Sleep-disordered Breathing and Neuropsychological Deficits

A Population-based Study

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The relationship of sleep-disordered breathing (SDB) to neuropsychological deficits was investigated with cross-sectional data from the Wisconsin Sleep Cohort Study, a population-based study of the natural history of SDB. A sample of 841 employed men and women ages 30 to 60 yr was studied by overnight polysomnography to assess the frequency of apneas and hypopneas per hour of sleep (apnea-hypopnea index, AHI). Prior to overnight polysomnography, the participants were given a battery of neuropsychological tests for functionally important capacities including motor skills, attention, concentration, information processing, and memory. Principal factor analysis of all the neuropsychological test data revealed a psychomotor efficiency and a memory factor. Multiple regression analysis showed a significant negative association between logarithmically transformed AHI (LogAHI) and psychomotor efficiency score independent of age, gender, and educational status ($p = 0.017$). The relationship was not explained by self-reported sleepiness. No significant relationship was seen between LogAHI and memory score. In assessing the clinical significance of mild SDB, we estimate that an AHI of 15 is equivalent to the decrement in psychomotor efficiency associated with 5 additional yr of age, or to 50% of the decrement associated with hypnosedative use. Kim HC, Young T, Matthews CG, Weber SM, Woodard AR, Palta M. Sleep-disordered breathing and neuropsychological deficits: a population-based study. AM J RESPIR CRIT CARE MED 1997;156:1813–1819.

There is a high prevalence of undiagnosed sleep-disordered breathing (SDB), ranging from mild to severe, in the general population (1). However, it is not known whether unrecognized SDB results in the same degree of morbidity and mortality as does clinically diagnosed SDB. Studies of sleep clinic patients (2–7) have associated SDB with pathologic sleepiness and other types of behavioral morbidity including problems with memory, decreased concentration, and poor task-performance. The goal of our study was to determine whether SDB in the general population is associated with the neuropsychological deficits seen in patients with clinically diagnosed SDB.

Several population-based studies of middle-aged adults have shown associations between SDB and neuropsychological deficits. The Finnish Twin Cohort Study (8) found an association between SDB and deficits in memory and spatial orientation in habitual snorers. Similarly, relationships between self-reported snoring and subjective memory and concentration problems were reported in an epidemiologic survey of 3,323 Danish men (9). A relationship between SDB and cognitive complaints was also reported in the Dan-MONICA II Study (10). Although these studies suggest that undiagnosed SDB is related to neuropsychological deficits, the findings are limited by a very small sample (8), lack of standardized method of measuring SDB (8, 10), self-reported snoring as a surrogate for SDB status (9), or self-reported neuropsychological deficits (9, 10).

We report here on the association between polysomnographically determined SDB and neuropsychological test battery parameters in 841 men and women enrolled in the Wisconsin Sleep Cohort Study, an ongoing population-based epidemiologic study of SDB. In addition, data on self-reported sleepiness afforded the opportunity to investigate the role of sleepiness in explaining or modifying associations of SDB with neuropsychological deficits.

METHODS

Sample

The Wisconsin Sleep Cohort Study is a prospective population-based study of the natural history of SDB. A two-stage sampling procedure, previously described in detail (1), was used to construct the cohort sample. First, all men and women, ages 30–60 yr, who were employed at one of five state agencies in the south-central region of Wisconsin were identified and surveyed on sleep characteristics and sociodemographic factors. There was a range of occupational categories including manual and skilled labor, service, technical support, and professional at each agency. A probability sample was drawn from the survey respondents and recruited by mail and telephone for participation in the Sleep Cohort Study. To increase study efficiency, men and women with self-reported snoring and breathing pauses were oversampled.

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Recruitment has been ongoing since 1989, and the response rate has averaged 50%. Comparison of participants and nonparticipants showed no differences in age, gender, ethnicity, income, marital status, prevalence of cardiovascular or pulmonary diseases, or sleep habits. Participants, as compared with nonparticipants, were more likely to be nonsmokers, less likely to have hypertension, had a higher educational status, and had a slightly higher body mass index. To confirm the absence of response bias, the effects of the latter variables on the association of interest were routinely examined by multivariable modeling.

At the time of this investigation, 841 men and women had successfully completed the entire study protocol. The characteristics of the sample are given in Table 1.

Data Collection

All participants underwent an overnight study at a sleep laboratory equipped with comfortable bedrooms. For the present analysis, the following components of the Sleep Cohort Study protocol were used: standard polysomnography, a 1-h neuropsychological test battery, and an extensive health interview of lifestyle, medical conditions and medication use.

