian disturbances might affect cognition [29]. On the other hand, sleep deprivation research has demonstrated that disturbed sleep can reduce neural activity [30], and sleep has also been hypothesized to affect synaptic strength [9]. Further research is needed to disentangle the mechanisms that evoke the distinct effects of circadian rhythms and sleep on cognition.

Moreover, the 24-h activity rhythm and sleep parameters showed diverse association patterns with the different cognitive tasks. Fragmentation of the rhythm was particularly important for non-memory tasks. This extends on previous research where fragmentation has been associated with all cognitive subdomains except for episodic memory [6] or where associations with memory disappeared after correction for confounders [5]. By contrast, a long sleep-onset latency was associated with worse memory performance and worse verbal fluency. While this association has not been demonstrated in population-based studies, it extends on the clinical research of sleep and memory. Thus, in our study, 24-h activity rhythms were related to non-memory executive tasks, whereas sleep characteristics, particularly sleep-onset latency, were related to memory and verbal fluency.

The association between disturbed rhythms and cognitive performance can be explained in multiple ways. First, the association could be a direct effect of disturbed rhythms on perceptual speed and executive functioning. Fragmentation, in our study, indicates fragmentation during the day as well as fragmentation during the night. It has been suggested that a high fragmentation indicates not only problems staying asleep during the night but also problems in staying awake during the day [31]. We cannot assess the temporality of the effect in our cross-sectional study, so we can only carefully infer that persons with high fragmentation may be less vigilant during the day, which directly worsens the performance on perceptual speed and executive functioning tasks. Second, a shared underlying factor could explain the association between disturbed rhythms and worse cognitive functioning in the non-memory tasks. For example, an unhealthy lifestyle has been related to disturbed activity rhythms [11] and to worse cognitive performance [32]. Third, the direction of the effect can also be reversed; worse cognitive functioning might also lead to more disturbed rhythms. For example, dementia is accompanied by highly disturbed patterns of sleep. It has even been suggested that this is a major reason for hospitalization of patients with dementia [12]. Severe cognitive deficits can disturb activity rhythms in this situation. However, in our sample, exclusion of participants who screened positive for dementia did not change the results largely.

The association of lengthened sleep-onset latency with poorer performance on the delayed recall of 15 words and generating animal names was not explained by disturbances in the activity rhythm. This is in line with the suggestion that memory performance is largely independent of the circadian rhythm disturbances [33]. It has been suggested that the association of sleep-onset latency with memory can be explained by attention deficits; the inability to direct and control attention is detrimental not only for memory performance but also for falling asleep as this requires outside stimuli and thoughts to be disregarded [34]. However, in our sample, sleep-onset latency was not related to any other tasks that draw more on attention.

We found that age modified the association of sleep-onset latency with non-memory tasks, as well as the association of fragmentation with performance on the Stroop interference trial. This demonstrates that age is an important factor in the relation of the 24-h activity rhythm and sleep with cognition. Although our study is cross-sectional, it suggests that older people are more vulnerable to disturbed sleep and activity rhythms with respect to their cognitive performance, specifically in non-memory tasks. Most likely, this is due to the aging of the brain, which diminishes the ability to compensate the effects of circadian and sleep disturbances on cognition.

The current study has several strengths. First, the embedding in an existing population-based study makes our findings more generalizable. Second, we assessed cognition with multiple, established cognitive tests. Third, activity rhythms and sleep have been assessed objectively over multiple nights. Fourth, we used nonparametric measures of the 24-h activity rhythm. The main advantage of a nonparametric indicator, over a parametric indicator, is that no assumptions are made about the nature of the rhythm; such an assumption is particularly problematic in elderly populations with less pronounced circadian rhythms [13]. However, there are some limitations that should be considered. First, we cannot draw any conclusions on the temporality of the observed associations as our study is cross-sectional. In addition, the design of our study was particularly suited to assess the 24-h activity rhythm, as an indicator of the circadian rhythm. Actigraphy allows us to estimate sleep parameters, but it lacks the precision of polysomnography, which is considered the gold standard in sleep research [15]. Also, we did not formally assess chronotype. Therefore, we cannot comment on the association of chronotype with cognitive function or the possible confounding effects of chronotype on the associations between 24-h rhythms and cognition. Next, we had self-rated but no objective information about sleep-disordered breathing, which may be a mediator between sleep and activity rhythm disturbances and cognition. Although a study in community-dwelling older men was not able to find an association between the apnea/hypopnea index and cognition [35], it is not clear to what extent sleep-disordered breathing affected our results. In addition, persons with better cognitive functioning might be overrepresented in our study because they are less likely to refuse cognitive testing. Last, cognitive tests usually measure a multitude of cognitive constructs. The differential associations of 24-h rhythms and sleep with the different cognitive

domains found in this study might partially reflect the somewhat nonspecific nature of the cognitive tests commonly used in neuropsychological research. For example, the categorical fluency test, also known as the semantic fluency test, has been described as a test for verbal abilities, semantic memory, working memory, and executive functioning. Recent research suggests that working memory and semantic word retrieval are particularly related to the categorical fluency test, where the phonetic fluency test is more related to processing speed and verbal intelligence [36].

In conclusion, activity rhythm and sleep disturbances are independently related to cognition. Fragmentation of the activity rhythm is related to tasks that depend more strongly on executive functioning and perceptual speed, while sleep-onset latency is associated with worse performance memory and verbal fluency tasks. Lastly, our research suggests that non-impaired circadian rhythms and good sleep are important for good cognitive functioning, particularly in the elderly who might be more vulnerable to the effects of circadian rhythm and sleep on cognition. Some cognitive problems can be possibly ameliorated by treating circadian disturbances, for example, with lifestyle change or medication.

Conflict 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.2015.03.012.

Acknowledgments

This research was supported by a Netherlands Organisation for Scientific Research grant (NWO-VIDI: 017.106.370) awarded to H. Tiemeier. The Rotterdam Study is funded by the Erasmus Medical Center and Erasmus University Rotterdam; the Netherlands Organisation for Health Research and Development (ZonMw); the Research Institute for Diseases in the Elderly (RIDE); the Ministry of Education, Culture and Science, Netherlands; the Dutch Ministry of Health, Welfare and Sport; the European Commission (DG XII); and the Municipality of Rotterdam. The authors are grateful to the study participants, the staff from the Rotterdam Study, and the participating general practitioners and pharmacists.

Appendix: Supplementary material

Supplementary data to this article can be found online at doi:10.1016/j.sleep.2015.03.012.

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