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ORIGINAL ARTICLE

Actigraphic Sleep Duration and Fragmentation in Older Women: Associations With Performance Across Cognitive Domains

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Study Objectives: To determine the association of actigraphic sleep duration and fragmentation with cognition in community-dwelling older women.
Methods: We studied 782 women (mean age = 87.4) of varied cognitive status from the Study of Osteoporotic Fractures who completed wrist actigraphy and the Modified Mini-Mental State Examination (3MS), California Verbal Learning Test-II-Short Form, digit span, verbal fluency tests, and the Trailmaking Test, Part B (Trails B). Total sleep time (TST) and wake after sleep onset (WASO) tertiles were our primary predictors.
Results: There were few significant associations in adjusted analyses. Compared to women with intermediate TST (mean = 430.1 minutes), those with the longest (508.7 minutes) had significantly poorer performance on the 3MS and phonemic and semantic fluency. Compared to women with the least WASO (31.5 minutes), those in the middle tertile (61.5 minutes) had significantly poorer delayed recall and those in the middle tertile and highest tertile (126.2 minutes) had poorer total recall and semantic fluency. We observed significant adjusted associations of TST with impaired 3MS performance and of WASO with impaired delayed recall, semantic fluency, and digit span. After excluding participants with adjudicated dementia diagnoses or indeterminate cognitive status, some adjusted associations remained but decreased in magnitude, others became nonsignificant, and a new association emerged.
Conclusions: In community-dwelling older women, longer objectively measured sleep duration and greater sleep fragmentation are associated with poorer performance and impairment in only a subset of cognitive domains. Some of these associations may be driven by women with dementia in whom disturbed sleep and cognitive performance share an underlying neuropathological basis.
Keywords: older adults, actigraphy, cognition, neuropsychological, impairment.

Statement of Significance
Sleep disturbance is gaining increasing attention as a potential risk factor for later-life cognitive impairment. However, most studies have relied on self-report measures of sleep, rather than objective measures (eg, wrist actigraphy). Given cognitive impairment may affect the validity of self-reported sleep, studies with objective sleep measures are valuable, especially in populations at elevated risk for cognitive impairment, such as older adults. Most studies with objective sleep measures have investigated only one or two cognitive domains, or a global measure of cognition, limiting our understanding of how sleep is related to a broader range of cognitive abilities in older people. We investigated the association of actigraphically measured sleep duration and fragmentation with performance across multiple cognitive domains in community-dwelling older women.

INTRODUCTION

Cognitive impairment is common in the rapidly growing US population of older adults, with about one-third of adults aged 71 and older meeting criteria for mild cognitive impairment (MCI) or dementia.[1,2] Sleep disturbances also are prevalent among older people; more than half of those aged 65 and older have a chronic sleep-related complaint.[3] Numerous studies have examined the association between poor sleep and cognitive function among older adults. For example, comparisons of neuropsychological test performance in older adults with and without insomnia have shown insomnia-related decrements in attention and executive function,[4,5] and community-based cohort studies have linked insomnia symptoms to a greater risk of cognitive decline.[6,7] [For a detailed review see a 2015 article by Scullin and Bliwise.[8]] These, and most other studies of sleep and cognition, however, have used self-report measures (eg, questionnaires, insomnia complaints) to assess sleep, rather than objective methods. Because self-reported estimates of sleep often are weakly correlated with objective measures[9] and can be affected by factors including cognitive deficits,[10] objective sleep measures have special utility in studies attempting to quantify the association between sleep parameters and cognitive impairment.

Wrist actigraphy is an unobtrusive, objective method of sleep/wake assessment. In a study of actigraphic sleep and cognition in over 3000 older men in the Osteoporotic Fractures in Men Study (MrOS), long sleep duration, and indices of sleep fragmentation were associated with lower performance on a measure of global cognition; greater sleep fragmentation also was associated with lower executive function.[11] Among older women in the Study of Osteoporotic Fractures (SOF) (the current cohort) who completed wrist actigraphy, greater sleep fragmentation was associated with lower global cognitive performance and lower executive function, and shorter sleep duration was weakly associated with lower global cognitive performance.[12] Although these studies have advanced our knowledge, they have included only two or three tests representing a limited range of cognitive domains. We are aware of only one study that investigated associations between actigraphic data and performance on a broader range of cognitive tests.[13] Although that study found that greater rest/activity fragmentation was associated with lower performance in a range of cognitive domains, it did not include

an assessment of sleep duration.[13] It is important to consider sleep duration in addition to sleep fragmentation because fragmentation does not address the total amount of sleep obtained, and sleep duration does not account for sleep consolidation. Here, we determined the extent to which objectively measured sleep duration and sleep fragmentation—two fundamental dimensions of sleep—each are associated with performance and impairment on multiple neuropsychological tests in older women from the SOF cohort who completed actigraphy and an expanded neuropsychological test battery at a later time of data collection than previously reported by Blackwell et al.[12] We hypothesized that, compared to women with intermediate total sleep time (TST) and the least wake after sleep onset (WASO), those with shorter or longer TST and greater WASO would have poorer performance, and a greater odds of impairment, on neuropsychological tests.

