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Research Article

Cognitive Performance Trajectories Before and After Sleep Treatment Initiation in Middle-Aged and Older Adults: Results From the Health and Retirement Study

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Abstract

Background: Sleep disturbances are associated with risk of cognitive decline but it is not clear if treating disturbed sleep mitigates decline. We examined differences in cognitive trajectories before and after sleep treatment initiation.

Method: Data came from the 2006–2014 Health and Retirement Study (HRS). At each of 5 waves, participants were administered cognitive assessments and scores were summed. Participants also reported if, in prior 2 weeks, they had taken medications or used other treatments to improve sleep. Our sample (N = 3 957) included individuals who at HRS 2006 were 50 years and older, had no cognitive impairment, reported no sleep treatment, and indicated experiencing sleep disturbance. We identified differences between those receiving versus not receiving treatment in subsequent waves and, among those treated (n = 1 247), compared cognitive trajectories before and after treatment.

Results: At baseline, those reporting sleep treatment at subsequent waves were more likely to be younger, female, Caucasian, to have more health conditions, to have higher body mass index, and more depressive symptoms (all ps ≤ .015). Decline in cognitive performance was mitigated in periods after sleep treatment versus periods before (B = –0.20, 95% CI = [–0.25, –0.15], p < .001 vs B = –0.26, 95% CI = [–0.32, –0.20], p < .001), and this same trend was seen for self-initiated and doctor-recommended treatments. Trends were driven by those with higher baseline cognitive performance—those with lower performance saw cognitive declines following sleep treatment.

Conclusions: In middle-aged and older adults with sleep disturbance, starting sleep treatment may slow cognitive decline. Future research should assess types, combinations, and timing of treatments most effective in improving cognitive health in later life.

Keywords: Cognitive decline, Sleep, Sleep treatment

There is an emerging interest in the role that sleep may have on neurodegeneration and cognitive aging. Sleep disturbances (which may include insomnia, obstructive sleep apnea [OSA], restless legs syndrome, circadian rhythm disorders, etc.) are highly prevalent in middle-aged and older adults with estimates ranging from 40% to 70% experiencing sleep disorders and/or transient difficul-

ties sleeping (1–3). At the same time, there is evidence suggesting poor sleep to be associated with increased risk of cognitive impairment and cognitive decline (4–8) in epidemiological cohorts. There is some biological plausibility for this relationship—for example, sleep has been shown to serve as a clearance mechanism for neurotoxins built up throughout waking hours (9), and poor sleep is associated with accumulation of beta-amyloid burden in humans (10,11). Sleep apnea is characterized by intermittent hypoxia and reoxygenation which can lead to oxidative stress (12), one factor thought to be important in the pathogenesis of Alzheimer's disease (AD) (13), and sleep fragmentation—inherent in sleep apnea—has been shown to increase deposition of amyloid and tau proteins in both rodent models and in humans (14,15). There is also some evidence from genetic analyses showing APOE ε4 gene is associated with both sleep apnea and AD, suggesting some possible genetic link (16). Taken together, considerable evidence exists to suggest an important role for sleep health in maintaining brain and cognitive health.

A variety of treatments exist for sleep disturbances (17), which may be recommended by a doctor or be self-initiated. For example, clinicians may prescribe sleep medications (eg, benzodiazepines and other hypnotics) or deliver behavioral treatments (eg, cognitive behavioral therapy for insomnia [CBT-I]) for the treatment of insomnia, or prescribe continuous positive airway pressure (CPAP) and mandibular advancement devices for the treatment of sleep apnea (17). While there is limited availability of behavioral sleep treatments like CBT-I (18), use of prescription hypnotics and CPAP is quite common in older persons. For example, previous estimates indicate that between 5% and 7% of older adults aged 65 and older have used sleep medications in the past month (19). There are also a number of other marketed treatments available directly to patients including herbal supplements (eg, melatonin) or other "over-the-counter" (OTC) medications. The actual prevalence of use of these patient-initiated treatments among older persons remains largely unknown, although one previous estimate showed 17.5% of older adults with sleep disturbance used OTC sleep aids (20). Past research has shown that sleep treatment may be more common among women (21), and those with more comorbid health conditions and mental health symptoms (eg, depressive symptoms) (22).

At present, the effect of treating sleep disturbance on cognitive function remains unclear. In theory, treatments that consolidate sleep might facilitate its restorative role, which may lead to improved cognition (23). For example, a study by Ancoli-Israel et al. found that CPAP among patients with mild–moderate AD and OSA improved cognitive functioning over 3 weeks (24). On the other hand, some insomnia treatments such as benzodiazepines and other hypnotics may worsen memory and lead to cognitive impairment (25). Indeed, benzodiazepines have been shown to be associated with AD risk in some (26–29) but not all studies (30–32). It should be noted that many OTC medications (eg, Benadryl), while commonly used, are not recommended for use to address sleep and there are limited data about their efficacy for sleep treatment (20). More research is needed to determine whether improving poor sleep could have the potential to mitigate cognitive decline, and whether there might be differences based upon the type of treatment (eg, self-initiated or doctor-recommended).

