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Modifying pathways by age and sex for the association between combined sleep disordered breathing and long sleep duration with neurocognitive decline in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL)

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Abstract

INTRODUCTION: To determine if obesity or metabolic syndrome (MetS) modifies associations between sleep-disordered breathing (SDB), self-reported sleep duration (SD) and phenotypes of combined SDB/SD with 7-year neurocognitive decline (ND) in a community based-cohort of U.S. Hispanic/Latinos (N=5,500) in different age and sex groups.

METHODS: The exposures were baseline SDB (REI ≥ 15), sleepiness (ESS ≥ 10), SD (<6 hours, 6–9 hours, ≥ 9 hours). The outcome was 7-year ND.

RESULTS: Mean age was 56.0 years, 54.8% females. Obesity modified the association between SDB/SD and ND in memory (F=21.49, p<0.001), global cognition (F=9.14, p<0.001) in the oldest age group. Women without MetS with combined long sleep/SDB exhibited most pronounced decline in global cognition (F=3.07, p=0.010).

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DISCUSSION: The association between combined SDB/long sleep and declines in memory and global cognition was most pronounced in obese older adults. Among women, MetS status modified the association between long sleep/SDB and decline in global cognition.

Keywords

Cohort Studies; sleep; Neurocognitive decline; Age; Sex; Risk factors in epidemiology; Hispanic/Latino

1. INTRODUCTION

The median age of the world's population is rising rapidly [1]. In the United States, the proportion of the population aged ≥65-years is projected to grow from 12.4% in 2000 to 19.6% in 2030 [2]. Older age is associated with sleep problems; in fact, more than half of adults over the age of 65 years report at least one sleep complaint [3]. Poor sleep quality in older adults is linked with neurocognitive decline [4] and incident dementia [5]. The literature on older adults with chronic insomnia further suggests a high incidence of cognitive impairment, particularly on measures of executive function [6, 7]. Poor sleep quality can predict declines on simple measures of memory and global cognitive functioning in older adults at one year of follow-up [8]. Sleep disordered breathing (SDB), insomnia and sleep duration (SD) associates with increased risk of Alzheimer's disease (AD) [9] in recent meta-analyses. Given that neurocognitive function is the most important predictor of functional ability and quality of life in older adults [10], it is critically important to uncover the nuances associated with sleep-related neurocognitive decline in order to develop targeted interventions in at risk-groups.

Common correlates of SDB and short sleep in older adults include the metabolic syndrome (MetS) and some of its components (i.e. obesity, hypertension, and diabetes mellitus) [11–14]. Hispanic/Latinos [19] have significantly higher risk for MetS [20] and a 4-fold risk for Alzheimer's disease and Related Dementias (ADRD) compared to non-Hispanic whites [21]. Longitudinal research has also demonstrated that symptoms of insomnia and SDB predict incident MetS after three years [15]. We also observed strong associations between short SD and daytime napping with obesity in our diverse cohort of Hispanic/Latino adults [16]. MetS is a strong predictor of neurocognitive decline [17, 18], therefore it is important to examine the sleep characteristics modified by MetS that affects cognition.

Our prospective data also showed a higher prevalence of MetS and obesity among older Hispanic/Latino adults aged >65 years [24]. Despite these findings, there is a paucity of research directly examining the metabolic pathways through which sleep measures predict neurocognitive decline across different age and sex groups, especially among vulnerable Hispanic/Latino participants. Our published data reported a high prevalence of sleep disorders [25, 26] associated with neurocognitive dysfunction and decline [27] in a diverse sample of Hispanic/Latino participants [28]. The current study builds upon previous observation by examining the effect modification of MetS and obesity on the relationship between sleep phenotypes and neurocognitive dysfunction and decline in Hispanic/Latino adults within different age and sex groups. We hypothesize that MetS and obesity modify the

associations between sleep phenotypes and neurocognitive function and decline differently between age and sex groups. Due to the high prevalence of insomnia and extremes of SD in individuals with SDB [29] we examined combined phenotypes of SDB/SD as our primary exposures.

2. METHODS

2.1 Population:

We analyzed data from participants of *Study of Latinos-Investigation of Neurocognitive Aging* (SOL-INCA), an ancillary study of the *Hispanic Community Health Study/Study of Latinos* (HCHS/SOL). Additional information about design and scientific rationale of SOL-INCA have been previously published [30]. Details about HCHS/SOL study design and data collection have been described elsewhere [31, 32] and are publicly available: https://sites.cscc.unc.edu/hchs/. Briefly, the initial sample of 16,145 Hispanic/Latino aged 18–74 years underwent Visit-1 (V1) examination (2008 to 2011) in four U.S. field centers (Chicago, IL; Miami, FL; Bronx, NY; San Diego, CA). Eligible participants self-identified as Hispanic/Latino background. At baseline, we gathered information on sleep disorders, demographics, socioeconomic status, lifestyle habits (smoking, physical activity), medical history and biological measures (e.g., anthropometrics, blood draw). Neurocognitive function was also obtained at baseline (n=9,623) in participants 45–75 years-old.

SOL-INCA is an ancillary study designed to evaluate the prevalence and determinants of neurocognitive decline and disorders in HCHS/SOL. SOL-INCA data (2015 to 2018) was collected concurrent with HCHS/SOL Visit-2 (V2), (2014 to 2017). All participants provided informed consent and the study was approved by the institutional review board for each institution.

2.2 Outcomes: Description of Neurocognitive test, at baseline and follow-up:

Neurocognitive tests administered at baseline and follow up were described elsewhere [33]. Briefly, we administered (1) Six-Item Screener (**SIS**; mental status); (2) Brief Spanish English Verbal Learning Test (B-**SEVLT**; verbal episodic learning and memory); (3) Controlled Oral Word Association (or Word Fluency; **WF**; verbal fluency) Test of the Multilingual Aphasia Examination; and (4) Digit Symbol Subtest (**DSS**; processing speed) at V1 and during V2, which took place at approximately 7-years post initial evaluation. To evaluate neurocognitive decline, SOL-INCA repeated the above neurocognitive battery at V2 and also administered the Trail Making Test parts A and B (**TMT**). For the consistently assessed cognitive measures a change score indicator was generated using regression-based techniques. These change scores were calculated using survey linear regression to predict cognitive performance at V2 as a function of V1 cognitive performance, adjusting for age, education, and lapsed time (in days) between cognitive assessments.

2.3 Main Exposures: Description of sleep variables:

V1 sleep quality was assessed using a self-report questionnaires and objective measures of sleep disordered breathing. The sleep heart health study **S**leep Habits questionnaire evaluates weekday and weekend bedtime and wake time, napping behaviors, as well as

related SDB symptoms (snoring, witnessed apneas) [25]. The following questions were used to determine SD: *What time do you usually go to bed?* and *What time do you usually wake up?* Average SD was computed as the weighted average of weekday and weekend sleep [26]. We also categorized SD into short SD (<6 hours), intermediate SD (6–9 hours) and long SD (>9 hours) [19, 34]. HCHS/SOL also obtained the Epworth Sleepiness Scale (ESS) [35], insomnia was assessed with the Women's Health Initiative Insomnia Rating Scale (WHIIRS) [36], as a continuous variable ranging from 0 – 20 and a binary variable of insomnia (yes vs. no) based on a score ≥10. All questionaires were administered in English or Spanish, based on participant's preference.