METHODS

Participants

Participants were women enrolled in a prospective cohort study of aging, the SOF. Between September 1986 and October 1988, SOF enrolled 9704 women aged ≥65 years from the Monongahela Valley (Pittsburgh region), Pennysylvania; Portland, Oregon; Baltimore, Maryland; and Minneapolis, Minnesota. Inclusion criteria required participants to be community-dwelling women, free of bilateral hip replacement, and able to ambulate without another person's help. Since then, participants have repeated study visits on a 2- to 4-year basis. In 1997 and 1998, a total of 662 African-American women were recruited to increase the diversity of the sample. After attrition by death or loss to follow-up, a total of 2368 women participated in the Year-20 SOF Visit (2006–2008). Of these, 1534 women from three SOF sites completed an expanded battery of neuropsychological tests; 837 of those participants from two of the SOF sites (Monongahela Valley and Minneapolis) also completed wrist actigraphy at the Year-20 Visit as part of an ancillary study on sleep and cognition. Specifically, cognitive tests were administered at the SOF clinical centers, and the actigraph was applied at that same visit, with the recording starting at 09:00 am the following day. Of these women, 830 had usable actigraphy data for TST or WASO. We studied 782 of these participants with these actigraphy data who were community-dwelling (ie, had a residence in a private home or apartment, or retirement home/senior complex, and not in a nursing home, personal care home, adult foster home, or assisted living facility) and completed at least one test from the expanded neuropsychological test battery.

Actigraphy

At the Year-20 SOF Visit, participants from the Monongahela Valley and Minneapolis study sites were asked to wear a wrist actigraph (SleepWatch-O, Ambulatory Monitoring, Inc., Ardsley, New York) for a minimum of three 24-hour periods on the nondominant wrist. Sleep parameters were derived in the proportional integration mode (PIM) using Action W-2 software (Ambulatory Monitoring, Inc.). Nocturnal sleep duration was quantified by TST (number of minutes slept while in bed) and nocturnal sleep fragmentation was quantified as WASO (number of minutes awake following the first 20-minute bout of sleep). Each of these parameters was averaged across the number of nights of actigraphy data collected. To assist with actigraphy data processing, participants used sleep logs to record time into and out of bed, naps, and other sleep variables. Although several indices of sleep fragmentation are available from actigraphy, we selected WASO because it is a commonly used actigraphic measure of sleep fragmentation derived from a PSG-validated algorithm[14] that is not directly influenced by participant recall (ie, in sleep logs) and reflects the amount of time spent awake after sleep onset, rather than simply the number of awakenings.

The utility of actigraphy for sleep assessment has been demonstrated repeatedly, including in older adults,[15] and there is evidence for its validity in the SOF cohort. Among 68 older women in the SOF cohort who simultaneously completed polysomnography (PSG) and actigraphy, actigraphy data corresponded most closely to PSG data when derived in PIM.[16] When analyzed in PIM, there was no statistically significant difference between WASO measured by actigraphy and PSG-derived WASO; however, actigraphy data overestimated TST by 17.9 minutes on average.[16]

Cognitive Tests and Adjudication of Cognitive Status

Women enrolled in the ancillary cognitive study completed an expanded battery of neuropsychological tests, including the Modified Mini-Mental State Examination (3MS),[17] a test of general cognitive function; the California Verbal Learning Test-II-Short Form (CVLT-SF),[18] which measures memory for nine words in various metrics, including total recalled after four learning trials (total possible score = 36) and after various delays, digit span forwards, which measures attention[19] and digit span backwards, a measure of working memory.[19] They also completed two tests of verbal fluency: a phonemic fluency task in which they named as many words beginning with the letter "f" within 1 minute as they could and a semantic (category) fluency task in which they named as many vegetables in 1 minute as they could. These tests are also considered measures of executive function. Finally, they completed a modified version of the Trailmaking Test, Part B (Trails B),[20] a timed test of executive function, in which they drew a line between circles containing numbers and letters, in alternating alphanumeric order. Participants were allotted 180 seconds to complete Trails B. For participants who did not complete the test in this interval, extrapolated completion times were derived based on the amount of the test completed in 180 seconds; extrapolated times were truncated at 420 seconds.

The SOF cognitive adjudication procedure has been described in detail elsewhere.[21] Briefly, it involved a two-stage process in which participants' data were first screened for potential indicators of cognitive impairment (eg, participant report of dementia diagnosis or nursing home residence, performance below particular cutoffs on neuropsychological tests, or informant ratings on the Informant Questionnaire on Cognitive Decline in the Elderly[22]). Those who screened negative were considered cognitively normal and those screening positive had cognitive, functional, medical history, medication, and other data from Visit 9 and prior SOF visits referred to clinical adjudicators

(ie, a neurologist, psychologists) who diagnosed participants as having MCI according to modified Petersen criteria,[23] dementia, according to Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision criteria,[24] or determined that their cognitive status was normal or indeterminate/ambiguous.