Based on this conceptual framework, the overall purpose of this study was to determine in a large community-based sample of older adults whether treatment for sleep disturbances was associated with subsequent improvements in cognitive performance and, therefore, whether sleep treatment might have the potential to modify cognitive performance trajectories over time. Specifically, we aimed (i) to identify participant demographic and health characteristics associated with obtaining sleep treatment and (ii) to determine the association between sleep treatment initiation and concurrent and subsequent trajectories of cognitive functioning. We hypothesized that receipt of sleep treatment would be greater among women, those with more health conditions, and those with elevated depressive symptoms, and that treatment for sleep issues would be associated with improved subsequent cognitive performance and mitigation in cognitive decline longitudinally.

Methods

Data Source and Participants

We examined data from the 2006, 2008, 2010, 2012, and 2014 waves of the Health and Retirement Study (HRS). The HRS is a biennial longitudinal cohort study of a nationally representative sample of older adults. The study was initiated in 1992 and has continued with follow-up interviews every 2 years. Each wave consists of approximately 20 000 older adults who are contacted via telephone or in-person interviews. Subjects were eligible for the study if they were noninstitutionalized adults older than age 50+ years and primary U.S. residents. The HRS is sponsored by the National Institute on Aging (U01AG009740) and is conducted by the University of Michigan.

Measures

Cognitive performance

All HRS participants were asked to complete several cognitive measures, and those older than age 65 years were additionally asked to complete a small subset of naming tasks. Consistent with previous literature (33), we focused only on those measures administered to the entire sample. For *Immediate and Delayed Word Recall*, the interviewer read aloud 10 nouns, and participants repeated as many words as possible after the 10 words were read. After 5 minutes of answering other survey questions, participants again recalled as many words as possible. To account for practice effects, 4 word-lists were rotated across successive interviews and 2 members of same household were never administered the same list in an interview. For *Serial 7's*, participants were asked to start at 100 and subtract 7 consecutively, 5 times. *Backwards Counting* consisted of asking participants to count backwards for 10 consecutive numbers from 20 (point was given for correct response). Consistent with other research (33), we focused on the total cognition score (sum of all measures; 0–27) and the scores on individual tests: immediate word recall (up to 10 points), delayed word recall (up to 10 points), Serial 7's (up to 5 points), and backwards counting (up to 2 points).

Sleep complaints

At each wave, subjects were asked to report how often (ie, "rarely or never," "sometimes," "most of the time") they had "trouble falling asleep," "trouble staying asleep," "trouble with waking up too early and being unable to fall asleep again," and "feeling really rested in the morning."

Sleep treatment

Respondents were also asked at each wave "In the past 2 weeks, have you taken any medications or used other treatments to help you sleep?" with response options being "yes" or "no." If a respondent gave an affirmative response, they were subsequently asked "Were these medications or other treatments recommended to you by a doctor?" ("yes" or "no").

Table 1. Comparison of Baseline Characteristics by Treatment Type, Health and Retirement Study, 2006–2014