Information about SDB [25] was collected using the ARES Unicorder 5.2; B-Alert (Carlsbad, CA). Sleep records were scored at the HCHS/SOL Sleep Reading Center. Respiratory events were identified as a 50% or greater reduction in airflow lasting greater than or equal to 10 seconds with desaturations greater than or equal to 3% and defined as the respiratory event index (REI). SDB was used as a continuous variable and dichotomized with an REI ≥15.

The specific exposures analyzed in this study were: REI, Sleepiness, SD, combined Sleepiness/REI and combined SD/REI.

2.4 Definition of age and sex groups:

Age in years and sex were determined by self-report at baseline. For subsequent analyses participants were grouped into younger adults (aged 45–54 years), middle aged adults (aged between 55–64 years) and older adults (aged 65–74 years).

Metabolic Modification Variables: Obesity and MetS were derived from component variables at baseline. Obesity was operationalized as a dichotomous variable with categories grouping underweight/normal/overweight (BMI <29.9 kg/m^2) and obese (BMI 30+ kg/m^2). MetS was also operationalized as a binary variable (MetS present/not present) using the International Diabetes Federation definition [37].

Main Covariates: Time lapse between V1 sleep assessments and SOL-INCA cognitive testing, depressive symptoms using the Center for Epidemiologic Studies Depression scale (CESD-10) [38] and self-reported frequency of sleep medication use in the past 4 weeks were included in subsequent data analyses models as covariates. All models also controlled for Field Center site.

2.5 Analytical Subpopulation.

SOL-INCA enrolled 6,377 HCHS/SOL participants out of the 9,714 participants aged 45–74 years. For the current study, we excluded participants who did not participate in the baseline sleep module, participants who reported a stroke or transient ischemic attack at baseline, individuals with an SIS ≤3 at V1 and participants with missing values on any of the covariates of interest. The final analytic sample size was 5,500. Excluded participants had similar sex and education distributions but were older (64.9 years vs. 63-years; p <0.001) than those in the analytic sample.

2.6 Statistical Analysis.

SOL-INCA cognitive outcomes were z-scored (generated using [Y_I-*Mean* Y_i]/*Standard Deviation*) for analyses[28]. To examine modification in associations between sleep exposures and cognitive performance at SOL-INCA by categorical age and sex, we fit survey linear regression models with two-way interactions between age, sex and sleep exposures. Age interaction models were adjusted for sex, CESD-10, sleep medication usage, and field center site; sex interaction models were adjusted for age, CESD-10, sleep medication usage, and Field Center site. Change scores for repeated cognitive tests were estimated using survey linear regression to predict cognitive performance at SOL-INCA as a function of baseline cognitive performance, adjusting for age, education, and lapsed time (in days) between cognitive assessments [21]. Test specific standardized measures of change were subsequently calculated using $T2 - T2_{pred}/SEE$ where $T2$ was the respondent cognitive score at SOL-INCA, $T2_{pred}$ their predicted score and SEE is the standard error of the regression estimator [28]. Subsequently, we used survey linear regression with interactions between age, sex, and sleep exposures to independently examine the modification in associations between each sleep phenotype and the standardized measures of cognitive change. The *z*-scores that represented change in performance over time were calculated using a regression-based approach that accounted for age and education and therefore these variables were not included as covariates in the analytic models. Covariate adjustments in the models remained the same as the models for cognitive performance at SOL-INCA.

Post-hoc estimates of adjusted marginal means and their 95% confidence intervals were calculated for cognitive performance and cognitive change. ANOVA-based contrasts were used to test differences between sleep phenotypes over age groups.

Lastly, the SOL-INCA target population was stratified by sex (female/male) and age (<65 years and ≥65 years) groups independently. Within each stratum, we used survey linear regression to test interactions between (1) obesity and (2) MetS, independently, and sleep exposures to examine cardiometabolic modifications in the associations between each sleep phenotype and (1) cognitive performance at SOL-INCA and (2) cognitive change. In line with the above described models, we maintained the same covariates adjustment. Post-hoc estimates of crude and adjusted marginal means and their 95% confidence intervals derived from these models were calculated along with the ANOVA-based contrasts to examine differences in cognitive outcomes over sleep and cardiometabolic risk groups. We developed a dynamic dashboard using the R package `*Shiny*`to visualize the marginal means and contrasts. The dashboard allows users to view all combinations of marginal estimates and contrasts by selecting the stratifying variable (age or sex groups), cognitive outcome (cognitive performance or change), metabolic modifier (obesity or MetS), and sleep exposure of interest. The dashboard can be accessed permanently at https://solincalab.shinyapps.io/esanar2/.

3. RESULTS

Demographic and clinical characteristics of the target population are presented in Table 1. The mean age at SOL-INCA was 63±8.1 years. More than half were females (54.8%) and a large proportion had <12-years education (37.8%). Seventeen percent of the population had

REI ≥ 15, 1-in-5 had daytime sleepiness, one third had insomnia but 83.6% did report use of sleep medication in the past 4 weeks, 6.43% had short SD (<6 hours) and 14.81% percent had long (>9 hours) SD.

3.1 Cognitive performance.

Results are summarized in Figures 1A/B and Table 2. We found significant age modifications in the association between SD/REI phenotype and B-SEVLT-Recall ($p_{obesity}$=0.018; p_{MetS}=0.013). The worst performance in memory was seen among individuals age ≥65 years who had long sleep and REI ≥15 [$\Delta_{obesity}$ = −1.58 (SE =0.38), p<0.001; Δ_{MetS} = −1.57 (SE =0.38), p<0.001] relative to the youngest group. We also found that individuals age ≥65 who had long sleep and REI ≥15 had the worst performance in global cognition [$\Delta_{obesity}$ = −1.19 (SE =0.36), p=0.001; Δ_{MetS} = −1.17 (SE =0.37), p=0.001] relative to the youngest group, although the overall interaction with age was not statistically significant ($p_{obesity}$=0.108; p_{MetS}=0.141). Age also modified the association between the SD/REI phenotype and DSS ($p_{obesity}$=0.059; p_{MetS}=0.055). Individual age ≥65 with short sleep and REI ≥15 showed the worst performance in the DSS [$\Delta_{obesity}$ = −1.23 (SE =0.23), p<0.001; Δ_{MetS} = −1.24 (SE =0.25), p<0.001], relative to the youngest age group.

Finally, age also modified the associations between the Sleepiness/REI phenotype and DSS ($p_{obesity}$=0.006; p_{MetS}=0.008). Individuals age ≥65 years had worse performance regardless of Sleepiness/REI phenotype. However, older aged participants (≥65 years) who reported no excessive sleepiness and REI <15 had the worst performance on DSS relative to their younger age counterparts [Δ = −counterparts [$\Delta_{obesity}$= −1.13 (SE =0.14), p<0.001; Δ_{MetS} = −1.11 (SE =0.14), p<0.001].