Additional Measures

Upon enrollment in SOF, participants provided demographic data. At each study visit, they were weighed and measured, permitting calculation of body mass index (BMI; kg/m^2). They also completed several questionnaires, including the 15-item Geriatric Depression Scale (GDS)[25] and the Goldberg Anxiety Scale (GAS),[26] and they indicated whether they had been told that they have any of multiple medical conditions. They also were asked to bring to study visits all medications taken over the prior 30 days. These were entered in a computerized coding system, by brand or generic names.[27]

Statistical Analysis

After examining the distributions of variables and patterns of missingness in the data, we compared participant characteristics across tertiles of TST and WASO using chi-square or Fisher's exact tests for categorical variables and Kruskal–Wallis tests for continuous variables. Next, we determined the association between TST and WASO using Spearman's correlations. To examine the association between TST or WASO and cognitive outcomes, we fit a series of linear and logistic regression models with TST or WASO tertiles as the primary predictor and either performance (linear models) or impaired performance (logistic models) on a given cognitive test as the outcome. Our outcomes were 3MS score, CVLT delayed recall and total number of words recalled across learning trials, digit span forward and backward, phonemic fluency, category fluency, and Trails B score. We defined impairment as a score > 1.5 standard deviations (SDs) below our sample mean on a test, in an effort to approximate the cutoffs used in diagnosis of MCI.[28] For each cognitive outcome, we fit unadjusted and multivariable (MV)-adjusted models. Potential confounders were included in MV models based on either known associations with cognitive outcomes or on their association with either TST or WASO tertiles and at least one cognitive test at the $p < .10$ level. Specifically, we adjusted for age, race, education, BMI, alcohol use, walking for exercise, heart failure, stroke, 15-item GDS score, GAS score, and use of antidepressant medications. We also explored interactions of TST with WASO by entering an interaction term (TST tertiles X continuously measured WASO) in MV models.

Finally, we performed two sets of sensitivity analyses. First, to examine the extent to which results were driven by participants with significant cognitive impairment, in whom disturbed sleep is more likely to be a consequence of neurodegeneration than a cause of cognitive impairment, we excluded those with an adjudicated dementia diagnosis ($n = 99$) or indeterminate cognitive status ($n = 4$) and reran analyses using the same tertile cutoffs with a continuous variable as the outcome in the combined sample of 679 participants with normal cognition ($n = 481$) or MCI ($n = 198$) who remained. In addition, we repeated regression analyses in the full sample after dropping a participant with a TST of only 39 minutes and 23 others with fewer than three nights of actigraphy and reran analyses for continuous and dichotomous outcomes, retaining the cutoffs for tertiles and cognitive impairment. Although some results that were significant in the full sample became stronger after excluding participants with fewer than three nights of data and some nonsignificant or trend-level results became significant, others decreased in magnitude and/or fell below statistical significance. However, significant results from the original analyses remained in the same direction regardless of whether participants with adjudicated dementia or indeterminate cognitive status were included. Because several changes in significance appeared to be due to reductions in statistical power, we retained the data from participants who completed fewer than three nights of actigraphy data in our main analyses. An $\alpha < 0.05$ was used to indicate statistical significance. All analyses were performed in Stata version 12.1 (StataCorp, College Station, Texas).

RESULTS

Compared to women who participated in the Year-20 Visit but were excluded from our sample, those in our sample had a younger mean ± SD age (88.5 ± 3.9 vs. 87.4 ± 3.1) and higher 3MS scores (85.4 ± 12.3 vs. 84.4 ± 8.9), consumed more caffeine (0.17 ± 0.16 vs. 0.15 ± 0.15 g/day), and were more likely to drink alcohol (38.7% vs. 27.7%) and to walk for exercise (40.2% vs. 34.9%) (all $p < .05$). They had fewer depressive symptoms (2.4 ± 2.4 vs. 2.7 ± 2.5) and were less likely to use antidepressant medications (12.3% vs. 23.3%) or to have heart failure (11.3% vs. 14.6%) (all $p < .05$). They did not differ by race, education, BMI, smoking status, anxiety symptoms, benzodiazepine or nonbenzodiazepine sleep medication use, hypertension, diabetes, coronary artery disease (CAD), or chronic obstructive pulmonary disease (COPD).

The women in our analytic sample ranged in age from 78 to 98 years. Overall, 694 (88.8%) were white and 285 (36.5%) had an education beyond high school. They completed 4.2 ± 0.8 nights of wrist actigraphy (range 1–9) (Supplementary Table 1). Mean TST was 426.9 ± 80.4 minutes and mean WASO was 73.0 ± 47.3 minutes; when examined as continuous variables, TST and WASO were modestly and inversely correlated (Spearman's rho = −0.30, $p < .001$). Across TST tertiles, participants differed significantly by BMI, alcohol use, depressive symptoms, heart failure, and adjudicated dementia diagnosis (Table 1). Across WASO tertiles (Table 1 footnote), participants differed significantly by race, BMI, walking for exercise, anxiety symptoms, antidepressant use, heart failure, COPD, and adjudicated dementia diagnosis. Mean sleep onset latency (interval between time into bed and initial sleep onset) was 31.3 ± 30.6 minutes and mean sleep efficiency (proportion of time in bed spent asleep) was 80.5% ± 11.2. Descriptive statistics for cognitive test scores and cutoffs for impaired performance are displayed in Table 2.