Characteristic	No Treatment n = 2 710 n (%)	Self-Initiated Treatment n = 350 n (%)	Comparison AOR (95% CI), p Value	Doctor-Recommended Treatment n = 897 n (%)	Comparison AOR (95% CI), p Value
Baseline age, mean (*SD*)	67.3 (9.83)	65.7 (9.14)	**0.98 (0.97, 1.00), p = .010**	66.9 (9.55)	**0.99 (0.98, 1.00), p = .013**
Gender					
Male	1 195 (44.1)	123 (35.1)	Ref.	301 (33.6)	Ref.
Female	1 515 (55.9)	227 (64.9)	**1.37 (1.07, 1.75), p = .011**	596 (66.4)	**1.49 (1.25, 1.76), p < .001**
Race					
Caucasian	2 305 (85.1)	311 (88.9)	Ref.	805 (89.7)	Ref.
African American	289 (10.7)	25 (7.1)	**0.58 (0.37, 0.89), p = .014**	63 (7.0)	**0.51 (0.38, 0.69), p < .001**
Other	116 (4.3)	14 (4.0)	0.67 (0.35, 1.27), p = .217	29 (3.2)	0.67 (0.42, 1.06), p = .090
Hispanic ethnicity					
No	2 531 (93.4)	323 (92.3)	Ref.	843 (94.0)	Ref.
Yes	179 (6.6)	27 (7.7)	1.18 (0.72, 1.91), p = .512	54 (6.0)	0.85 (0.59, 1.22), p = .369
Education					
<High school	415 (15.3)	41 (11.7)	Ref.	162 (18.1)	Ref.
High school degree or GED	1 033 (38.1)	143 (40.9)	1.37 (0.93, 2.04), p = .113	337 (37.6)	0.82 (0.64, 1.04), p = .094
Some college	643 (23.7)	93 (26.6)	1.46 (0.96, 2.21), p = .077	214 (23.9)	0.85 (0.65, 1.10), p = .215
>College	618 (22.8)	73 (20.9)	1.26 (0.81, 1.97), p = .305	184 (20.5)	0.85 (0.65, 1.12), p = .254
Number of health conditions, mean (*SD*)	2.1 (1.39)	1.9 (1.31)	0.94 (0.86, 1.03), p = .184	2.3 (1.40)	**1.15 (1.08, 1.22), p < .001**
BMI, mean (*SD*)	28.4 (5.97)	28.9 (6.06)	1.01 (0.99, 1.03), p = .379	28.6 (6.13)	0.99 (0.98, 1.01), p = .467
CES-D, mean (*SD*)	1.7 (1.98)	2.0 (2.30)	**1.07 (1.01, 1.13), p = .015**	2.3 (2.25)	**1.10 (1.06, 1.14), p < .001**
Current smoking					
No	2 293 (85.2)	298 (85.6)	Ref.	743 (84.0)	Ref.
Yes	399 (14.8)	50 (14.4)	0.84 (0.60, 1.18), p = .318	142 (16.1)	0.94 (0.75, 1.18), p = .608
Ever drink					
No	1 235 (45.6)	162 (46.3)	Ref.	438 (48.8)	Ref.
Yes	1 475 (54.4)	188 (53.7)	1.03 (0.78, 1.35), p = .855	459 (51.2)	0.99 (0.82, 1.20), p = .909
# days drink per week, mean (*SD*)	1.2 (2.16)	1.0 (1.86)	0.96 (0.89, 1.04), p = .334	1.0 (2.03)	0.99 (0.94, 1.04), p = .705
# drinks per day, mean (*SD*)	0.7 (1.37)	0.6 (1.05)	1.00 (0.88, 1.13), p = .988	0.6 (1.26)	1.00 (0.92, 1.08), p = .940

Notes: AOR = adjusted odds ratio; CI = confidence interval; BMI = body mass index; CES-D = Center for Epidemiologic Studies Depression Scale; GED = general equivalency diploma; SD = standard deviation. All percentages are column percentages unless otherwise specified. AORs control for baseline age, gender, race, ethnicity, education, number of health conditions, BMI, CES-D, smoking, drinking, # days drink/week, and # drinks/day. All bolded values denote statistical significance at $p < .05$.

Other covariates

We also considered respondent age (years), gender (male, female), race (Caucasian, African American, other), Hispanic ethnicity, education (which we categorized as less than high school, high school diploma or equivalent, some college, higher than college degree), number of health conditions, body mass index (BMI; calculated from self-reported height and weight), depressive symptoms (as measured by the 8-item version of the Center for Epidemiologic Studies Depression Scale [CES-D] (34)), and current smoking status (yes vs no). Because alcohol use is associated with sleep quality (35) and may interact with sleep medications (36), we also assessed whether participants ever drink alcohol (yes vs no), the number of times per week they drank, and the average number of drinks per day they drank.

Participants

Our analyses focused on HRS respondents in the 2006 wave who had normal cognition (based on previous research (33) defined as a total cognition score between 12 and 27), who self-reported no sleep treatment, and who reported sleep difficulty. We defined "sleep difficulty" as the respondent indicating at baseline they experienced any of the sleep disturbance symptoms "all of the time" (or "rarely or never" for feeling rested in the morning). We then excluded those who were <50 years old. In total, our sample consisted of $N = 3\,957$ participants.

Statistical Analyses

Analyses were conducted in 4 stages. We first sought to determine the baseline (HRS 2006) demographic and health characteristics that may predict future receipt of treatment for sleep disturbances. We compared baseline measures using multinomial logistic regression among those who in the years after 2006 reported (i) no future treatment (which served as the reference), (ii) future treatment not recommended by a doctor (hereafter referred as "self-initiated treatment"), and (iii) future treatment recommended by a doctor ("doctor-recommended treatment"). If they reported both self-initiated treatment and doctor-recommended treatment, we categorized them as receiving doctor-recommended treatment. For these models, the main outcome was treatment type (self-initiated and doctor-recommended treatment both compared to no future treatment) and the predictors were the various baseline measures in HRS 2006; analyses controlled for all variables assessed.

Second, we focused on those who received any sleep treatment and examined the association between treatment for sleep disturbance and cognitive performance at the same wave across years of our study (ie, HRS 2006–2014). In order to account for clustering of observations within subjects, we employed generalized estimating equations (37) with an identity link for continuous outcomes. Specifically, the cognitive performance scores served as the outcomes and treatment type (ie, no treatment [reference], self-initiated treatment, doctor-recommended treatment) was the main predictor of interest. These analyses controlled for baseline age, gender, race, ethnicity, education, number of health conditions, BMI, CES-D, current smoking status, ever alcohol use, and alcohol use frequency and quantity, all of which we allowed to be time varying. In order to isolate the effect of treatment on cognitive performance regardless of changes over time, we also controlled for HRS interview year.