3.2 Cognitive Change.

Results are summarized in Figures 2A/B and Table 3. Age modified the associations between SD/REI phenotype and change in memory (B-SEVLT-Recall; $p_{obesity}$=0.036; p_{MetS}=0.030) and processing speed (DSS; $p_{obesity}$=0.018; p_{MetS}=0.012). Older individuals (ages (≥65 years) with long SD and REI ≥15 had more pronounced decline in B-SEVLT-Recall [$\Delta_{obesity}$ = −1.00 (SE =0.42), p=0.016; Δ_{MetS} = −1.00 (SE =0.42), p=0.017], and global cognition, relative to their younger aged counterparts. Age also modified the associations between SD and change in DSS (p_{MetS}=0.046), but we found no statistical evidence to support modifications in change in memory or global cognition.

We found no statistical evidence that sex modified associations between the sleep exposures and cognitive performance (Supplemental Table 1).

3.3 Metabolic modifications

MetS and obesity modifications—Obesity and MetS did not significantly modify any of the associations between sleep exposures and cognitive outcomes in the overall target population (Supplemental Tables 4 and 5).

Age specific—Results for the tested modifications in the associations between sleep exposures and cognitive outcomes by obesity and MetS within age groups are presented in

Supplemental Figures 1–7 and Supplemental Tables 6 (marginal estimates) and 7 (contrast of marginal estimates). The MetS modified the associations between SD/REI phenotype and both change in memory (p=0.021) (Supplemental Figure 1), processing speed (p=0.003) (Supplemental Figure 2) and global cognition (p<0.001) (Supplemental Figure 3) among younger middle-aged (45–54 years) individuals. In this age group, individuals not meeting criteria for MetS who had long sleep and REI≥15 had significantly more pronounced decline across processing speed and global cognition, and to a less consistent extent in memory, compared to age matched individuals both with and without MetS. Among older individuals (≥65 years), obesity modified the associations between SD/REI phenotype and both change in memory (p<0.001) (Supplemental Figure 4) and global cognition (p<0.001) (Supplemental Figure 5). In particular, individuals who were not obese and had short sleep and REI ≥15 had more pronounced decline in memory and global cognition compared to both other obese as well as non-obese counterparts. Furthermore, older obese individuals who had long sleep and REI ≥15 were consistently more likely to decline in memory and global cognition compared to other age matched obese individuals across the spectrum of SD/REI phenotype. Lastly, in the older cohort, we also found that obesity modified the association between SD and memory (p=0.001) (Supplemental Figure 6) whereby obese individuals reporting longer SDs had more pronounced decline in memory compared to their non-obese counterparts. We found no consistent evidence for modifications in associations between sleep exposures and executive function through obesity or the MetS.

Sex specific—Obesity status and MetS did not significantly modify associations between sleep exposures and cognitive outcomes among either males or females. However, we found some notable differences in how MetS influences the associations between SD/REI phenotype and change in global cognition (p=0.010) (Supplemental Figure 7) among females. In particular, women not meeting criteria for MetS who had long sleep and REI ≥15 had more pronounced declines in global cognitive function compared to all other considered groups with and without MetS.

4. DISCUSSION

We found that combined SDB/extremes of SD (<6 hours and >9 hours) were associated with poorer performances on measures of processing speed, mental flexibility and verbal memory in our diverse sample of middle-aged and older Hispanics/Latinos. In addition, these sleep phenotypes predicted declines in verbal memory and processing speed at 7-year follow up. We further demonstrated that age, but not sex differences, significantly modified these relationships. In particular, these sleep measures predicted accelerated neurocognitive decline in participants who were age ≥65 years at V1. More importantly, we highlight important age and sex differences in the ways in which MetS and obesity modify the relationships of these sleep phenotypes with neurocognitive function and decline. Specifically, younger middle-aged individuals (50–64 years) with long SD and REI ≥15 without MetS had significant declines in executive function, global cognition, and memory. However, among adults aged ≥65 years, obesity modified the relationships between combined long sleep and REI ≥15 phenotype with declines in memory and global cognition. Furthermore, females with combined long SD and REI ≥15 without MetS exhibited decline

in all cognitive measures when compared to males with and without MetS as well as females with MetS. The results were significant after stringent control for cardiovascular risk, depression and use of sleep medications. These results contrast with prior studies demonstrating attenuated effects of self-reported sleep apnea risk on cognition in older adults, ≥70 years [22]. However, other research has demonstrated a significant relationship between poor sleep efficiency and working memory task in older adults aged >60 years [39]. The literature thus appears to suggest a complex relationship between sleep quality and cognition across the lifespan, with possible accelerated declines in older adults' age ≥65 years from diverse Hispanic/Latino backgrounds.

A key finding involves the modification effects of MetS and obesity on the relationships between sleep phenotypes and neurocognitive function and decline in different age groups. Specifically, the relationship between long SD and REI ≥15 with 7-year neurocognitive declines was stronger in middle-aged adults without MetS and in the obese older adults (≥65 years). These appear to contradict published work highlighting an effect of MetS on memory in middle age [40]. SDB in middle-age has been found to independently predict development of insulin resistance syndrome [42], even when controlling for the effects of obesity [43]. It is possible that SDB worsened insulin resistance in middle age and predicts subsequent neurocognitive decline in our sample independent of MetS.

An additional finding involved the association between the long SD/REI ≥15 phenotype and decline in all cognitive domains among females without MetS. Non-human models of sleep and cognition have demonstrated sex differences in hippocampal kynurenic acid, a key N-Methyl-D-Aspartate (NMDA) antagonist after sleep deprivation [45]. Women have a unique sleep phenotype characterized by shorter apneas, lower arousal threshold and greater desaturation per arousal [46]. These findings are reportedly independent of age and obesity. It is possible that the combined long SD/ REI ≥15 phenotype could be indicative of a unique autonomic responsive SDB phenotype that drives cognitive decline in women without the competing influence of MetS.

A strength of our study is the large sample of middle-aged and older Hispanic/Latinos from different countries of origin, who are generally underrepresented in studies of sleep risk factors for neurocognitive decline. In addition, we employed stringent controls for covariates that may be associated with markers of poor sleep and neurocognitive decline. The study also had several limitations. First, there are a limited number of measures available for SDB assessment from the home sleep apnea test, preventing evaluation of arousal, sleep architecture and central sleep apnea. Secondly, as SD was a self-report measure, the variable could be subject to reporting bias. However, a separate study has demonstrated that individuals who report long SD spend more time asleep and in bed as measured by actigraphy and polysomnography [47]. Third, HCHS/SOL was designed to address gaps in research associated with U.S. Hispanic/Latino health. However, factors such as low health literacy, low education and the implementation of cultural specific protocols may serve as unknown confounders. Importantly, the chosen questionnaires are available and validated in Spanish and English.