TST and Cognitive Performance

In unadjusted analyses, women with the longest TST (mean = 508.7 ± 46.6 minutes, 459.8 to 702.8) had 3MS scores 2.89 points on average below those of participants with intermediate

Table 1—Participant Characteristics by TST Tertiles, Mean ± SD or *n* (%).

Characteristics	Total Sleep Time (minutes)			TST *p*-value
	Tertile 1 (*n* = 262) 342.6 ± 55.4 minutes, 39.0 to 399.2	Tertile 2 (*n* = 260) 430.1 ± 17.0 minutes, 399.4 to 459.5	Tertile 3 (*n* = 260) 508.7 ± 46.6 minutes, 459.8 to 702.8	
Age	87.4 ± 3.1	87.4 ± 3.0	87.5 ± 3.1	.750
Racial/ethnic minority	31 (11.8)	27 (10.4)	30 (11.5)	.858
Education > high school	97 (37.0)	102 (39.2)	86 (33.1)	.336
BMI	26.9 ± 4.5	26.1 ± 4.6	26.2 ± 5.1	.046
Current smoker	5 (1.9)	5 (1.9)	4 (1.5)	1.000
Alcohol use (≥1 drink/past 30 days)	85 (32.4)	105 (40.4)	112 (43.2)	.032
Caffeine intake (g/day)	0.2 ± 0.2	0.2 ± 0.2	0.2 ± 0.1	.451
Walks for exercise	114 (44.4)	100 (38.9)	95 (37.4)	.240
Geriatric Depression Scale	2.1 ± 2.1	2.5 ± 2.6	2.6 ± 2.5	.049
Goldberg Anxiety Scale	2.1 ± 2.5	2.1 ± 2.4	2.1 ± 2.5	.947
Antidepressant use	26 (10.0)	30 (11.5)	40 (15.4)	.151
Benzodiazepine use	14 (5.4)	19 (7.3)	25 (9.7)	.179
Nonbenzodiazepin sleep meds	6 (2.3)	7 (2.7)	6 (2.3)	.949
Diabetes	46 (17.6)	36 (13.9)	37 (14.2)	.430
Hypertension	169 (64.5)	174 (66.9)	175 (67.3)	.763
Coronary artery disease	52 (19.9)	43 (16.5)	61 (23.5)	.142
Heart failure	43 (16.4)	12 (4.6)	33 (12.7)	<.001
COPD	34 (13.0)	27 (10.4)	30 (11.5)	.652
Osteoarthritis	114 (43.5)	109 (41.9)	108 (41.5)	.890
Stroke	20 (7.6)	30 (11.5)	36 (13.9)	.072
Dementia (adjudicated diagnosis)	23 (8.9)	32 (12.4)	44 (17.0)	.020

N ranges from 768 to 782. *p*-values are from Kruskal–Wallis tests (with rank ties) for skewed variables and from χ^2 or Fisher's exact (only smoking) tests for categorical variables.
BMI = body mass index; COPD = chronic obstructive pulmonary disease; SD = standard deviation; TST = total sleep time; WASO = wake after sleep onset. WASO Tertile 1: *n* = 261; mean = 31.5 ± 10.4 minutes, 4.3 to 46.8; Tertile 2: *n* = 260; mean = 61.5 ± 9.6 minutes, 47.0 to 80.5; Tertile 3: *n* = 260, mean = 126.2 ± 42.9 minutes, 80.8 to 319.0.

Table 2—Cognitive Test Performance.

Cognitive test	*N*	Mean ± SD	Impairment	*N* (%) impaired*
3MS	782	88.4 ± 8.9	score < 75.1	66 (8.4)
CVLT 10-minute delayed recall	770	5.2 ± 2.6	< 1.29 words	96 (12.5)
CVLT total recalled	768	23.6 ± 5.2	< 15.8 words	64 (8.3)
Digit span forward	773	7.5 ± 2.1	< 4.4 digits	50 (6.5)
Digit span backward	772	5.6 ± 2.1	< 2.5 digits	49 (6.4)
Phonemic fluency	773	10.7 ± 4.3	< 4.3 words	45 (5.8)
Category fluency	773	10.7 ± 3.4	< 5.6 words	48 (6.2)
Trails B (extrapolated)	668	169.9 ± 87.2	> 300.8 seconds	58 (8.7)

*Impairment refers to performance > 1.5 SD below sample mean.
3MS = Modified Mini-Mental State Examination; CVLT = California Verbal Learning Test.

TST (mean = 430.1 ± 17.0 minutes, 399.4 to 459.5; unstandardized regression coefficient (B) = −2.89, 95% confidence interval (CI) −4.40, −1.38) (Table 3). This association decreased but remained significant after MV adjustment (B = −2.11, 95% CI −3.46, −0.75). Similarly, in both unadjusted and MV-adjusted analyses, women in the longest TST tertile had poorer performance compared to those in the middle tertile in both phonemic fluency (adjusted B = −1.05, 95% CI −1.77, −0.33) and semantic fluency (adjusted B = −0.69, 95% CI −1.27, −0.10). Moreover, in unadjusted analyses, women in the longest TST tertile recalled an average of 0.45 fewer words on a delayed recall task (B = −0.45, 95% CI −0.90, −0.002) and an average of 0.92 fewer words in total across list-learning trials (B = −0.92, 95% CI −1.81, −0.02); however, these associations fell to the trend level after MV adjustment (both $p \leq .10$). There were no associations between TST and performance on digit span forward or backward or on Trails B.