Neuropsychological Test Battery

Neuropsychological tests were chosen to cover a range of cognitive function factors expected to be affected by sleep-disordered breathing. Fine motor control and eye-hand coordination skills were primarily assessed by the Grooved Pegboard Test (11). Time to completion (on right and left hand trial) was measured for inserting 25 grooved pegs into randomly slotted holes as quickly as possible. Verbal cognitive speed and the ability to retrieve words from lexical memory in a rapid and effective fashion were assessed by the Controlled Oral Word Association Test (12). Verbal learning, retention, and recognition were assessed by the Rey Auditory-Verbal Learning Test (13). The test consisted of five presentations with immediate recall of a 15-word list, one presentation of a second 15-word list to provide a distractor task, and then a sixth recall trial of the original word list. Delayed recall was tested 30 min after the sixth recall trial. Learning was measured as the sum of the first five trials and retention was measured as the percentage of test words recalled after a 30-min delay. Recognition was measured as number of target words circled in a story. Visual search speed, attention, mental flexibility, and motor function were assessed by the Trail Making Test, Part B (14), on which time to connect 25 circles, numbered from 1–13 and lettered from A–L, alternating between numbers and letters was recorded. Sustained attention and visual scanning were assessed by the Digit Cancellation Test (15). Time to cross out a target number randomly interspersed in rows of other numbers was measured. The Symbol Digit Modalities Test (16) was used to assess motor persistence, sustained attention, response speed, and visuomotor coordination. The test consists of quickly substituting a series of symbols for numbers from a given key; the number of correct responses made in 90 s was scored.

All neuropsychological tests were administered by a trained technician before SDB status was determined. Information on educational status (highest degree earned and years of school completed) was obtained after the test battery.

TABLE 1

CHARACTERISTICS OF THE SAMPLE (n = 841)

Apnea-Hypopnea Index (AHI), median (range)	1.24 (0–97.5)
Age in years, mean (SD)	44.9 (7.6)
Male gender, n (%)	503 (59.8)
Highest educational attainment, n (%)	
Less than high school graduate	8 (1.0)
High school graduate	440 (52.3)
College graduate	251 (30.0)
Post-college graduate	142 (16.7)
Alcohol consumption	
Units*/week, mean (SD)	4.2 (7.0)
Alcohol taken 24 hours prior to neuropsychological testing, Yes, n (%)	178 (21.2)
Medications taken prior to overnight study, Yes, n (%)	
β-adrenergic blockers or α-2 agonists	38 (4.5)
ACE inhibitors	21 (2.5)
Hypnosedatives	20 (2.4)
Anti-depressants	20 (2.4)
Health history, Yes, n (%)	
Head injuries or unconsciousness	76 (9.0)
Epileptic seizures	15 (1.8)
Encephalitis or meningitis	11 (1.3)
Self-reported sleepiness variables†, Yes, n (%)	
Fatigue‡	459 (59.4)
Daytime sleepiness§	217 (26.0)
Uncontrollable sleepiness interferes with everyday life‖	144 (18.6)

* Number of beers, glasses of wine, and shots of hard liquor.

† Due to missing data, analysis for fatigue, daytime sleepiness, and uncontrollable sleepiness interferes with everyday life were based on sample size of 772, 835, and 775 subjects, respectively.

‡ Usually feeling tired or fatigued during the day.

§ Experiencing sleepiness when it is difficult to fight an uncontrollable urge to fall asleep.

‖ Experiencing uncontrollable sleepiness which interferes with any of the following: mood, relationship with people, enjoyment of life, ability to concentrate, or motivation.

Polysomnograph Recordings

The nocturnal polysomnogram consisted of continuous polygraphic (polygraph model 78; Grass Instruments, Quincy, MA) recording of electrooculography (EOG), electroencephalography (EEG), electrocardiography (single lead ECG), tracheal sounds (microphone), nasal airflow (end-tidal carbon dioxide concentration), oral airflow (thermocouple), thoracic and abdominal respiratory effort (inductance plethysmography, Respitrace; Ambulatory Monitoring, Ardsley, NY), and oxyhemoglobin saturation (finger-pulse oximeter, Ohmeda 3740; Englewood, CO). All monitoring allowed normal positional changes during sleep.

