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Association of sleep disturbances with cognitive impairment and depression in maintenance hemodialysis patients

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Abstract

Background—There are few data on the relationship of sleep with measures of cognitive function and symptoms of depression in dialysis patients.

Methods—We evaluated the relationship of sleep with cognitive function and symptoms of depression in 168 hemodialysis patients, using multivariable linear and logistic regression. Sleep disturbances were assessed using the sleep subscale battery of the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Health Experience Questionnaire. The cognitive battery assessed a broad range of functioning including global ability, verbal intelligence, supraspan learning, auditory retention, visual retention, attention/mental processing speed, visual construction/fluid reasoning and motor speed. Depressive symptoms were assessed using the Center for Epidemiological Studies of Depression (CESD) Scale, with depression indicated by a CESD score 16.

Results—Mean (SD) age of participants was 62 (17) years, 49% were women, 30% were African American and 33% had diabetes. There was no significant relationship between sleep score and performance on any neurocognitive test (p>0.13, for all multivariable analyses). The prevalence of depression increased from 16% in the highest quartile (best) of sleep score, to 31% in the lowest quartile (worst) of sleep score. In multivariable analyses, each 1 SD increase in sleep score was associated with a 2.18 (95% confidence interval, 1.07–3.29, p<0.001) lower CESD score. Results were consistent when considering individual components of both the CESD and sleep score.

Conclusions—Disturbances in sleep are associated with symptoms of depression but not measures of cognitive function. Dialysis patients with disturbances in sleep should be screened for depression.

Conflict of interest statement: The authors have no conflicts of interest to declare.

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Keywords

Cognitive function; Depression; Hemodi-alysis; Sleep

Introduction

Cognitive impairment is common in individuals with chronic kidney disease (CKD) (1), with the prevalence of cognitive impairment increasing as kidney function declines. In dialysis patients, cognitive impairment is associated with increased resource utilization, worse quality of life and higher risks of hospitalization and all-cause mortality (2). Depression is also common in dialysis patients, with studies suggesting a prevalence of approximately 20%–40% (3–6). Similar to cognitive impairment, depression may impact quality of life and is associated with adverse outcomes, including increased rates of hospitalizations, cardiovascular disease and mortality (5, 6).

The etiology of cognitive impairment and depression in dialysis patients is likely multifactorial (6), but abnormal sleep is a potential risk factor. Sleep disorders are highly prevalent in hemodialysis patients and are associated with adverse outcomes (7). However, there are few studies that have evaluated the relationship between sleep and either cognitive impairment or depression in hemodialysis patients. A recent study in the general population noted that sleep deprivation adversely affects cognitive function and the biological pathways that support cognitive performance (8), while another study concluded that sleep deprivation reduced attention and resulted in impaired central processing (9). In both peritoneal dialysis and hemodialysis patients, Kutner et al reported associations between both depression and sleep difficulty with lower levels of cognitive function, as assessed by screening questions included in the cognitive function subscale of the Kidney Disease Quality of Life, Short Form (KDQOL-CF) (10). In the current study we evaluated the association between sleep and both cognitive function, ascertained using an extensive battery of established neurocognitive tests, and depression.

Subjects and methods

Participants

All patients receiving hemodialysis at 5 Dialysis Clinic Inc. (DCI) units as well as one hospital-based unit (St. Elizabeth's Medical Center) in the greater Boston, Massachusetts, area were screened for the Cognition and Vascular Disease in Dialysis Patients Study. Eligibility criteria included English fluency, sufficient visual and auditory acuity to complete cognitive testing, absence of preexisting advanced dementia or confusion (based on provider testimony, medical chart review, or Mini-Mental State Examination (MMSE) score 10), medically stable condition without urgent non-access-related hospitalization within 1 month, receipt of maintenance hemodialy-sis therapy for at least 1 month and single-pool Kt/V >1.0. Demographic information was obtained through participant report, medical charts and electronic medical records. Data on use of antidepressants (heterotricyclic compounds, mono-amine oxidase inhibitors, selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, bupropi-on, mirtazapine,

trazodone), antipsychotics (first generation [typical], second generation [atypical]), benzodiazepines and zolpidem were collected at the time of cognitive testing. The Tufts Medical Center Human Investigation Review Board approved the study, and all participants signed informed consent and research authorization forms.