Third, to determine whether there were differences in cognitive trajectories before and after sleep treatment initiation, we defined a "treatment initiation" variable that began with a value of 0 at each

Table 2. Association Between Treatment Type and Concurrent Cognitive Performance, Health and Retirement Study, 2006–2014

Cognitive Score	Total Cognition *B* (95% CI), *p* Value	Immediate Word Recall *B* (95% CI), *p* Value	Delayed Word Recall *B* (95% CI), *p* Value	Serial 7's *B* (95% CI), *p* Value	Backwards Counting *B* (95% CI), *p* Value
No treatment	Ref.	Ref.	Ref.	Ref.	Ref.
Self-initiated treatment	0.01 (−0.22, 0.25), $p = .901$	0.02 (−0.08, 0.12), $p = .696$	0.02 (−0.10, 0.14), $p = .742$	−0.04 (−0.13, 0.05), $p = .394$	0.01 (−0.02, 0.04), $p = .500$
Doctor-recommended treatment	−0.09 (−0.28, 0.10), $p = .369$	−0.05 (−0.14, 0.03), $p = .240$	−0.02 (−0.12, 0.08), $p = .689$	−0.02 (−0.10, 0.05), $p = .526$	0.00 (−0.02, 0.03), $p = .813$

Notes: Beta coefficient comes from generalized estimating equations and corresponds to association between treatment type and each cognitive test averaged across all years. Results control for time, baseline age, gender, race, ethnicity, education, number of health conditions, body mass index, Center for Epidemiologic Studies Depression Scale, smoking, drinking, # days drink/week, and # drinks/day. All bolded values denote statistical significance at $p < .05$.

wave (ie, before treatment began), and changed to a value of 1 for the first and all subsequent waves in which treatment was reported. This variable was created for any treatment, self-initiated treatment, and doctor-recommended treatment. We stratified analyses for years before and years after initiation of sleep treatment and determined differences in these trajectories via an interaction term for time and treatment period while adjusting for confounds.

Finally, because the effect of sleep treatment on cognitive performance may depend on baseline cognitive functioning, we also repeated analyses for stages 2 and 3 stratified by those with the highest and lowest cognitive performance in the normal range at baseline. Specifically, among all respondents (whether treatment received or not), we divided the sample at the median by which half of the sample had the highest and half had the lowest cognitive performance. While the HRS provides variables and weights to account for the study's complex sampling design, all analyses do not incorporate these variables as we were focused on examining the impact of treatment among those with sleep disturbance rather than nationally representative estimates. All analyses were conducted in Stata version 15 (StataCorp, College Station, TX).

Results

Baseline Demographic and Health Characteristics

Overall, 8.9% of respondents in our analysis sample reported future self-initiated treatment, and 22.7% reported future doctor-recommended treatment. Compared to those with no future treatment, those reporting self-initiated treatment were younger (adjusted odds ratio [AOR] = 0.98, 95% confidence interval [CI] = [0.97, 1.00], $p = .010$), more likely to be female (AOR = 1.37, 95% CI = [1.07, 1.75], $p = .011$), to have more depressive symptoms (AOR = 1.07, 95% CI = [1.01, 1.13], $p = .015$), and were less likely to be African American (AOR = 0.58, 95% CI = [0.37, 0.89], $p = .014$) versus Caucasian. Compared to no future treatment, those receiving doctor-recommended treatment were younger (AOR = 0.99, 95% CI = [0.98, 1.00], $p = .013$), more likely to be female (AOR = 1.49, 95% CI = [1.25, 1.76], $p < .001$), have a greater number of health conditions (AOR = 1.15, 95% CI = [1.08, 1.22], $p < .001$), and more depressive symptoms (AOR = 1.10, 95% CI = [1.06, 1.14], $p < .001$), and were less likely to be African American (AOR = 0.51, 95% CI = [0.38, 0.69], $p < .001$) versus Caucasian (Table 1).

Association Between Treatment and Concurrent Cognitive Performance

Among those who received treatment at any time point from 2006 to 2014, we observed no association between treatment type and concurrent cognitive performance on the total cognition score or on individual cognitive test scores, indicating that sleep treatment (both self-initiated and doctor-recommended treatment) did not correspond to differences in concurrent cognitive performance as compared to no treatment (Table 2).