Each 30-s epoch of the recordings was scored by a team of technicians and sleep specialists for sleep, respiration, oxyhemoglobin changes, and movement. Sleep stage was scored by the criteria of Rechtschaffen and Kales (17). Respiration was evaluated for apnea (cessation of airflow for 10 s or more) and hypopnea (reduction in respiratory effort accompanied by a 4% drop in oxyhemoglobin saturation). Apnea-hypopnea index (AHI) was defined as the number of apneas plus hypopneas per hour of total sleep time. Minimum requirements for acceptable quality were adequate signals throughout the night, at least 240 min of objectively measured sleep, and at least one REM period. On average participants were asleep for 352 min (SD = 65 min); of this, 10% (SD = 6%) was spent in stage 1 sleep, 62% (SD = 10%) in stage 2 sleep, 10% (SD = 8%) in slow wave sleep (stages 3 and 4), and 18% (SD = 6%) in REM sleep.

Health Interview

A structured health interview was conducted by a trained interviewer prior to the polysomnogram. Data relevant to this investigation were medication use (β-adrenergic blockers, α-2 agonists, angiotensin catalyzing enzyme [ACE] inhibitor, hypnosedatives, and anti-depressants), history of epileptic seizures, head injuries, unconsciousness, encephalitis or meningitis, typical weekly intake of alcohol and alcohol intake in the last 24 h (number of beers, glasses of wine, and shots of hard liquor), and sleepiness. Questions about fatigue and daytime sleepiness were constructed to assess physical fatigue, daytime sleepiness, and uncontrollable sleepiness that interferes with everyday life. Fatigue was assessed by the question: "Do you usually feel tired or fatigued at times during the day?" Daytime sleepiness was assessed by the question: "Many people have periods of low energy or fatigue, but do you experience excessive sleepiness, when it is difficult to fight an uncontrollable urge to fall asleep?" If the response was positive, a question of uncontrollable sleepiness that interferes with everyday life was asked: "Does your sleepiness interfere with any of the following: work, mood, relationships with people, enjoyment of life, ability to concentrate, or motivation?" Reporting sleepiness that interferes with at least one of these aspects was considered a positive response.

Statistical Analysis

A principal factor analysis with varimax rotation was performed on the neuropsychological variables to reduce dimensionality and thereby increase the precision in measuring common factors as well as to minimize Type I error resulting from numerous comparisons. A factor with a minimum eigen value of 1.0 was retained in the analysis. Factor scores were computed for each subject based on the loadings.

Data were analyzed using SAS and SUDAAN (18) software. To account for the stratified sampling of the Sleep Cohort, all analyses were weighted to give unbiased estimates. The SUDAAN software was used to compute appropriate standard errors for the weighted analyses.

For regression analysis, AHI was transformed as the natural logarithm of AHI + 1 (LogAHI) to meet the assumption of linearity between AHI and derived factor scores. Graphical methods, including scatter and residual versus predicted plots, were used to assess linearity and normality.

Multiple regression analysis was used to estimate the relationship between LogAHI and factor scores. Age, gender, and educational status were included with LogAHI in all models. Additional potential confounding variables (the use of β-blockers or α-2 agonists, ACE inhibitors, hypnosedatives, antidepressants, history of encephalitis or meningitis, history of head injury or unconsciousness, history of epileptic seizures, and alcohol consumption per week and alcohol taken 24 h prior to neuropsychological testing) were added singly to the model with LogAHI, age, gender, and educational status to determine if adjusting for those variables changed the relationship between LogAHI and neuropsychological performance. A variable was considered to be a confounder when it changed the regression coefficient of LogAHI by more than 15%. Age in years and alcohol intake per week were entered into the regression models as continuous variables. Educational status was entered into the models as indicator variables with high school graduate or less as the reference category. The indicator variables and all other variables were binary. Interaction effects between LogAHI and covariates were assessed. Multiple linear regression was also used to investigate the relationship of self-reported sleepiness and fatigue with neuropsychological factor scores.

General Linear Model (GLM) analysis of variance was used to investigate the differences in least squares mean neuropsychological factor scores adjusted to the mean age, gender and educational status distributions between SDB categories.

Student's *t*-test (two-tailed) was used to determined statistical significance of linear regression coefficients and differences in group means. Statistically significant differences in proportions were determined by the Chi-square test and Fisher's exact test. The Wilcoxon Sum Rank Test was used to determine the significance of differences in distribution of AHI. Spearman rank and Pearson correlations were used where appropriate. Data from continuous variables were summarized as mean ± SEM. Two-tailed p values < 0.05 were considered to indicate statistical significance.