TST and Cognitive Impairment

Compared to women in the middle TST tertile, those with the longest TST had approximately 2.5 times the odds of impaired performance (> 1.5 SD below the mean) on the 3MS (unadjusted odds ratio (OR) = 2.45, 95% CI 1.32, 4.54; MV-adjusted OR = 2.47, 95% CI 1.23, 4.93) (Supplementary Table 2). In addition, women with the shortest TST had approximately half the odds of impairment on digits forward in unadjusted analyses, compared to those in the middle tertile (OR = 0.45, 95% CI 0.21, 0.94), but this was at the trend level after adjustment ($p \leq .10$). There were no other associations between TST and impaired test performance.

WASO and Cognitive Performance

In unadjusted analyses, the 3MS scores of women in the intermediate WASO tertile (mean = 61.5 ± 9.6 minutes, 47.0 to 80.5) were on average 1.6 points lower than those with the least WASO (mean = 31.5 ± 10.4 min, 4.3 to 46.8; B = −1.60, 95% CI −3.12, −0.08), but this was nonsignificant after adjustment (Table 4). Similarly, women with the most WASO (mean = 126.2 ± 42.9 minutes, 80.8 to 319.0) had 3MS scores 2.1 points lower than those with the least in unadjusted analyses (B = −2.09, 95% CI −3.61, −0.57), but this decreased to a trend after adjustment. Compared to women with the least WASO, those in the middle tertile had lower scores on CVLT delayed recall in unadjusted (B = −0.71, 95% CI −1.16, −0.26) and adjusted analyses (B = −0.54, 95% CI −0.98, −0.09). Women with the most WASO had lower delayed recall scores than those with the least but only in unadjusted analyses (B = −0.45, 95% CI −0.90, −0.01). Women in the middle and highest WASO tertiles recalled fewer words in total across all CVLT trials compared to those with the least WASO in unadjusted and adjusted analyses (adjusted middle tertile B = −1.19, 95% CI −2.06, −0.33, adjusted highest tertile B = −1.15, 95% CI −2.04, −0.27). On phonemic fluency, women with the most WASO generated 0.94 fewer words than those with the least in unadjusted analyses (B = −0.94, 95% CI −1.67, −0.20), but this association fell to the trend level after adjustment. Unadjusted and adjusted comparisons of phonemic fluency between women in the middle and lowest WASO tertiles also yielded trend-level

Table 3—Associations [B (95% CI)] Between Total Sleep Time and Test Performance.

Cognitive test	Unadjusted	MV-adjusted*
3MS	*n* = 782	*n* = 749
Tertile 1	0.17 (−1.33, 1.68)	−0.53 (−1.90, 0.83)
Tertile 2	(ref)	(ref)
Tertile 3	**−2.89 (−4.40, −1.38)**	**−2.11 (−3.46, −0.75)**
CVLT delayed recall	*n* = 770	*n* = 743
Tertile 1	0.21 (−0.23, 0.66)	0.09 (−0.36, 0.54)
Tertile 2	(ref)	(ref)
Tertile 3	**−0.45 (−0.90, −0.002)**	−0.41 (−0.85, 0.03)†
CVLT total recalled	*n* = 768	*n* = 741
Tertile 1	0.09 (−0.80, 0.99)	−0.25 (−1.12, 0.63)
Tertile 2	(ref)	(ref)
Tertile 3	**−0.92 (−1.81, −0.02)**	−0.78 (−1.65, 0.09)†
Phonemic fluency	*n* = 773	*n* = 746
Tertile 1	−0.08 (−0.81, 0.65)	−0.20 (−0.93, 0.53)
Tertile 2	(ref)	(ref)
Tertile 3	**−1.07 (−1.81, −0.33)**	**−1.05 (−1.77, −0.33)**
Semantic fluency	*n* = 773	*n* = 745
Tertile 1	0.02 (−0.56, 0.61)	−0.19 (−0.78, 0.39)
Tertile 2	(ref)	(ref)
Tertile 3	**−0.70 (−1.29, −0.12)**	**−0.69 (−1.27, −0.10)**
Digits forward	*n* = 773	*n* = 746
Tertile 1	0.16 (−0.20, 0.52)	0.08 (−0.29, 0.45)
Tertile 2	(ref)	(ref)
Tertile 3	−0.17 (−0.53, 0.20)	−0.17 (−0.54, 0.20)
Digits backward	*n* = 772	*n* = 746
Tertile 1	0.15 (−0.21, 0.51)	0.12 (−0.24, 0.48)
Tertile 2	(ref)	(ref)
Tertile 3	−0.10 (−0.46, 0.26)	−0.11 (−0.47, 0.25)
Trails B	*n* = 668	*n* = 652
Tertile 1	−7.27 (−23.36, 8.81)	−5.80 (−21.30, 9.70)
Tertile 2	(ref)	(ref)
Tertile 3	10.50 (−5.86, 26.85)	7.26 (−8.26, 22.79)

Bold values indicate $p < .05$.
*Adjusted for age, race, education, body mass index, alcohol use, walking for exercise, heart failure, stroke, 15-item Geriatric Depression Scale score, Goldberg Anxiety Scale score, and use of antidepressant medications.
†$p \leq .10$.
Tertile 1: *n* = 262; mean = 342.6 ± 55.4 minutes, 39.0 to 399.2; Tertile 2: *n* = 260; mean = 430.1 ± 17.0 minutes, 399.4 to 459.5; Tertile 3: *n* = 260, mean = 508.7 ± 46.6 minutes, 459.8 to 702.8.
3MS = Modified Mini-Mental State Examination; CI = confidence interval; CVLT = California Verbal Learning Test; MV = multivariable; Trails B = Trailmaking Test, Part B.