4.1 Conclusion

In the largest longitudinal study of U.S. Hispanic/Latinos, the SDB and long SD phenotype experience 7-year neurocognitive decline, especially in middle-aged individuals without MetS, women without MetS and obese older adults. Our findings highlight the importance of a precision medicine approach that takes into account possible differential trajectories of cognitive decline by metabolic risk factors, age and sex among vulnerable Hispanic/Latino participants who exhibit poor sleep. Finally, our use of combined SDB/SD as well as sleepiness phenotypes is unique and may yield important information about nuanced relationships between sleep and cognitive decline. A future direction would be to examine the effect of race/ethnicity as a potential modifier of the relationships between sleep phenotypes and neurocognitive decline in a multi-ethnic dataset to highlight potential sleep and health disparities in diverse ethnic/racial groups.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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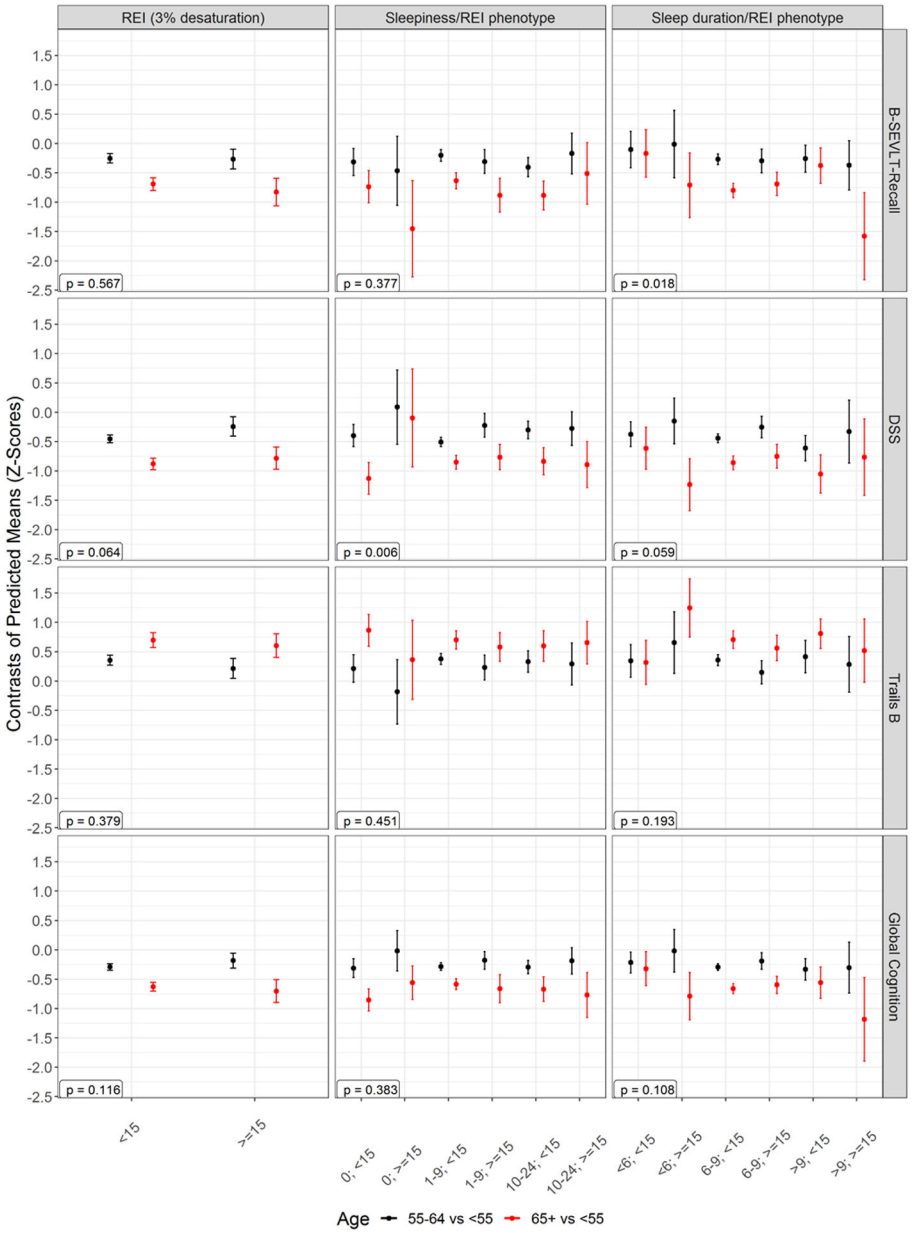

Figure 1A.

Contrasts of predictive margins for cognitive performance at SOL-INCA adjusting for obesity.

Notes:

REI: Respiratory Event Index; B-SEVLT: Brief-Spanish English Verbal Learning Test; DSS: Digit Symbol Substitution

Age <55 is 50–54 given the target population.

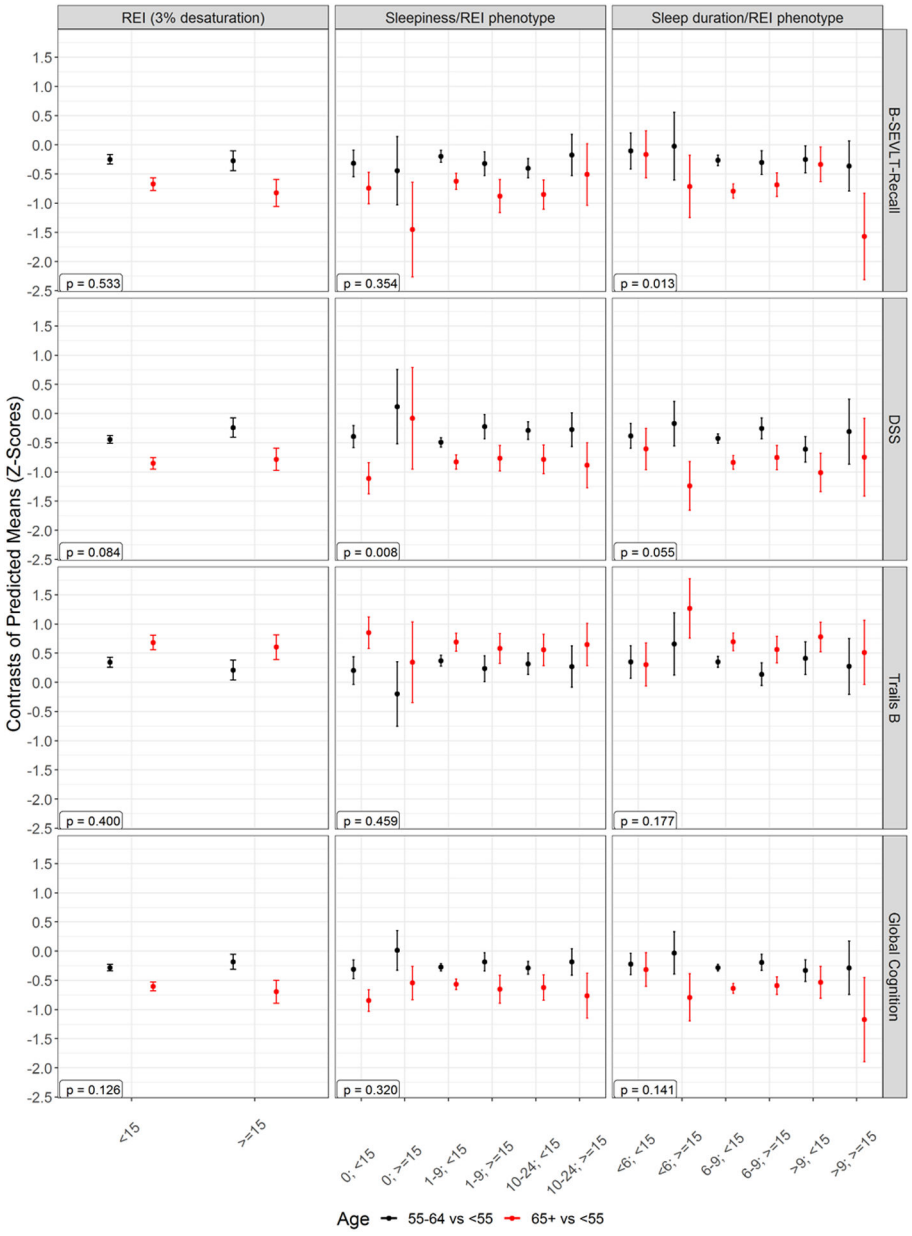

Figure 1B.