Exposure: sleep quality assessment

Sleep disturbances were assessed using the sleep subscale of the Choices for Healthy Outcomes in Caring for ESRD (CHOICE) Health Experience Questionnaire (CHEQ) (11). The CHEQ is a patient-centered instrument that provides specific scores for domains important to patients with end-stage renal disease (ESRD). The consistency and reliability of the scale was based on a Cronbach's α of 0.70, which measures the standardization of items in a scale around a consistent variable. The assessments of sleep in the CHEQ were based on sleep initiation (have trouble falling asleep), sleep maintenance (awaken during sleep and have trouble falling asleep again) and sleep adequacy (get enough sleep to feel rested upon waking in the morning). The sleep questions ask individuals to quantify their responses on a 6-point scale: (i) all of the time, (ii) most of the time, (iii) good bit of the time, (iv) some of the time, (v) a little of the time and (vi) none of the time. The CHEQ sleep score was defined as the sum of the raw values for the 3 sleep questions and then converted to a 100-point scale, with a higher value indicating better sleep.

Outcomes

Cognitive Impairment—Participants were administered a detailed battery of neurocognitive tests by trained research assistants. To ensure quality and inter-rater reliability, reassessment of research assistants by the study neuropsychologist (T.S.) with either mock training sessions or witnessed testing of study participants occurred at 3- to 6month intervals. The neuropsycho-logical battery included well-validated and commonly used cognitive tests that possess high inter- and intra-rater reliability, and many of the tests have established age-, sex- and/ or education-matched normative scores. To limit participant fatigue, all testing was completed during the first hour of hemodialysis. The tests administrated included Mini-Mental State Examination (MMSE), North American Adult Reading Test (NAART) (12), Trail Making Test A&B (TMT) (13), Wechsler Memory Scale-III Word List Learning subtest (WMS-III) (14), Wechsler Adult Intelligence Scale-III (WAIS-III) Block Design, Digit Span, and Digit Symbol-Coding Tasks (14), Controlled Oral Word Association Test (COWAT) (15) and Mental Alternations Test (MAT) (16). The overall battery assesses a broad range of functioning including global ability, verbal intelligence, supraspan learning, auditory retention, visual retention, attention/mental processing speed, visual construction/ fluid reasoning and motor speed (Tab. I).[AUTHORS: please note: the style guidance for the J Nephrol indicates that all tables should be numbered consecutively as cited in text.] In addition to using raw scores, neurocognitive performance outcomes were evaluated with principal components analysis (17). For 15 individuals who were missing results on 1 cognitive test (or 2 results if derived from the same test), singleitem imputation was performed using multivariable linear regression models based on performance on other tests in the cognitive battery. Imputation results were incorporated to derive the principal components analysis but were not used for evaluating performance on individual cognitive tests. Principal component analysis with varimax rotation was used to

derive composite scores for separate cognitive domains. Following application of this datareduction technique, 2 principal components with eigenvalues >1 were obtained. The first component, with explained variance of 3.3 following rotation, consisted primarily of the Trails A and B, Block Design, Digit Symbol–Coding, Digit Span, Mental Alternations and COWAT tasks, and was considered to reflect executive functioning, attention and processing speed. The second component, with explained variance of 3.5 following rotation, consisted primarily of the Word List Learning Recall and Recognition tasks, also modestly incorporated Digit Symbol–Coding and the COWAT tasks, and was interpreted as reflecting memory.

Depression—Depression was evaluated using the Center for Epidemio-logical Studies of Depression (CESD) Scale (Tab. II) (18). For the purpose of analyses in the current study, we did not include question number 11 of the CESD, as this question directly evaluates sleep. Depression was defined as a score of 16; a value consistent with the presence of major depression in the general population (18). Use of the CESD has been validated in both the general population and dialysis patients (4). Depression was also divided into 4 subgroups commonly used in CESD analyses, including "depression affect," "positive affect," "somatic and retarded activity" and "interpersonal" (18).