Table 4—Associations [B (95% CI)] Between Wake After Sleep Onset and Test Performance.

Cognitive test	Unadjusted	MV-adjusted*
3MS	*n* = 781	*n* = 748
Tertile 1	(ref)	(ref)
Tertile 2	**−1.60 (−3.12, −0.08)**	−0.57 (−1.93, 0.79)
Tertile 3	**−2.09 (−3.61, −0.57)**	−1.24 (−2.63, 0.15)†
CVLT delayed recall	*n* = 769	*n* = 742
Tertile 1	(ref)	(ref)
Tertile 2	**−0.71 (−1.16, −0.26)**	**−0.54 (−0.98, −0.09)**
Tertile 3	**−0.45 (−0.90, −0.01)**	−0.38 (−0.83, 0.07)
CVLT total recalled	*n* = 767	*n* = 740
Tertile 1	(ref)	(ref)
Tertile 2	**−1.39 (−2.28, −0.50)**	**−1.19 (−2.06, −0.33)**
Tertile 3	**−1.46 (−2.35, −0.57)**	**−1.15 (−2.04, −0.27)**
Phonemic fluency	*n* = 772	*n* = 745
Tertile 1	(ref)	(ref)
Tertile 2	−0.64 (−1.38, 0.09)†	−0.67 (−1.39, 0.06)†
Tertile 3	**−0.94 (−1.67, −0.20)**	−0.71 (−1.44, 0.03)†
Semantic fluency	*n* = 772	*n* = 744
Tertile 1	(ref)	(ref)
Tertile 2	**−0.74 (−1.32, −0.16)**	**−0.68 (−1.26, −0.09)**
Tertile 3	**−1.01 (−1.59, −0.43)**	**−0.87 (−1.46, −0.28)**
Digits forward	*n* = 772	*n* = 745
Tertile 1	(ref)	(ref)
Tertile 2	0.12 (−0.25, 0.48)	0.09 (−0.28, 0.45)
Tertile 3	−0.03 (−0.40, 0.33)	−0.12 (−0.50, 0.25)
Digits backward	*n* = 771	*n* = 745
Tertile 1	(ref)	(ref)
Tertile 2	−0.17 (−0.53, 0.20)	−0.13 (−0.49, 0.23)
Tertile 3	−0.21 (−0.57, 0.15)	−0.03 (−0.40, 0.34)
Trails B	*n* = 667	*n* = 651
Tertile 1	(ref)	(ref)
Tertile 2	12.33 (−3.71, 28.37)	12.41 (−2.89, 27.72)
Tertile 3	**16.45 (0.38, 32.53)**	6.15 (−9.60, 21.90)

Bold values indicate $p < .05$.
*Adjusted for age, race, education, body mass index, alcohol use, walking for exercise, heart failure, stroke, 15-item Geriatric Depression Scale score, Goldberg Anxiety Scale score, and use of antidepressant medications.
†$p \leq 0.10$.
Tertile 1: *n* = 261; mean = 31.5 ± 10.4 minutes, 4.3 to 46.8; Tertile 2: *n* = 260; mean = 61.5 ± 9.6 minutes, 47.0 to 80.5; Tertile 3: *n* = 260, mean = 126.2 ± 42.9 minutes, 80.8 to 319.0.
3MS = Modified Mini-Mental State Examination; CI = confidence interval; CVLT = California Verbal Learning Test; MV = multivariable; Trails B = Trailmaking Test, Part B.

results. On semantic fluency, however, women in the middle and highest WASO tertiles named fewer vegetables than those with the least WASO in unadjusted and MV-adjusted analyses (adjusted middle B = −0.68, 95% CI −1.26, −0.09; adjusted highest tertile B = −0.87, 95% CI −1.46, −0.28). Women with the most WASO also took longer to complete Trails B in unadjusted analyses (B = 16.45, 95% CI 0.38, 32.53), but this association did not remain after adjustment. There were no associations between WASO and performance on digit span forward or backward.