RESULTS

Of the 966 participants who completed the overnight study, 30 were excluded because the polysomnography results did not meet the quality criteria. Because of late arrival, complete neuropsychological data were not available on all participants. Ninety-five people were not given the neuropsychological test battery, resulting in a sample of 841 participants for this investigation. Those who did complete the neuropsychological test battery, compared with those who did not, did not differ on AHI, age, gender, educational status, alcohol consumption, health history, or medication use ($p > 0.3$).

The unadjusted mean neuropsychological test scores by SDB categories are shown in Table 2. Compared with those with AHI greater or equal to 5, those with AHI of less than 5 had better scores on the learning and retention variable of the auditory verbal learning test, symbol digit modalities, controlled oral word association, grooved pegboard, trail making, and digit cancellation test, but the differences were not statistically significant.

TABLE 2

UNADJUSTED MEAN NEUROPSYCHOLOGICAL TEST SCORES BY SDB CATEGORIES

	SDB Category	
Test	AHI < 5 (Mean ± SD) (*n = 642*)	AHI ⩾ 5 (Mean ± SD) (*n = 199*)
AVLT Learning*	53 ± 8	51 ± 8
AVLT Retention†	82 ± 17	80 ± 18
AVLT Recognition‡	14 ± 1.5	14 ± 1.8
Grooved Pegboard§	135 ± 22	141 ± 20
Symbol Digit Modalities Test‖	55 ± 9	52 ± 9
Trail Making Test, Part B¶	67 ± 24	74 ± 28
Digit Cancellation¶	364 ± 72	380 ± 78
Controlled Oral Word Association Test**	42 ± 11	40 ± 11

* Sum of trials 1–5.
† Number of words in delayed recall/highest of trials 1–5 times 100.
‡ Numbers of words correctly circled in a story.
§ Sum of dominant and nondominant hand scores.
‖ Number of correct responses.
¶ Time to completion.
** Sum of trials C, F, and L.

The rotated principal factor analysis of the neuropsychological tests resulted in two common factors being identified with eigenvalues greater than one, accounting for 53.7% of the variance (Table 3). Based on the clustering of high factor loadings, the two factors were interpreted as psychomotor efficiency (I) and memory (II). The logarithmic transformation of AHI resulted in a linear relationship between AHI and both factor scores. Both factors were normally distributed and were scaled to have means of 0 and standard deviations of 1. Both psychomotor efficiency and memory scores were coded so that increase in the scores indicated better performance.

Univariate analysis (Table 4) showed that LogAHI and age were negatively and significantly ($p < 0.05$) associated with both the psychomotor efficiency and memory score, while educational status was positively and significantly associated with both the psychomotor efficiency and memory score. Alcohol consumption per week was negatively and significantly associated with the memory score. Use of β-adrenergic blockers or

TABLE 3

ROTATED (VARImax) FACTOR LOADINGS FOR NEUROPSYCHOLOGICAL TEST BATTERY

	Factor	
Test	Psychomotor Efficiency	Memory
AVLT Learning*	−0.3007	0.7659
AVLT Retention†	−0.0858	0.7907
AVLT Recognition‡	−0.0177	0.8215
Grooved Pegboard§	0.6263	−0.0685
Symbol Digit Modalities Test‖	−0.7529	0.2527
Trail Making Test, Part B¶	0.7209	−0.1236
Digit Cancellation¶	0.6583	0.0622
Controlled Oral Word Association Test**	−0.5238	0.1847
Eigenvalue	2.285	2.009
% Variance	28.56	25.11

* Sum of trails 1–5.
† Number of words in delayed recall/highest of trials 1–5 times 100.
‡ Number of words correctly circled in a story.
§ Sum of dominant and nondominanat hand scores.
‖ Number of correct responses.
¶ Time to completion.
** Sum of trials C, F, and L.

TABLE 4

CORRELATIONS OF NEUROPSYCHOLOGICAL FACTOR SCORES WITH LogAHI* AND COVARIATES

	Psychomotor Efficiency		Memory	
Variable	r	p Value	r	p Value
LogAHI†	−0.18	0.0001	−0.10	0.004
Age, yr†	−0.33	0.0001	−0.11	0.0009
Educational status‡	0.24	0.0001	0.11	0.002
Alcohol consumption per week‡	−0.02	0.61	−0.11	0.0009

* ln (AHI + 1).

† Pearson correlation for the relationlships between factor scores and both LogAHI and age.

‡ Spearman correlation for the relationships between factor scores and both educational status and alcohol consumption per week.

α-2 agonists, ACE inhibitors, antidepressants, alcohol consumption 24 h prior to testing, and self-reported sleepiness and fatigue were significantly associated with neuropsychological scores (Table 5).