Statistical analysis

Baseline characteristics of dialysis patients with measures of sleep, cognitive function and depression were compared using the chi-square test, *t*-test and ANOVA as appropriate. Linear regression was used to explore the association between sleep and performance by each principal component as well as individual cognitive tests, with principal component scores and raw test scores serving as the dependent variables. Sleep scores were modeled linearly with parameter estimates (β coefficients) calculated per 1 standard deviation (SD) increase. Analyses where performance on the Trails B test was the outcome used Tobit regression, censoring for failure to complete the task within 5 minutes (19). Models initially adjusted for age, sex, race (African American vs. non-African American), education (did not graduate high school, high school graduate and/or 1 year of college, 2+ years of college) and cause of ESRD. Subsequent models adjusted for other variables that differed in baseline characteristics – namely, stroke and heart failure. In additional analyses, we evaluated the association between sleep and either total CESD score or CESD components using linear regression for continuous scores and logistic regression using a CESD cutpoint of 16 (depression). In these latter analyses, the sleep exposure term was evaluated both per SD increase as well as in quartiles. We also evaluated the association between each sleep question separately and the CESD score, using linear regression. All analyses were performed using SAS, version 9.2 (SAS Institute, Cary, NC, USA). All hypothesis tests were 2-sided, and differences were considered statistically significant at a p value of <0.05.

Results

One hundred and sixty-eight individuals completed both the sleep questionnaire and the neurocognitive battery, including the CESD. Mean (SD) age of participants was 62 (17) years, 49% were women, 30% were African American, 33% had diabetes as the primary

cause of kidney failure, 45% graduated high school while an additional 45% had at least 2 years of college, and the median dialysis vintage was 32 months (Tab. III). Forty-two patients (25%) had a symptom burden consistent with depression (Tab. IV). The prevalence of depression increased from 16% in quartile 4, consisting of those with the best sleep score, to 31% in quartile 1, comprising individuals with the worst sleep score. Demographics, patient characteristics and medications overall were similar across sleep score quartiles, although the prevalence of stroke was higher in those with better sleep score, and the prevalence of heart failure was higher in those with worse sleep score. We noted no significant relationship between sleep score and performance on neurocognitive tests in either univariate or multivariable analyses (Tab. V). Both CESD scores and the prevalence of depression were highest in those with the worst sleep score, and this relationship was present in both univariate and multivariable analyses (Tab. VI). In multivariable analyses, each 1 SD increase in sleep score was associated with a 2.18 (95% confidence interval [95% CI], 1.07–3.29, p<0.001) lower CESD score. In multivariable analysis, each 1 unit increase in sleep initiation, sleep maintenance and sleep adequacy (higher score consistent with better sleep), was associated with 1.34 (95% CI, 0.67–2.00, p<0.001), 1.16 (95% CI, 0.42–1.89, p<0.002) and 0.72 (95% CI, 0.00–1.44, p=0.051) lower CESD score, respectively. When the subcomponents of CESD were considered, higher sleep score was associated with lower "depression affect," "somatic and retarded activity" and "interpersonal effect" (Tab. VI). We also noted that better sleep score was associated with a trend toward lower prevalence of depression in univariate and multivariable models in both quartile and continuous analyses (Tab. VII).

Discussion

Among maintenance hemodialysis patients, individuals with worse sleep have more symptoms of depression but no apparent difference in performance on cognitive tests. These results remained consistent in subgroup analyses and following multivariable adjustment, suggesting that sleep does not have overt effects on cognitive function in hemodialysis patients, but rather, that hemodialysis patients with sleep disturbances should be screened for depression.

There are limited studies evaluating the relationship between sleep and cognitive function in dialysis patients. Kutner et al studied the relationship between sleep disorders with cognitive function using responses to the 3 questions comprising the KDQOL-CF to estimate cognitive function in 2,286 dialysis patients included in the Dialysis Morbidity and Mortality Study (DMMS) Wave 2 cohort (10). The authors noted that patients with lower KDQOL-CF scores were more likely to report sleep difficulty. However, this study was limited by relying on a single yes/no question to assess sleep and the KDQOL-CF to assess cognitive function, an instrument with poor sensitivity and only modest specificity (20).