Contrasts of predictive margins for cognitive performance at SOL-INCA adjusting for MetS.

Notes:

REI: Respiratory Event Index; B-SEVLT: Brief-Spanish English Verbal Learning Test; DSS: Digit Symbol Substitution

Age <55 is 50–54 given the target population.

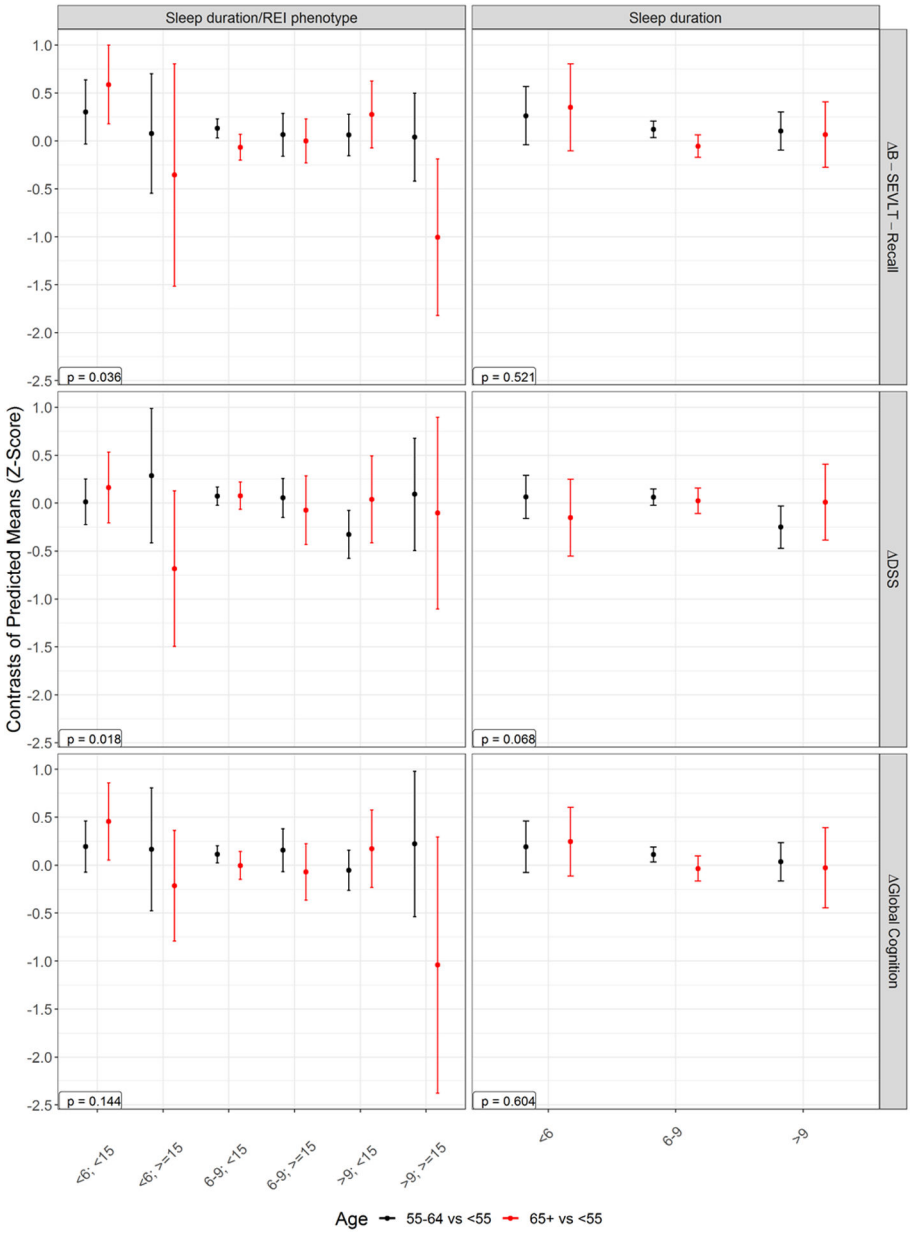

Figure 2A.

Contrasts of predictive margins for change in cognitive performance adjusting for obesity.

Notes:

REI: Respiratory Event Index; B-SEVLT: Brief-Spanish English Verbal Learning Test; DSS: Digit Symbol Substitution

Age <55 is 50–54 given the target population.