WASO and Cognitive Impairment

In unadjusted models, compared to women with the least WASO, those in the middle and third tertile had at least twice the odds of impairment on the 3MS (middle tertile OR = 2.03, 95% CI 1.01, 4.06, third tertile OR = 2.30, 95% 1.16, 4.55), but these associations decreased and became nonsignificant or statistical trends after adjustment (Supplementary Table 3). In addition, women in the middle WASO tertile had a greater odds of impaired delayed recall on the CVLT in unadjusted (OR = 2.10, 95% CI 1.23, 3.61) and adjusted analyses (OR = 1.82, 95% CI 1.03, 3.22). In unadjusted models, women in the middle and third tertiles had approximately four times the odds of impaired semantic fluency (middle tertile OR = 4.00, 95% CI 1.59, 10.03 and third tertile OR = 3.53, 95% CI 1.39, 8.94) compared to those with the least WASO, and these associations decreased but remained significant after adjustment. In addition, women in the second and third WASO tertiles had 2.7–2.9 times the odds of impaired performance on digit span forward (middle tertile OR = 2.68, 95% CI 1.16, 6.21 and third tertile OR = 2.91, 95% CI 1.27, 6.67) in unadjusted analyses; these associations decreased but retained significance in adjusted analyses. Finally, in unadjusted analyses, women in the middle and third WASO tertiles had more than twice the odds of impaired performance on digit span backward (middle tertile OR = 2.26, 95% CI 1.0005, 5.08 and third tertile OR = 2.45, 95% CI 1.10, 5.46), but this decreased to the trend level (middle tertile only) in adjusted analyses. There was no consistent evidence of interaction between WASO and TST across cognitive tests (data not shown).

Sensitivity Analyses

After removing the 103 participants with adjudicated dementia diagnoses or indeterminate cognitive status, in adjusted analyses, women with the longest TST still had poorer performance than those in the middle TST tertile on tests of phonemic fluency (B = −1.02, 95% CI −1.81, −0.23) but this decreased to the trend level for semantic fluency (B = −0.58, 95% CI −1.17, 0.01) (Supplementary Table 4). Associations with performance on the 3MS and CVLT delayed and total recall that were significant or near significant in the full sample were no longer so in this restricted sample. For WASO, significant adjusted associations remained with lower performance on CVLT delayed (middle tertile B = −0.46, 95% −0.87, −0.05) and total recall (middle tertile B = −1.00, 95% CI −1.82, −0.17), although the magnitude of these associations decreased. A new significant adjusted association emerged with Trails B performance (middle tertile B = 15.92, 95% CI 0.89, 30.94) (Supplementary

Table 5) but associations decreased and became nonsignificant or statistical trends for the 3MS and semantic fluency.

DISCUSSION

In this study of older community-dwelling women, longer TST and greater WASO, measured by wrist actigraphy, were only associated with poorer performance or impairment in a subset of cognitive domains. Compared to those with intermediate TST, women with the longest TST exhibited lower performance in global cognition and phonemic and semantic verbal fluency and impaired performance in global cognition after adjusting for numerous potential confounders. The only association we observed between shorter sleep and our outcomes was for digits forward, on which women with the shortest TST had a reduced odds of impairment compared to those in the middle tertile in unadjusted analyses. Regarding WASO, compared to the women with the least, those with more had lower scores on tests of delayed recall and total number of words recalled and semantic fluency and a greater odds of impairment on tests of delayed recall, semantic fluency, and attention in adjusted models. In general, these significant associations were modest in magnitude, and although there were some trend-level associations, it is important to note that we also observed many null associations. It is also noteworthy that some of the significant associations we observed decreased in magnitude and/or significance when participants with adjudicated diagnoses of dementia or indeterminate cognitive status were excluded from analyses, suggesting that, among community-dwelling older women, links between sleep duration or fragmentation and cognitive performance or impairment may be driven by individuals with significant cognitive impairment, in whom disturbed sleep and cognitive impairment are likely to arise from a shared neuropathological process.

Our findings are partially consistent with those from the few prior studies of actigraphic sleep and cognition. A study from an earlier wave of SOF found that longer sleep was weakly associated with better global cognitive function, and that greater WASO was associated with poorer performance and impairment in global cognition (Mini-Mental State Examination) and on Trails B.[12] We observed a different pattern in adjusted analyses in the same cohort: participants with the longest (vs. intermediate) TST had poorer global cognitive performance, and there was no significant association between WASO and global cognition. Although we found no significant adjusted associations with Trails B in our main analyses, longer (vs. intermediate) TST and greater WASO were associated with lower scores and greater WASO with impairment in verbal fluency, which taps verbal ability and—like Trails B—executive function.[29] Differences between findings in the two SOF waves may be due to the larger sample, younger mean age, and shorter mean TST and greater WASO in the earlier paper, and to differences in tests of global cognitive function.

Our findings concerning longer sleep and lower global cognitive performance are consistent with cross-sectional findings in older men in MrOS[11] but differ from those from a recent prospective study in that cohort, in which actigraphic TST was not associated with cognitive decline.[30] The inconsistencies in associations of longer sleep duration and cognition, even when objectively measured, highlights the challenges in analyzing longer sleep, which may reflect different types of sleep quality across different samples and may also be influenced by preclinical medical illnesses that our statistical models did not capture, or by sleep-disordered breathing (SDB) that results in greater sleep propensity.[31,32]

In contrast to our findings, Lim et al.[13] found associations between greater actigraphically measured rest/activity fragmentation and poorer global cognitive performance and no association between rest/activity fragmentation and episodic memory in community-dwelling older adults. However, the use of k_{RA} and k_{AR} fragmentation indices in the Lim et al. paper versus a more conventional actigraphic index (WASO) in the present study complicate their comparison. Additional studies that use more comprehensive measurements of sleep, including electroencephalogram (EEG), may help resolve discrepancies between studies in this domain.