There are several reasons sleep may not be associated with cognitive impairment in our study. First, it is possible that indeed no association exists between sleep and cognitive function in dialysis patients. Second, it is possible that the prevalence of both sleep abnormalities and cognitive impairment is so high that it is difficult to discern relationships between these entities because there is an insufficient range in the exposure and outcome

variables. The range of sleep scores in our study does not however support this premise. Furthermore, we used multiple measures of cognitive function and noted no suggestion of a relationship using any of these measures. Third, it is possible that both the sleep questionnaire and the cognitive function battery are not sensitive enough to appreciate this association.

We did observe a significant relationship between sleep and measures of depression. These results were consistent when the sleep questions were considered separately and were reproduced within 3 of the 4 CESD components, and also when depression was considered as a dichotomous variable. These findings are consistent with prior reports that have used other measures to assess sleep and depression in dialysis patients (21–23) as well as the general population (24, 25). While we acknowledge that disordered sleep may be considered a manifestation of depression, this does not detract from the importance of recognizing that depression is more prevalent in dialysis patients with sleep abnormalities and that the latter patients should therefore be screened more carefully for depression.

Our study has several strengths. First, we performed detailed neurocognitive testing, which allowed us to evaluate the relationship between sleep and cognition using well- validated tests of cognitive function. Second, both the CESD and CHEQ have been validated in dialysis patients (4, 26). Third, although the dialysis patients evaluated in this study were healthier than those not eligible for inclusion, the cohort recruited is not dissimilar from the broader US dialysis population (27).

Our study also has several limitations. First, despite the fact that our assessment of sleep includes more questions than several other studies (10), we did not perform a detailed sleep evaluation and therefore were not able to evaluate objective components of sleep, such as sleep quality, sleep latency, sleep duration and daytime dysfunction, in order to validate participants' self-assessments of their sleep. Third, cognitive testing was performed at the start of the dialysis procedure. Although this in theory may affect the prevalence of cognitive impairment, it should not bias toward affecting the relationship between sleep with either cognitive function or depression. Fourth, we examined the association between sleep and depressive effect rather than a current or prior diagnosis of depressive symptoms, we did not adjust for antidepressant use. Fifth, this is a cross-sectional study, precluding our ability to ascribe cause and affect relationships and to evaluate whether sleep abnormalities lead to depressive symptoms or vice versa.

In summary, these results demonstrate that patients with worse sleep are more likely to have symptoms of depression but are not more likely to perform poorly on neurocognitive testing. Future studies should evaluate these relationships in prospective longitudinal studies using more detailed measures of sleep. In addition, hemodialysis patients with complaints of abnormal sleep should be screened for depression.

Acknowledgments

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TABLE I

COMPONENTS OF THE NEUROPSYCHIATRIC BATTERY

Function assessed	Test	Scoring	Test details
Cognitive screen	Mini-Mental State Examination	Number correct	Thirty-point questionnaire that samples abilities such as arithmetic, memory and orientation.
Intelligence	North American Adult Reading Test	$128.7 - (0.89 \times \text{number})$ of errors)	Estimation of verbal intelligence quotient that requires subjects to read a list of 61 words out loud.
Supraspan learning & word recall	Immediate Recall [*]	Total initially correct	A test of memory in which a list of 12 words is presented during 4 trials, and retention of these
word recail	Percent Retention*	Percentage recall after delay	words is tested after a delay of 25 to 35 minutes. Calculated scores include <i>immediate</i>
	Delayed Recognition [*]	Number of correctly identified words	<i>recall</i> (which is the sum of words recalled during the 4 trials), <i>percentage retention</i> [(delayed recall / trial 4 of immediate recall) x 100] and <i>delayed recognition</i> .
Visual construction & fluid reasoning	Block Design [†]	Number completed weighted for time	Subjects are required to reproduce de- picted patterns using a set of colored blocks.
Attention, mental processing speed &	Digit Symbol–Coding †	Number of copied symbols in 2 minutes	Symbols are decoded by matching a given symbol to a digit provided in an answer key.
executive function	Trail Making Test A	Time to completion	"Connect-the-dots" for a consecutive number sequence from 1 to 25.
	Trail Making Test B	Time to completion	"Connect-the-dots" alternating betwe- en numbers (1 to 13) and letters (A to L).
Depression	Center for Epidemiological Studies of Depression Scale	Four-point scale (0-3)	Twenty-question questionnaire that samples self-analysis of past weekly mood

Derived from the Word List Learning subtest of the Wechsler Memory Scale-III (WMS-III).