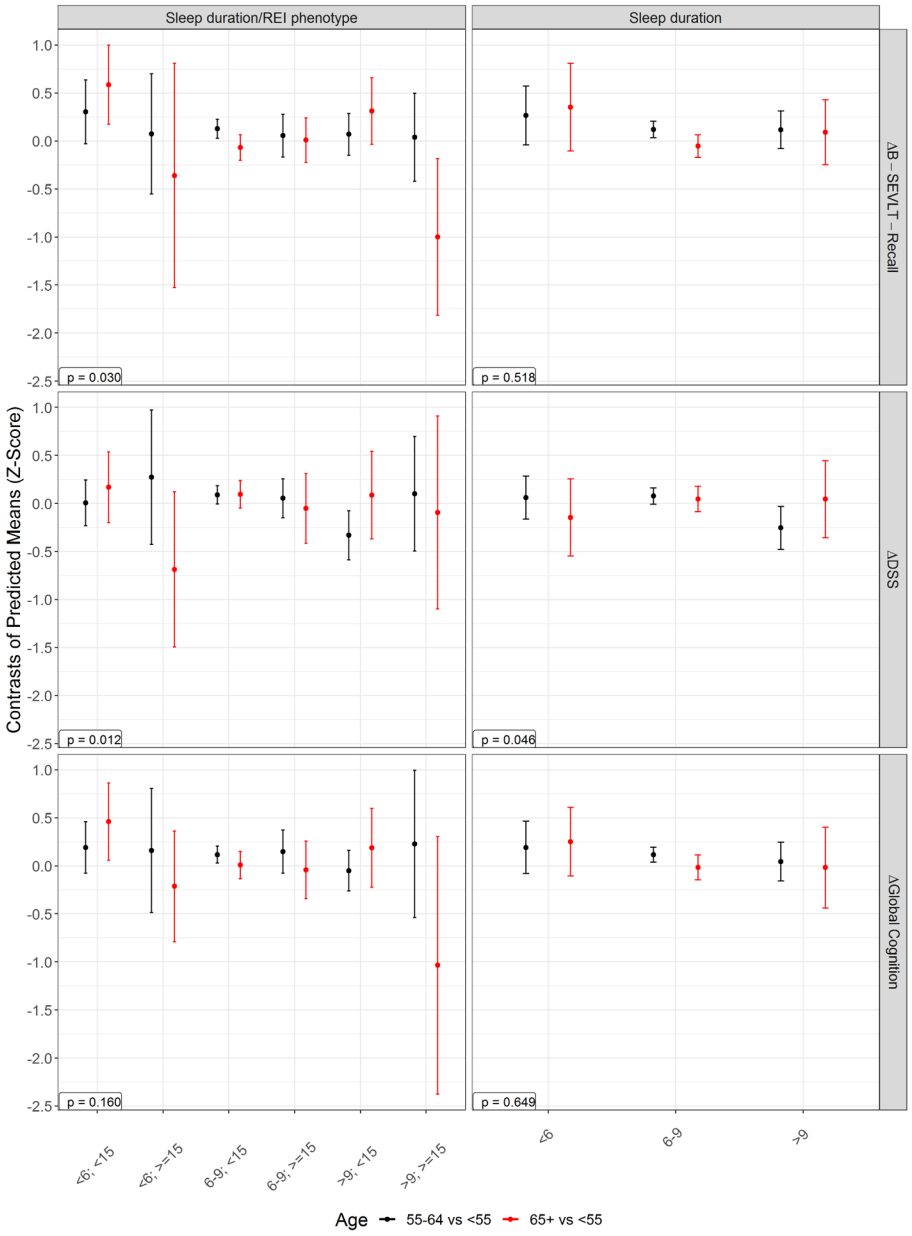

Figure 2B.

Contrasts of predictive margins for change in cognitive performance adjusting for MetS.

Notes:

REI: Respiratory Event Index; B-SEVLT: Brief-Spanish English Verbal Learning Test; DSS: Digit Symbol Substitution

Age <55 is 50–54 given the target population.

Table 1.

Demographics, vascular risk score, and sleep characteristics of the HCHS/SOL and SOL-INCA. Unweighted n = 5,500.

	%(SE)
Education	
Less than HS	37.68 (1.12)
HS or equivalent	21.55 (0.83)
Greater than HS	40.77 (1.07)
Sex	
Female	55.00 (0.93)
Male	45.00 (0.93)
Ethnicity	
Dominican	9.41 (0.77)
Central American	6.95 (0.55)
Cuban	24.34 (1.96)
Mexican	36.02 (1.80)
Puerto-Rican	14.41 (0.83)
South American	4.93 (0.38)
Other	3.94 (0.50)
Sleep medication frequency	
Not in the past 4 weeks	83.62 (0.79)
Less than once a week	3.06 (0.39)
1–2 times a week	3.20 (0.30)
3–4 times a week	2.19 (0.29)
5+ times a week	7.92 (0.55)
Obesity	
Underweight	59.42 (0.94)
Obese	40.58 (0.94)
MetS	
No	47.73 (0.98)
Yes	52.27 (0.98)
REI	
<15	82.74 (0.79)
>=15	17.26 (0.79)
Sleepiness (3 category)	
No Sleepiness (ESS = 0)	10.14 (0.60)
Mild Sleepiness (ESS 1–9)	69.49 (0.90)
Severe Sleepiness (ESS 10–24)	20.36 (0.86)
Sleep Phenotypes	
Short/No Insomnia	3.48 (0.35)
Short/Insomnia	2.99 (0.30)
Average/No Insomnia	53.84 (0.99)

Average/Insomnia	24.97 (0.80)
Long/No Insomnia	8.98 (0.61)
Long/Insomnia	5.74 (0.47)
Insomnia	
No	66.18 (0.88)
Yes	33.82 (0.88)
Sleep Duration (hours/day)	
<6	6.43 (0.45)
6 to 9	78.76 (0.80)
9+	14.81 (0.72)
Sleepiness/AHI Phenotype	
0; <15	8.93 (0.53)
0; >=15	1.21 (0.25)
1–9; <15	58.24 (0.95)
1–9;>=15	11.39 (0.61)
10–24;<15	15.71 (0.75)
10–24>=15	4.52 (0.43)
SD/REI Phenotype	
Short; <15	4.98 (0.38)
Short; >=15	1.51 (0.23)
Average; <15	65.62 (0.91)
Average; >=15	13.39 (0.74)
Long; <15	12.09 (0.65)
Long; >=15	2.42 (0.34)
	Mean (SD)
Age at INCA (years)	62.98 (8.05)
CESD-10	7.27 (6.31)
Time from baseline to sleep study (days)	−11.77 (44.08)
Time from sleep to inca study (days)	2541.54 (436.03)
REI Continuous (3%)	8.70 (13.34)

Notes

Abbreviations: HCHS/SOL= Hispanic Community Health Study/Study Of Latinos; SOL-INCA= Study Of Latinos -Investigation of Neurocognitive Aging;

SE = standard error; SD = standard deviation

HS= High School; REI=Respiratory Event Index; SD= Sleep Duration; CESD-10= Center for Epidemiological Studies of Depression 10-item; MetS = Metabolic Syndrome

Subpopulation: Participation in INCA, No prevalent Stroke/TIA, No mental status impairment, No missingness on age, education, CESD-10, obesity, and sleeping pill usage.

Table 2.

Test results and marginal estimates for the age modifications in associations between sleep risks and cognitive performance.