Several mechanisms may explain associations between sleep fragmentation and poorer cognitive performance, including the development of Alzheimer's disease (AD) pathology. Studies in humans demonstrate that poorer sleep quality and lower actigraphically measured sleep efficiency and greater sleep fragmentation are associated with amyloid deposition.[33,34] These results using AD biomarkers are complemented by findings that greater actigraphic sleep fragmentation is associated with an increased risk of incident clinical AD.[35] Similarly, studies in AD mouse and *Drosophila* models demonstrate that sleep loss promotes amyloid deposition.[36,37] Alternatively, fragmentation-related sleep loss may negatively impact cognitive performance by promoting endothelial dysfunction[38] and inflammation[39] and subsequent cerebrovascular changes. However, the causal mechanisms that might explain associations between longer duration sleep and reduced cognitive performance are unclear. Indeed, as mentioned above, these associations may be driven by medical morbidity or SDB.[31,32]

Another possibility is that the associations we observed between disturbed sleep and cognition simply reflect brain changes attributable to AD or other neurological illnesses that affect both sleep and cognitive function. Roh et al.[40] demonstrated in AD mice that amyloid deposition coincided with deteriorations in sleep/wake patterns. Indeed, the attenuated results that we observed in analyses that excluded participants with dementia diagnoses support the notion that findings in the full sample are driven in part by deteriorations of sleep and cognition due to neurological disease.

A related question is which brain regions might link TST and WASO to poorer performance in particular cognitive domains. The associations we observed between longer sleep duration and verbal fluency measures, which reflect language and executive function, are consistent with a recent study that found that longer sleep duration at baseline was associated with more rapid subsequent cortical thinning in frontal and temporal regions on magnetic resonance imaging.[41] In addition, Lim et al.[42] found that greater actigraphic rest/activity fragmentation, measured by k_{RA}, was associated with reduced volume in frontal regions and reduced total cortical gray matter volume, and these volumetric changes could explain WASO-related decrements in memory and semantic fluency. Studies integrating actigraphy and both cognitive and neuroimaging measures would help map sleep-related changes in brain structure to sleep-related changes in cognitive performance.

This study has several strengths. Most prior studies of sleep and cognitive performance have used self-report sleep measures,[4–7] and those that have included actigraphy have, with one exception,[13] focused on two or three cognitive tests.[11,12,30] The present study advances knowledge by using actigraphy in a large sample of older women who completed a full neuropsychological battery, but it also has limitations. First, it was cross sectional rather than prospective, so we could not evaluate whether TST or WASO is associated with subsequent declines on particular tests. Second, only PSG can definitively discriminate sleep from wakefulness and evaluate the extent to which SDB might affect sleep duration and fragmentation. As described above, in a subset of women in SOF who concurrently completed PSG and actigraphy at SOF Year 16, actigraphy overestimated TST.[16] It is possible that the present study's results would change if another unobtrusive sleep-assessment method was available that more closely approximated PSG. Moreover, in a prior SOF paper, SDB (measured by PSG at Year 16) was associated with greater odds of MCI or dementia at SOF Year 20, from which data for the present study came.[43] PSG was not performed at SOF Year 20, and it is unclear how incident, remitting, or persistent SDB at Year 20 may have affected results. Third, because our sample was 89% white and consisted entirely of women, it is unclear whether our findings will generalize to other race/ethnic groups or to men. Fourth, although we completed sensitivity analyses after excluding participants with adjudicated dementia diagnoses, they included participants with normal cognition and those with MCI. Studies of this sort in large community-based samples of cognitively normal participants could provide valuable information about links between sleep and cognitive functioning in the context of healthy cognitive aging. In addition, studies that include a broader range of actigraphic sleep parameters as well as self-report sleep measures and compare their associations with performance across cognitive domains would enrich the existing literature. Longer periods of assessment with actigraphy (eg, 1–2 weeks) would also enhance these studies by providing more reliable estimates of sleep/wake patterns. Moreover, we performed many analyses in this study. Although these were based on hypothesized associations, we did not adjust for multiple comparisons, and our results may be affected by type-one error. Replication in other samples of older adults is needed. Finally, all observational studies are vulnerable to selection bias. It is possible that selection into or out of the SOF cohort affected results, but it is uncertain how.

In conclusion, we found that longer sleep duration and greater sleep fragmentation are associated with lower cognitive performance or impairment in a limited number of domains of cognitive function among community-dwelling older women. These associations may be driven in part by individuals with dementia, in whom disturbed sleep and cognitive impairment co-occur due to neurological changes. Prospective studies using broad neuropsychological test batteries are needed to better understand associations of sleep duration and fragmentation with trajectories of decline across cognitive domains. Observing how patterns of decline across domains differ as a function of sleep, in concert with neuroimaging studies, will help elucidate the pathophysiology linking disturbed sleep to cognitive decline in later life and will inform potential interventions aimed at preventing poor cognitive outcomes.

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SUPPLEMENTARY MATERIAL

Supplementary material is available at *SLEEP* online.

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