 $^{\dagger} \mathrm{From}$ the Wechsler[AUTHORS: please advise: correct edit?] Adult Intelligence Scale.

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TABLE II

COMPONENTS OF THE DEPRESSION BATTERY

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tarded activity	Depression affect	I felt that I could not shake off the blues even with help from my family.				
tarded activity		I feel depressed.				
tarded activity		I thought my life had been a failure.				
tarded activity		I felt fearful.				
tarded activity		I felt lonely.				
tarded activity		I had crying spells.				
tarded activity		I felt sad.				
I felt hopeful about the fitute. I was happy. I was happy. I relioyed life. Somatic and retarded activity Vas bother by the things that usually don't bother me. Somatic and retarded activity I did not feel like earing: my appetite was poor. I did not feel like earing: my appetite was poor. I had trouble keeping my mind on what I was doing. I fielt that everything I did was an effort. My sleep was restless. (Eliminated) I talked less than usual. I could not "get going".	Positive affect	I felt that I was just as good as other people.				
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Е		I had trouble keeping my mind on what I was doing.				
My sleep was restless. (Eliminated) I talked less than usual. I could not "get going".		I felt that everything I did was an effort.				
I talked less than usual. I could not "get going".		My sleep was restless. (Eliminated)				
I could not "get going".		I talked less than usual.				
		I could not "get going".				

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Test factors	During the past week	Rarely or none of the time (<1 day)	Some or a little of the time (1–2 days)	Rarely or none of Some or a little of Occasionally or All of the tim the time (<1 day) the time (1-2 days) moderate amount of time (5-7 days) (3-4 days)	All of the time (5–7 days)
Interpersonal activity	People were unfriendly.				
	I felt that people disliked me.				

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TABLE III

CLINICAL CHARACTERISTICS OF PARTICIPANTS STRATIFIED BY SLEEP SCORE

	Sleep score quartile 1 (n=48, 29%)	Sleep score quartile 2 (n=41, 24%)	Sleep score quartile 3 (n=34, 20%)	Sleep score quartile 4 (n=45, 27%)	Total (n=168)	Trend p Value
Sleep score	27 ± 13	54 ± 5	70 ± 3	88 ± 7	58 ± 25	N/A
Age (years)	62 ± 17	60 ± 15	62 ± 18	62 ± 17	62 ± 17	0.76
Female sex	52	46	44	53	49	0.95
Black race	25	37	29	29	30	0.84
Education						
<12th grade	13	12	3	6	10	
High school graduate	42	54	44	42	45	0.58
2+ years college	46	34	53	49	45	
Peripheral artery disease	17	15	15	27	18	0.23
Coronary artery disease	31	39	29	29	32	0.63
Hypertension	94	88	100	87	92	0.52
Stroke	15	10	21	29	18	0.04
Diabetes	56	54	35	47	49	0.18
Heart Failure	54	34	24	24	35	0.002
Cause of ESRD						
Diabetes	35	41	24	31	33	
Glomerulonephritis	13	22	21	18	18	
Hypertension	19	17	24	20	13	0.84
Other	10	12	18	13	16	
Unknown	23	7	15	18	14	
Smoking						
Never	31	43	59	36	41	
Past	48	55	38	56	50	0.14
Current	21	3	3	6	10	
spKt/V	1.51 ± 0.22	1.50 ± 0.24	1.57 ± 0.24	1.57 ± 0.28	1.53 ± 0.25	0.22
Systolic BP (mm Hg)	139 ± 26	140 ± 21	139 ± 17	141 ± 21	140 ± 22	0.71
Diastolic BP (mm Hg)	73 ± 16	71 ± 12	74 ± 13	72 ± 13	72 ± 13	0.95
Body mass index (kg/m ²)	29 ± 7	32 ± 10	26 ± 4	30 ± 8	29 ± 8	0.60