	Cognitive Performance	
	Obesity[A]	MetS[B]
REI >=15		
B-SEVLT-Recall	**p-value=0.5673; F statistics=0.57; DF=2.00**	**p-value=0.5327; F statistics=0.63; DF=2.00**
DSS	**p-value=0.0639; F statistics=2.76; DF=2.00**	**p-value=0.0841; F statistics=2.49; DF=2.00**
Trails B	**p-value=0.3790; F statistics=0.97; DF=2.00**	**p-value=0.4007; F statistics=0.92; DF=2.00**
Global Cognition	**p-value=0.1155; F statistics=2.17; DF=2.00**	**p-value=0.1259; F statistics=2.08; DF=2.00**
Sleepiness /REI Phenotype		
B-SEVLT-Recall	**p-value=0.3767; F statistics=1.08; DF=10.00**	**p-value=0.3538; F statistics=1.11; DF=10.00**
DSS	**p-value=0.0062; F statistics=2.49; DF=10.00**	**p-value=0.0081; F statistics=2.41; DF=10.00**
ESS = 0 / REI <15 and Ages <55	0.34 [0.23;0.45]	0.33 [0.22;0.44]
ESS = 0 / REI <15 and Ages 55–64	−0.06 [−0.22;0.11]	−0.06 [−0.22;0.11]
ESS = 0 / REI <15 and Ages 65+	−0.79 [−1.03;−0.54]	−0.78 [−1.02;−0.53]
ESS = 0 / REI ≥15 and Ages <55	−0.15 [−0.57;0.27]	−0.15 [−0.57;0.28]
ESS = 0 / REI ≥15 and Ages 55–64	−0.06 [−0.50;0.39]	−0.03 [−0.47;0.42]
ESS = 0 / REI ≥15 and Ages 65+	−0.24 [−0.97;0.49]	−0.23 [−0.99;0.53]
ESS 1–9 / REI <15 and Ages <55	0.42 [0.36;0.49]	0.41 [0.35;0.48]
ESS 1–9 / REI <15 and Ages 55–64	−0.08 [−0.15;−0.01]	−0.08 [−0.15;−0.01]
ESS 1–9 / REI <15 and Ages 65+	−0.43 [−0.54;−0.32]	−0.42 [−0.53;−0.30]
ESS 1–9 / REI ≥15 and Ages <55	0.18 [0.04;0.32]	0.19 [0.05;0.33]
ESS 1–9 / REI ≥15 and Ages 55–64	−0.05 [−0.20;0.11]	−0.03 [−0.19;0.13]
ESS 1–9 / REI ≥15 and Ages 65+	−0.59 [−0.75;−0.42]	−0.57 [−0.74;−0.41]
ESS 10–24 / REI <15 and Ages <55	0.28 [0.16;0.39]	0.26 [0.14;0.37]
ESS 10–24 / REI <15 and Ages 55–64	−0.03 [−0.14;0.09]	−0.03 [−0.14;0.08]
ESS 10–24 / REI <15 and Ages 65+	−0.56 [−0.77;−0.35]	−0.53 [−0.75;−0.30]
ESS 10–24 / REI ≥15 and Ages <55	0.43 [0.27;0.58]	0.45 [0.30;0.60]
ESS 10–24 / REI ≥15 and Ages 55–64	0.15 [−0.10;0.40]	0.17 [−0.08;0.43]
ESS 10–24 / REI ≥15 and Ages 65+	−0.46 [−0.82;−0.11]	−0.44 [−0.79;−0.09]
Trails B	**p-value=0.4510; F statistics=0.99; DF=10.00**	**p-value=0.4588; F statistics=0.98; DF=10.00**
Global Cognition	**p-value=0.3830; F statistics=1.07; DF=10.00**	**p-value=0.3202; F statistics=1.15; DF=10.00**
Sleep Duration/ REI Phenotype		
B-SEVLT-Recall	**p-value=0.0184; F statistics=2.16; DF=10.00**	**p-value=0.0134; F statistics=2.26; DF=10.00**
Short Sleep / REI <15 and Ages <55	0.13 [−0.14;0.40]	0.13 [−0.14;0.40]
Short Sleep / REI <15 and Ages 55–64	0.03 [−0.17;0.23]	0.03 [−0.18;0.23]
Short Sleep / REI <15 and Ages 65+	−0.04 [−0.34;0.26]	−0.03 [−0.33;0.27]
Short Sleep / REI ≥15 and Ages <55	0.31 [0.01;0.62]	0.34 [0.03;0.64]
Short Sleep / REI ≥15 and Ages 55–64	0.30 [−0.18;0.77]	0.31 [−0.17;0.80]
Short Sleep / REI ≥15 and Ages 65+	−0.40 [−0.87;0.07]	−0.38 [−0.83;0.07]

Cognitive Performance		
	Obesity[A]	**MetS**[B]
Average Sleep / REI <15 and Ages <55	0.34 [0.29;0.40]	0.34 [0.28;0.40]
Average Sleep / REI <15 and Ages 55–64	0.07 [0.00;0.15]	0.07 [−0.00;0.15]
Average Sleep / REI <15 and Ages 65+	−0.46 [−0.57;−0.35]	−0.45 [−0.57;−0.34]
Average Sleep / REI ≥15 and Ages <55	0.34 [0.21;0.47]	0.35 [0.23;0.48]
Average Sleep / REI ≥15 and Ages 55–64	0.04 [−0.12;0.20]	0.05 [−0.11;0.21]
Average Sleep / REI ≥15 and Ages 65+	−0.35 [−0.50;−0.20]	−0.33 [−0.49;−0.17]
Long Sleep / REI <15 and Ages <55	0.14 [−0.01;0.30]	0.14 [−0.02;0.30]
Long Sleep / REI <15 and Ages 55–64	−0.11 [−0.28;0.06]	−0.11 [−0.28;0.06]
Long Sleep / REI <15 and Ages 65+	−0.23 [−0.49;0.03]	−0.19 [−0.44;0.06]
Long Sleep / REI ≥15 and Ages <55	0.27 [−0.04;0.57]	0.28 [−0.04;0.61]
Long Sleep / REI ≥15 and Ages 55–64	−0.10 [−0.39;0.18]	−0.08 [−0.37;0.21]
Long Sleep / REI ≥15 and Ages 65+	−1.31 [−1.99;−0.63]	−1.28 [−1.96;−0.61]
DSS	**p-value=0.0594; F statistics=1.79; DF=10.00**	**p-value=0.0547; F statistics=1.82; DF=10.00**
Trails B	**p-value=0.1934; F statistics=1.36; DF=10.00**	**p-value=0.1769; F statistics=1.4; DF=10.00**
Global Cognition	**p-value=0.1077; F statistics=1.58; DF=10.00**	**p-value=0.1408; F statistics=1.49; DF=10.00**
Sleep Duration (3 Categories)		
B-SEVLT-Recall	**p-value=0.1028; F statistics=1.94; DF=4.00**	**p-value=0.1007; F statistics=1.95; DF=4.00**
DSS	**p-value=0.4095; F statistics=1; DF=4.00**	**p-value=0.4531; F statistics=0.92; DF=4.00**
Trails B	**p-value=0.7369; F statistics=0.5; DF=4.00**	**p-value=0.7473; F statistics=0.48; DF=4.00**
Global Cognition	**p-value=0.3449; F statistics=1.12; DF=4.00**	**p-value=0.4484; F statistics=0.93; DF=4.00**

Notes:

Marginal estimates are only provided for the age modifications that were significant.

A: Models are adjusted for sex, CESD-10, obesity, sleeping pill usage, and Field Center.

B: Models are adjusted for sex, CESD-10, MetS, sleeping pill usage, and Field Center.

Abbreviations: REI=Respiratory Event Index; SD= Sleep Duration; B-SEVLT=Brief-Spanish English Verbal Learning Test; DSS= Digit Symbol Substitution test; DF = degrees of freedom.

Age <55 is 50–54 given the target population.

Table 3.

Test results and marginal estimates for the age modifications in associations between sleep risks and cognitive change.