Differences in Cognitive Performance Trajectories Before and After Initiation of Sleep Treatment

Among those who subsequently received any type of treatment, the total cognition score decreased on average –0.25 points per year (95% CI = [–0.28, –0.23], $p < .001$) between 2006 and 2014. During periods before sleep treatment initiation, declines in cognition were similar to the overall trend ($B = –0.26$, 95% CI = [–0.32, –0.20], $p < .001$); however, during periods after sleep treatment, the trend was less pronounced ($B = –0.20$, 95% CI = [–0.25, –0.15], $p < .001$). This change in trajectories before and after sleep treatment initiation was statistically significant (interaction p value = .031), indicating that cognitive decline slowed after initiating sleep treatment. When examining individual cognitive tests (eg, immediate and delayed word recall, etc.), we saw similar patterns, although only scores on Serial 7's showed statistically significant differences in trends before and after sleep treatment was initiated. For the most part, similar results were seen when focusing on either self-initiated or doctor-recommended treatment (Table 3).

Table 3. Trajectories of Cognitive Performance Before and After Sleep Treatment, Health and Retirement Study, 2006–2014

Cognitive Score	Before Sleep Treatment *B* (95% CI), *p* Value	After Sleep Treatment *B* (95% CI), *p* Value	Interaction *p* Value
Overall treatment			
Total cognition	**–0.26 (–0.32, –0.20), $p < .001$**	**–0.20 (–0.25, –0.15), $p < .001$**	**$p = .031$**
Immediate word recall	**–0.10 (–0.13, –0.07), $p < .001$**	**–0.08 (–0.10, –0.06), $p < .001$**	$p = .197$
Delayed word recall	**–0.10 (–0.13, –0.07), $p < .001$**	**–0.08 (–0.11, –0.06), $p < .001$**	$p = .265$
Serial 7's	**–0.05 (–0.07, –0.02), $p < .001$**	**–0.03 (–0.05, –0.01), $p = .002$**	**$p = .036$**
Backwards counting	**–0.01 (–0.02, 0.00), $p = .016$**	0.00 (–0.01, 0.00), $p = .265$	$p = .198$
Self-initiated treatment			
Total cognition	**–0.28 (–0.32, –0.25), $p < .001$**	**–0.17 (–0.24, –0.10), $p < .001$**	**$p = .003$**
Immediate word recall	**–0.11 (–0.12, –0.09), $p < .001$**	**–0.07 (–0.10, –0.04), $p < .001$**	**$p = .034$**
Delayed word recall	**–0.11 (–0.12, –0.09), $p < .001$**	**–0.08 (–0.12, –0.05), $p < .001$**	$p = .328$
Serial 7's	**–0.06 (–0.07, –0.04), $p < .001$**	–0.01 (–0.04, 0.01), $p = .351$	**$p = .003$**
Backwards counting	**–0.01 (–0.01, –0.01), $p < .001$**	0.00 (–0.01, 0.01), $p = .472$	**$p = .012$**
Doctor-recommended treatment			
Total cognition	**–0.25 (–0.28, –0.21), $p < .001$**	**–0.20 (–0.26, –0.14), $p < .001$**	**$p = .028$**
Immediate word recall	**–0.10 (–0.11, –0.08), $p < .001$**	**–0.08 (–0.11, –0.05), $p < .001$**	$p = .237$
Delayed word recall	**–0.11 (–0.13, –0.09), $p < .001$**	**–0.07 (–0.10, –0.04), $p < .001$**	**$p = .010$**
Serial 7's	**–0.04 (–0.05, –0.02), $p < .001$**	**–0.03 (–0.06, –0.01), $p = .004$**	$p = .252$
Backwards counting	0.00 (–0.01, 0.00), $p = .205$	–0.01 (–0.02, 0.00), $p = .066$	$p = .469$

Notes: Beta coefficient comes from generalized estimating equations and corresponds to change in cognitive score with 1-y change in time. Results control for baseline age, gender, race, ethnicity, education, number of health conditions, body mass index, Center for Epidemiologic Studies Depression Scale, smoking, drinking, # days drink/week, and # drinks/day. All bolded values denote statistical significance at $p < .05$.

Stratified Results by Baseline Cognitive Functioning

Fifty-nine percent had lower cognitive functioning (n = 2 314, total cognitive score range from 12 to 17) and the remaining 39.2% had higher cognitive functioning (n = 1 551, total cognitive score range from 18 to 27); n = 92 (2.3%) were excluded as their data for HRS 2006 were reported by proxies. Overall, among those with lower cognitive functioning and who received treatment, self-initiated treatment was associated with higher concurrent cognitive functioning for the total cognition score and immediate word recall as compared to no treatment, while we did not see differences for doctor-recommended treatment. Among those with better cognitive performance at baseline, both self-initiated treatment and doctor-recommended treatment were associated with lower concurrent cognitive functioning (Table 4). When examining trajectories of cognition before and after treatment initiation, the periods after sleep treatment for those with the lower cognitive performance at baseline were actually associated with a faster decline in cognitive performance for overall treatment and self-initiated treatment, while there were no statistically significantly different changes for doctor-recommended treatment. Among those with better cognitive performance at baseline, decline in cognitive performance slowed substantially for overall, self-initiated, as well as doctor-initiated treatment (Table 5).