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	Sleep score quartile 1 (n=48, 29%)	Sleep score quartile 2 (n=41, 24%)	Sleep score quartile 3 (n=34, 20%)	Sleep score quartile 2 (n=41, Sleep score quartile 3 (n=34, Sleep score quartile 4 (n=45, Total (n=168) Trend p Value $24\%_6$) $24\%_6$)	Total (n=168)	Trend p Value
Serum albumin (g/dL)	3.7 ± 0.4	3.8 ± 0.3	3.9 ± 0.4	3.8 ± 0.4	3.8 ± 0.4	0.49
Phosphate (mg/dL)	5.8 ± 1.7	5.8 ± 1.4	5.9 ± 1.6	5.5 ± 1.5	5.7 ± 1.6	0.65
Dialysis vintage (months)	34 (14–55)	24 (14–37)	29 (13–52)	32 (16-48)	32 (13-49)	0.80
Antidepressants	25	22	32	29	27	0.49
Antipsychotics	2	0	0	7	2	0.17
Benzodiazepines	23	10	21	16	17	0.58
Zolpidem	6	17	6	4	6	0.51

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Continuous variables shown are means ± standard deviation except for dialysis vintage which is median (25th-75th percentile); categorical data are presented as percentages; p values for dialysis vintage calculated using the Kruskal-Wallis test. Quartile 1 includes those with the worst performance based on the sleep score, while quartile 4 comprises the best performers. For 22 individuals (receiving dialysis at a non-Dialysis Clinic Inc. facility), blood pressure results are from a single dialysis session rather than a monthly average.

ESRD = end-stage renal disease; BP = blood pressure; spKt/V = single-pool Kt/V.

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TABLE IV

ASSOCIATION BETWEEN SYMPTOMS OF DEPRESSION AND SLEEP

	Sleep score quartile 1 (n=48, 29%)	Sleep score quartile 2 (n=41, 24%)	Sleep score quartile 3 (n=34, 20%)	Sleep score quartile 3 Sleep score quartile 4 $(n=34, 20\%)$ $(n=45, 27\%)$	Total (n=168) Trend p value	Trend p value
CESD raw score	16 ± 8	12 ± 6	12 ± 7	8 ± 7	12 ± 8	<0.0001
CESD raw score (excludes sleep question)	13 ± 8	11 ± 6	11 ± 7	7 ± 7	11 ± 7	< 0.0001
Prevalence of depression (CESD score 16)	31%	27%	26%	16%	25%	60.0

CESD = Center for Epidemiological Studies of Depression.

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TABLE V

ASSOCIATION BETWEEN SLEEP SCORE AND COGNITIVE TESTING

Cognitive test	Function tested	Z		Univariate			Multivariable	0
			β	95% CI	p Value	ß	95% CI	p Value
Executive Factor	Executive function	144	-0.14	-0.30, 0.02	60.0	-0.09	-0.24, 0.06	0.25
Memory Factor	Memory	144	0.06	-0.09, 0.22	0.43	0.04	-0.10, 0.18	0.56
MMSE	Cognition screen	168	-0.14	-0.57, 0.29	0.52	-0.16	-0.56, 0.25	0.44
Delayed Recall	Memory and supraspan learning	165	-0.33	-0.74, 0.08	0.12	-0.23	-0.62, 0.16	0.25
Short Delay		166	-0.24	-0.69, 0.20	0.28	-0.16	-0.57, 0.25	0.43
Recall Total		166	-0.14	-1.20, 0.93	0.80	0.05	-0.87, 0.97	0.92
Percent Retention	Primary cortical (memory)	160	-2.66	-6.84, 1.52	0.21	-1.72	-6.08, 2.64	0.44
Recognition		165	-0.24	-0.64, 0.15	0.22	-0.21	-0.59, 0.17	0.27
Block Design	Primary subcortical (executive function and processing speed)	162	-1.24	-2.84, 0.37	0.13	-1.03	-2.38, 0.32	0.13
Digit Symbol–Coding		136	1.09	-1.92, 4.10	0.48	0.92	-1.49, 3.33	0.45
Trails A		146	-2.54	-9.87, 4.78	0.49	-1.48	-8.89, 5.93	0.69
Trails B		146	-6.91	-25.34, 11.52	0.46	-6.34	-22.09, 9.41	0.43
COWAT Animal	Semantic verbal fluency	167	-0.26	-1.14, 0.61	0.55	-0.38	-1.21, 0.46	0.38
COWAT Market		168	-0.19	-1.18, 0.79	0.70	-0.06	-1.03, 0.92	0.91
Mental Alternations	Executive function	167	0.69	-0.48, 1.86	0.24	0.71	-0.37, 1.80	0.20
CESD Total	Depression screen	168	-2.34	-3.40, -1.27	<0.0001	-2.18	-3.29, -1.07	<0.0001