Cognitive Change		
	Obesity	**MetS**
REI >=15		
Δ B-SEVLT-Recall	**p-value=0.3876; F statistics=0.95; DF=2.00**	**p-value=0.3999; F statistics=0.92; DF=2.00**
Δ DSS	**p-value=0.2729; F statistics=1.3; DF=2.00**	**p-value=0.3037; F statistics=1.19; DF=2.00**
Δ Global Cognition	**p-value=0.1207; F statistics=2.12; DF=2.00**	**p-value=0.1787; F statistics=1.73; DF=2.00**
Sleepiness Phenotype		
Δ B-SEVLT-Recall	**p-value=0.5054; F statistics=0.93; DF=10.00**	**p-value=0.4117; F statistics=1.04; DF=10.00**
Δ DSS	**p-value=0.4554; F statistics=0.98; DF=10.00**	**p-value=0.4978; F statistics=0.94; DF=10.00**
Δ Global Cognition	**p-value=0.3702; F statistics=1.09; DF=10.00**	**p-value=0.3219; F statistics=1.15; DF=10.00**
Sleep Duration/ REI Phenotype		
Δ B-SEVLT-Recall	**p-value=0.0356; F statistics=1.96; DF=10.00**	**p-value=0.0298; F statistics=2.01; DF=10.00**
Short Sleep / AHI <15 and Ages <55	−0.19 [−0.49;0.10]	−0.19 [−0.49;0.11]
Short Sleep / AHI <15 and Ages 55–64	0.11 [−0.09;0.31]	0.11 [−0.08;0.31]
Short Sleep / AHI <15 and Ages 65+	0.40 [0.11;0.68]	0.39 [0.11;0.68]
Short Sleep / AHI ≥15 and Ages <55	0.01 [−0.26;0.28]	0.03 [−0.24;0.30]
Short Sleep / AHI ≥15 and Ages 55–64	0.09 [−0.47;0.65]	0.11 [−0.46;0.67]
Short Sleep / AHI ≥15 and Ages 65+	−0.34 [−1.48;0.79]	−0.33 [−1.46;0.81]
Average Sleep / AHI <15 and Ages <55	0.04 [−0.02;0.10]	0.04 [−0.02;0.10]
Average Sleep / AHI <15 and Ages 55–64	0.17 [0.09;0.25]	0.17 [0.09;0.25]
Average Sleep / AHI <15 and Ages 65+	−0.02 [−0.15;0.10]	−0.03 [−0.15;0.10]
Average Sleep / AHI ≥15 and Ages <55	0.03 [−0.12;0.17]	0.04 [−0.10;0.18]
Average Sleep / AHI ≥15 and Ages 55–64	0.09 [−0.09;0.27]	0.10 [−0.08;0.27]
Average Sleep / AHI ≥15 and Ages 65+	0.03 [−0.16;0.21]	0.05 [−0.13;0.24]
Long Sleep / AHI <15 and Ages <55	−0.10 [−0.26;0.06]	−0.11 [−0.27;0.05]
Long Sleep / AHI <15 and Ages 55–64	−0.04 [−0.18;0.10]	−0.04 [−0.18;0.10]
Long Sleep / AHI <15 and Ages 65+	0.17 [−0.13;0.48]	0.20 [−0.09;0.50]
Long Sleep / AHI ≥15 and Ages <55	0.04 [−0.28;0.36]	0.06 [−0.27;0.39]
Long Sleep / AHI ≥15 and Ages 55–64	0.08 [−0.26;0.42]	0.10 [−0.24;0.44]
Long Sleep / AHI ≥15 and Ages 65+	−0.96 [−1.71;−0.22]	−0.94 [−1.68;−0.19]
Δ DSS	**p-value=0.0183; F statistics=2.17; DF=10.00**	**p-value=0.0119; F statistics=2.3; DF=10.00**
Short Sleep / AHI <15 and Ages <55	0.05 [−0.10;0.21]	0.05 [−0.11;0.21]
Short Sleep / AHI <15 and Ages 55–64	0.07 [−0.12;0.26]	0.06 [−0.13;0.25]
Short Sleep / AHI <15 and Ages 65+	0.22 [−0.11;0.55]	0.22 [−0.11;0.56]
Short Sleep / AHI ≥15 and Ages <55	−0.08 [−0.69;0.53]	−0.07 [−0.69;0.54]
Short Sleep / AHI ≥15 and Ages 55–64	0.20 [−0.16;0.57]	0.20 [−0.16;0.56]
Short Sleep / AHI ≥15 and Ages 65+	−0.77 [−1.30;−0.23]	−0.76 [−1.29;−0.23]
Average Sleep / AHI <15 and Ages <55	0.00 [−0.06;0.06]	−0.01 [−0.07;0.05]
Average Sleep / AHI <15 and Ages 55–64	0.08 [0.00;0.15]	0.08 [0.01;0.16]

Cognitive Change		
	Obesity	**MetS**
Average Sleep / AHI <15 and Ages 65+	0.08 [−0.05;0.21]	0.09 [−0.05;0.22]
Average Sleep / AHI ≥15 and Ages <55	−0.02 [−0.16;0.12]	−0.02 [−0.16;0.12]
Average Sleep / AHI ≥15 and Ages 55–64	0.03 [−0.12;0.19]	0.04 [−0.12;0.19]
Average Sleep / AHI ≥15 and Ages 65+	−0.10 [−0.42;0.22]	−0.07 [−0.39;0.25]
Long Sleep / AHI <15 and Ages <55	0.16 [−0.01;0.33]	0.16 [−0.01;0.33]
Long Sleep / AHI <15 and Ages 55–64	−0.17 [−0.35;0.01]	−0.17 [−0.36;0.01]
Long Sleep / AHI <15 and Ages 65+	0.20 [−0.22;0.62]	0.24 [−0.18;0.67]
Long Sleep / AHI ≥15 and Ages <55	−0.24 [−0.71;0.23]	−0.23 [−0.72;0.25]
Long Sleep / AHI ≥15 and Ages 55–64	−0.15 [−0.47;0.18]	−0.13 [−0.46;0.20]
Long Sleep / AHI ≥15 and Ages 65+	−0.34 [−1.22;0.54]	−0.33 [−1.21;0.55]
Δ Global Cognition	**p-value=0.1443; F statistics=1.48; DF=10.00**	**p-value=0.1604; F statistics=1.44; DF=10.00**
Sleep Duration (3 Categories)		
Δ B-SEVLT-Recall	**p-value=0.5211; F statistics=0.81; DF=4.00**	**p-value=0.5182; F statistics=0.81; DF=4.00**
Δ DSS	**p-value=0.0683; F statistics=2.19; DF=4.00**	**p-value=0.0458; F statistics=2.44; DF=4.00**
< 6 Hours and Ages <55	0.04 [−0.12;0.20]	0.04 [−0.12;0.20]
< 6 Hours and Ages 55–64	0.11 [−0.06;0.28]	0.10 [−0.07;0.27]
< 6 Hours and Ages 65+	−0.11 [−0.49;0.27]	−0.10 [−0.48;0.28]
6–9 Hours and Ages <55	−0.00 [−0.06;0.05]	−0.02 [−0.07;0.04]
6–9 Hours and Ages 55–64	0.06 [−0.01;0.12]	0.06 [−0.00;0.13]
6–9 Hours and Ages 65+	0.02 [−0.10;0.14]	0.03 [−0.09;0.16]
9+ Hours and Ages <55	0.11 [−0.05;0.27]	0.11 [−0.06;0.27]
9+ Hours and Ages 55–64	−0.14 [−0.30;0.01]	−0.14 [−0.30;0.01]
9+ Hours and Ages 65+	0.12 [−0.24;0.48]	0.15 [−0.21;0.52]
Δ Global Cognition	**p-value=0.6040; F statistics=0.68; DF=4.00**	**p-value=0.6486; F statistics=0.62; DF=4.00**

Notes:

Marginal estimates are only provided for the age modifications that were significant.

A: Models are adjusted for sex, CESD-10, obesity, sleeping pill usage, and Field Center.

B: Models are adjusted for sex, CESD-10, MetS, sleeping pill usage, and Field Center.

Abbreviations: REI=Respiratory Event Index; SD= Sleep Duration; B-SEVLT=Brief-Spanish English Verbal Learning Test; DSS= Digit Symbol Substitution test; DF = degrees of freedom.

Age <55 is 50–54 given the target population.