Discussion

Our findings are important because they add to the existing literature regarding the influential role of sleep health on cognition (5–13,16,38,39). We sought to identify the role of sleep treatment on cognitive performance among older adults with sleep disturbances. While we did not find an association between sleep treatment and cognitive performance at the same time, we did find that, longitudinally, initiating treatment was associated with a mitigation in cognitive decline over an 8-year period, suggesting that short-term effects of treatment may be more subtle, whereas long-term effects may become more evident well after treatment. Our findings are clinically significant because we found an impact of treatment on cognition during an 8-year period, and given that dementia may take years if not decades to develop, it is possible our observed effect would be stronger when observed over longer time periods (eg, a decade or more). This mitigation we observed was seen for both self-initiated and doctor-recommended treatment and was particularly strong among those with the higher cognitive functioning at baseline as compared to those with functioning on the lower end. These findings are particularly notable, given the large burden of AD on modern society which has become more profound with the aging of the population (40).

Accelerated cognitive decline and development of dementia affects the lives of not only patients but also their families and caregivers. Thus, there have been efforts by the medical community to find a cure or therapy to prevent or effectively treat the disease. The search for pharmacological options, however, has not been fruitful to date. A number of promising drugs in development (eg, solanezumab) were deemed ineffective in larger clinical trials (41), and even medications which came to market and were approved for use in AD for the most part may be less effective. Donepezil, for example, has been approved for use in AD, although the observed benefits can be quite modest (42). Thus, the optimal therapy for AD and patients at risk of AD remains unclear.

Table 4. Association Between Treatment Type and Concurrent Cognitive Performance Stratified by Baseline Cognitive Functioning, Health and Retirement Study, 2006–2014

Cognitive Score	Total Cognition *B* (95% CI), *p* Value	Immediate Word Recall *B* (95% CI), *p* Value	Delayed Word Recall *B* (95% CI), *p* Value	Serial 7's *B* (95% CI), *p* Value	Backwards Counting *B* (95% CI), *p* Value
Lowest cognitive functioning					
No treatment	Ref.	Ref.	Ref.	Ref.	Ref.
Self-initiated treatment	**0.36 (0.05, 0.66), p = .022**	**0.17 (0.03, 0.30), p = .014**	0.11 (−0.04, 0.27), p = .161	0.06 (−0.07, 0.19), p = .385	0.01 (−0.04, 0.05), p = .770
Doctor-recommended treatment	0.22 (−0.02, 0.46), p = .078	0.05 (−0.05, 0.16), p = .319	0.12 (−0.01, 0.24), p = .071	0.04 (−0.06, 0.15), p = .421	0.00 (−0.04, 0.04), p = .920
Highest cognitive functioning					
No treatment	Ref.	Ref.	Ref.	Ref.	Ref.
Self-initiated treatment	**−0.39 (−0.74, −0.05), p = .026**	−0.15 (−0.31, 0.00), p = .055	−0.10 (−0.28, 0.08), p = .282	**−0.15 (−0.27, −0.04), p = .008**	0.02 (−0.02, 0.05), p = .395
Doctor-recommended treatment	**−0.57 (−0.86, −0.28), p < .001**	**−0.23 (−0.36, −0.10), p = .001**	**−0.23 (−0.38, −0.08), p = .003**	**−0.12 (−0.22, −0.02), p = .016**	0.01 (−0.02, 0.04), p = .478

Notes: Beta coefficient comes from generalized estimating equations and corresponds to association between treatment type and each cognitive test averaged across all years. Results control for time, baseline age, gender, race, ethnicity, education, number of health conditions, body mass index, Center for Epidemiologic Studies Depression Scale, smoking, drinking, # days drink/week, and # drinks/day. All bolded values denote statistical significance at $p < .05$.

Table 5. Trajectories of Cognitive Performance Before and After Sleep Treatment Stratified by Baseline Cognitive Functioning, Health and Retirement Study, 2006–2014