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Multivariable linear regression models adjusted for age, sex, race, education, cause of end-stage renal disease, history of stroke and history of heart failure. For all neurocognitive assessments, higher values are consistent with better performance, except Trails A and B where lower scores are better. Higher values on the sleep score are consistent with better self-identified sleep. All β coefficients are per 1 SD increase in sleep score. Trails B models used Tobit regression.

CESD = Center for Epidemiological Studies of Depression; COWAT = Controlled Oral Word Association Test; MMSE = Mini-Mental State Examination; NAART = North American Adult Reading Test; 95% CI = 95% confidence interval.

TABLE VI

ASSOCIATION BETWEEN SLEEP SCORE AND CESD*

			Univariate			Multivariable	e
	Number of questions	ß	95% CI p Value β	p Value	β	95% CI p Value	p Value
CESD raw score *	19	-2.34	-2.34 -3.40, -1.27 <0.0001 -2.18 -3.29, -1.07 <0.0001	<0.0001	-2.18	-3.29, -1.07	<0.0001
Subcomponents of CESD*							
Depression affect	7	-1.02	-1.02 -1.52, -0.52 <0.0001 -0.89 -1.40, -0.38	<0.0001	-0.89	-1.40, -0.38	0.001
Positive affect	4	-0.36	-0.36 -0.84, 0.12	0.14	-0.30	-0.82, 0.21	0.25
Somatic & retarded activity *	6	-0.79	-0.79 -1.21, -0.37	<0.0001	-0.83	-1.27, -0.39	<0.0001
Interpersonal	2	-0.16	-0.16 -0.29 , -0.04 0.01 -0.03 -0.30 , -0.03 0.02	0.01	-0.03	-0.30, -0.03	0.02

Multivariable models adjusted for age, sex, race, education, cause of end-stage renal disease, history of stroke and history of heart failure. For CESD and its subcomponents, lower values are consistent with better performance. Higher values on the sleep score are consistent with better self-identified sleep. All β coefficients are per 1 SD increase in sleep score.

CESD = Center for Epidemiological Studies of Depression; 95% CI = 95% confidence interval.

 $^{*}_{\mathrm{Excludes}}$ question 11 on the CESD, which specifically queries regarding sleep.

TABLE VII

ASSOCIATION BETWEEN SLEEP SCORE AND THE PREVALENCE OF DEPRESSION

			Univariate	e		Multivariable [*]	le*
	Percentage depressed OR 95% CI p Value OR 95% CI p Value	OR	95% CI	p Value	OR	95% CI	p Value
Sleep score (per 1 SD increase)	25%	0.74	0.52, 1.05	0.09	0.71	0.74 0.52, 1.05 0.09 0.71 0.47, 1.07 0.10	0.10
Quartile of sleep score							
Quartile1	31%		1			1	
Quartile 2	27%	0.81	0.81 0.32, 2.03	0.65	0.72	0.72 0.26, 1.98	0.52
Quartile 3	26%	0.79	0.30, 2.10	0.64	0.86	0.86 0.29, 2.56	0.79
Quartile 4	16%	0.41	0.41 0.15, 1.11	0.08	0.39	0.39 0.13, 1.19	0.10

Quartile 1, consistent with the worst sleep, serves as the reference.

95% CI = 95% confidence interval; OR = odds ratio.

* Multivariable models adjusted for age, sex, race, education, cause of end-stage renal disease, history of stroke and history of heart failure. The p value for univariate analysis is 0.10 and for multivariable analysis 0.14.