Cognitive Score	Before Sleep Treatment *B* (95% CI), *p* Value	After Sleep Treatment *B* (95% CI), *p* Value	Interaction *p* Value
Lowest cognitive functioning			
Overall treatment			
Total cognition	−0.03 (−0.10, 0.04), $p = .448$	**−0.25 (−0.32, −0.19), $p < .001$**	**$p < .001$**
Immediate word recall	−0.01 (−0.04, 0.03), $p = .627$	**−0.10 (−0.13, −0.08), $p < .001$**	**$p < .001$**
Delayed word recall	0.01 (−0.03, 0.05), $p = .605$	**−0.10 (−0.13, −0.07), $p < .001$**	**$p < .001$**
Serial 7's	−0.03 (−0.06, 0.01), $p = .193$	**−0.04 (−0.07, −0.02), $p = .001$**	$p = .949$
Backwards counting	0.00 (−0.01, 0.01), $p = .702$	0.00 (−0.01, 0.01), $p = .741$	$p = .906$
Self-initiated treatment			
Total cognition	**−0.18 (−0.23, −0.14), $p < .001$**	**−0.26 (−0.35, −0.17), $p < .001$**	$p = .071$
Immediate word recall	**−0.07 (−0.08, −0.05), $p < .001$**	**−0.11 (−0.15, −0.07), $p < .001$**	**$p = .036$**
Delayed word recall	**−0.06 (−0.08, −0.04), $p < .001$**	**−0.12 (−0.17, −0.07), $p < .001$**	**$p = .006$**
Serial 7's	**−0.05 (−0.07, −0.03), $p < .001$**	−0.03 (−0.07, 0.00), $p = .081$	$p = .397$
Backwards counting	**−0.01 (−0.02, 0.00), $p = .003$**	0.00 (−0.01, 0.01), $p = .641$	$p = .124$
Doctor-recommended treatment			
Total cognition	**−0.15 (−0.20, −0.11), $p < .001$**	**−0.23 (−0.31, −0.15), $p < .001$**	$p = .336$
Immediate word recall	**−0.06 (−0.08, −0.04), $p < .001$**	**−0.09 (−0.13, −0.06), $p < .001$**	$p = .113$
Delayed word recall	**−0.07 (−0.10, −0.05), $p < .001$**	**−0.08 (−0.12, −0.04), $p < .001$**	$p = .785$
Serial 7's	**−0.03 (−0.05, 0.00), $p = .016$**	**−0.04 (−0.08, −0.01), $p = .008$**	$p = .980$
Backwards counting	0.00 (−0.01, 0.01), $p = .801$	0.00 (−0.02, 0.01), $p = .469$	$p = .743$
Highest cognitive functioning			
Overall treatment			
Total cognition	**−0.58 (−0.66, −0.50), $p < .001$**	**−0.12 (−0.19, −0.05), $p = .001$**	**$p < .001$**
Immediate word recall	**−0.24 (−0.28, −0.20), $p < .001$**	**−0.05 (−0.08, −0.02), $p = .003$**	**$p < .001$**
Delayed word recall	**−0.25 (−0.30, −0.21), $p < .001$**	**−0.06 (−0.09, −0.02), $p = .004$**	**$p < .001$**
Serial 7's	**−0.08 (−0.10, −0.05), $p < .001$**	−0.01 (−0.03, 0.02), $p = .470$	**$p < .001$**
Backwards counting	**−0.02 (−0.03, −0.01), $p < .001$**	−0.01 (−0.01, 0.00), $p = .097$	**$p = .030$**
Self-initiated treatment			
Total cognition	**−0.42 (−0.47, −0.37), $p < .001$**	−0.08 (−0.18, 0.03), $p = .151$	**$p < .001$**
Immediate word recall	**−0.17 (−0.19, −0.15), $p < .001$**	−0.03 (−0.09, 0.02), $p = .182$	**$p < .001$**
Delayed word recall	**−0.17 (−0.20, −0.15), $p < .001$**	−0.05 (−0.11, 0.00), $p = .068$	**$p < .001$**
Serial 7's	**−0.07 (−0.08, −0.05), $p < .001$**	0.01 (−0.03, 0.05), $p = .608$	**$p < .001$**
Backwards counting	**−0.01 (−0.02, −0.01), $p < .001$**	0.00 (−0.01, 0.01), $p = .510$	**$p = .018$**
Doctor-recommended treatment			
Total cognition	**−0.38 (−0.43, −0.33), $p < .001$**	**−0.14 (−0.23, −0.05), $p = .003$**	**$p < .001$**
Immediate word recall	**−0.15 (−0.17, −0.13), $p < .001$**	**−0.06 (−0.10, −0.02), $p = .005$**	**$p < .001$**
Delayed word recall	**−0.17 (−0.20, −0.14), $p < .001$**	−0.05 (−0.09, 0.00), $p = .057$	**$p < .001$**
Serial 7's	**−0.05 (−0.07, −0.04), $p < .001$**	−0.02 (−0.05, 0.01), $p = .214$	**$p = .019$**
Backwards counting	−0.01 (−0.01, 0.00), $p = .050$	**−0.01 (−0.02, 0.00), $p = .017$**	$p = .326$

Notes: Beta coefficient comes from generalized estimating equations and corresponds to change in cognitive score with 1-y change in time. Results control for baseline age, gender, race, ethnicity, education, number of health conditions, body mass index, Center for Epidemiologic Studies Depression Scale, smoking, drinking, # days drink/week, and # drinks/day. All bolded values denote statistical significance at $p < .05$.

As efforts to find pharmacotherapies for AD have yet to be successful, investigators have searched for "actionable" risk factors that may serve as targets for behavioral intervention efforts for AD, including physical activity, diet, and sleep. These lifestyle factors may account for 40% of dementia cases worldwide (43). While there is uncertainty about whether poor sleep is causal for developing AD, our new findings suggest that sleep issues may be important considerations when optimizing therapy for these patients to improve and/or preserve their cognitive health.

In the context of our main findings, it should be noted that only a third of our sample reported receiving sleep treatment. This result suggests an unmet need for therapies to improve the care of those with sleep disturbances. Findings indicated that individuals who received treatment were on average more likely to be female, Caucasian, report more depressive symptoms, have a higher BMI, and have greater number of health conditions. More research is needed to determine how best to offer these treatments so as to prevent health disparities. Efforts to make treatments more available may also further help in prevention of cognitive decline.

While we did not see associations between treatment type and concurrent cognitive performance, we saw a mitigation of cognitive decline longitudinally following initiating sleep treatment. This finding suggests the benefits of sleep treatment on cognition may accumulate long after treatment began, while the immediate effects are minimal. This warrants further investigation, specifically examining the timing of treatment delivery (whether treatments are used consistently, intermittently, or long-term), and type of treatment or combination of treatments used.

Paradoxically, the protective effect of sleep treatment was seen exclusively in those with higher cognitive functioning at baseline, whereas those with lower cognitive functioning actually showed precipitous declines in performance following treatment. Those with

poorer cognition were likely those at greater risk for subsequent impairment, and cognitive declines after sleep treatment may be explained simply by worsening cognition due to a neurodegenerative disease that was also causing sleep disturbance. It is also possible that sleep treatment was initiated as part of a holistic strategy for memory-related problems introduced when cognitive impairment was significant—it should be noted that sleep problems are commonly seen in those with dementia, including AD (44).

A number of sleep treatments are available. Self-initiated treatments may include use of melatonin, OTC sleep aids, and smartphone applications including mindfulness and sleep tracking applications. While our findings suggest that self-initiated treatment could have the potential to slow cognitive decline, more research is needed to assess the efficacy of specific self-initiated treatments, as well as how use patterns of these treatments over time might also impact cognitive performance trajectories and cognition more broadly. It may also be important to assess characteristics of these treatments that are associated with sustained use over time and that impact on cognitive health. There are also a number of therapies overseen by a doctor that are available depending upon the underlying cause. For example, CBT-I is considered the first-line treatment for many patients with insomnia (45), particularly given the concerns about potential side-effects of pharmacotherapy. Nasal CPAP and mandibular advancement devices are efficacious for patients with OSA (46), although adherence can be a challenge particularly in older patients (47) and those with impaired cognition (48). The HRS question we relied upon to characterize sleep treatment was quite vague and there is considerable uncertainty about the type of treatment received or whether multiple therapies were used (eg, medications and CBT-I). Given the heterogeneity of treatments for various sleep conditions, we support further research into the optimal treatment strategy to preserve cognitive health in later life.

Our study had a number of strengths including a large population-based sample, with extensive follow-up, in a well-characterized population and with a detailed health profile including various domains of cognitive function. However, we acknowledge a number of limitations. First, we do not have granular data regarding sleep treatments as we relied on self-report and could not fully characterize what treatments were actually received. Moreover, the assessment period for receipt of sleep treatment was over the past 2 weeks, and it is possible treatments were received in the prior weeks. Thus, more research is needed to identify the sleep treatments and timing of these treatments that have greatest utility in modulating cognitive decline. Second, our study used observational data and we did not conduct a randomized controlled trial limiting our ability to assess causality. Nonetheless we view the findings as important since such data are critical to optimize the design of a robust randomized trial with adequate follow-up time. We are also supportive of "Big Data" approaches using electronic medical records and other large data sets to address these important questions. Third, although this study used carefully selected cognitive assessments, a number of cognitive tests of importance may also be important to characterize fully the cognitive impact of sleep treatment. As such, we are supportive of more extensive evaluations which may be possible using other data sets or via prospective data collection.

In summary, our study highlights the important role of sleep in cognitive outcomes and suggests that intervention for poor sleep, even in later adulthood, could have the potential to at a very minimum slow cognitive decline. While this study presents promising results, more research is needed to determine which sleep treatments are most effective in mitigating cognitive decline, and fuller assessment of the risks and benefits of various treatment options for other outcomes. These efforts could not only improve sleep health in these individuals but also could have the potential to contribute to AD prevention efforts.

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Conflict of Interest

S.A-I. has previously served as a consultant for Eisai, Merck, Biogen, and Pear. A.P.S. has received payment for serving as a consultant to Merck and from Springer Nature Switzerland AG for Guest Editing Special Issues of *Current Sleep Medicine Reports*. C.N.K., M.W.B., W.K.T., and A.M. declare no conflict of interest.

Author Contributions

C.N.K. conceived the study, analyzed the data, and wrote the manuscript. A.M. wrote the manuscript. M.W.B., W.K.T, A.P.S., and S.A-I. provided feedback on manuscript and analyses.

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