The regression models for psychomotor efficiency and memory factor scores are given in Table 6. LogAHI was negatively associated with the psychomotor efficiency factor, independent of age, gender, and educational status (coefficient of LogAHI = −0.07, p = 0.017). After adding age, gender, and educational status, LogAHI was no longer significantly associated with the memory score. The multiple regression analysis also showed that older age, male gender, and lower educational status were significantly related to lower scores on both psychomotor efficiency and memory factors.

The associations of LogAHI and the psychomotor efficiency and memory factor scores were not affected by the use of β-blockers and α-2 agonists, ACE inhibitors, hypnosedatives, antidepressants, history of encephalitis or meningitis, history of head injury or unconsciousness, history of epileptic seizures, and alcohol consumption per week and alcohol taken 24 h prior to neuropsychological testing.

The difference in mean psychomotor efficiency scores, adjusted for age, gender, and education, between those with AHI of less than 5 and those with AHI greater or equal to 5 was statistically significant ($p < 0.05$). However, the difference in adjusted mean memory score between the SDB categories was not statistically significant (Table 7).

The contribution of self-reported sleepiness and fatigue to the relationship between SDB and neuropsychological factor scores was assessed by adding the self-reported sleepiness and fatigue variables singly into the models (Table 8). None of these variables had an impact on the regression coefficient for LogAHI, indicating that neither self-reported sleepiness nor fatigue seemed to account for these associations. These analyses, however, did show that self-reported sleepiness and fatigue were independently related to the factor scores. Self-

TABLE 5

NEUROPSYCHOLOGICAL FACTOR SCORES ACCORDING TO COVARIATES

		Psychomotor Efficiency		Memory	
Variable	n	Mean ± SEM	p Value	Mean ± SEM	p Value
Gender					
Male	503	−0.07 ± 0.05	0.01	−0.14 ± 0.05	0.0001
Female	338	0.10 ± 0.05		0.21 ± 0.05	
Use of β-adrenergic blockers or α-2 agonists					
Yes	38	−0.51 ± 0.16	0.003	−0.12 ± 0.17	0.47
No	801	0.02 ± 0.04		0.009 ± 0.04	
Uses of ACE inhibitors					
Yes	21	−0.96 ± 0.22	0.0003	−0.54 ± 0.29	0.07
No	818	0.02 ± 0.03		0.02 ± 0.03	
Use of hypnosedatives					
Yes	20	−0.43 ± 0.34	0.21	0.24 ± 0.20	0.27
No	819	0.01 ± 0.03		−0.003 ± 0.03	
Use of antidepressants					
Yes	20	−0.28 ± 0.20	0.18	0.56 ± 0.16	0.002
No	819	0.01 ± 0.035		−0.01 ± 0.03	
Previous head injuries or unconsciousness					
Yes	76	−0.14 ± 0.13	0.26	−0.14 ± 0.12	0.21
No	765	0.01 ± 0.04		0.01 ± 0.04	
Previous epileptic seizures					
Yes	15	−0.55 ± 0.39	0.17	−0.02 ± 0.32	0.94
No	824	0.01 ± 0.03		0.003 ± 0.03	
Alcohol was taken 24 h prior to test					
Yes	178	−0.03 ± 0.08	0.064	−0.19 ± 0.08	0.006
No	663	0.01 ± 0.04		0.05 ± 0.04	
Usually fatigued					
Yes	459	0.02 ± 0.05	0.44	0.08 ± 0.04	0.001
No	313	−0.03 ± 0.06		−0.17 ± 0.06	
Experiencing daytime sleepiness					
Yes	217	−0.16 ± 0.07	0.011	0.10 ± 0.06	0.10
No	618	0.06 ± 0.04		−0.03 ± 0.04	
Experiencing uncontrollable sleepiness that interferes with everyday life					
Yes	144	−0.26 ± 0.10	0.003	0.08 ± 0.08	0.17
No	631	0.06 ± 0.04		−0.04 ± 0.04	

TABLE 6

MODELS* FOR NEUROPSYCHOLOGICAL FACTORS FITTED BY LogAHI†, AGE, GENDER, AND EDUCATIONAL STATUS

	Psychomotor Efficiency Model			Memory Model		
Variable	β‡	(SE)§	p Value	β	(SE)	p Value
Intercept	1.63	(0.20)	0.0001	0.29	(0.21)	0.162
LogAHI	−0.07	(0.03)	0.017	−0.03	(0.03)	0.41
Age, yr	−0.04	(0.004)	0.0001	−0.01	(0.005)	0.007
Gender (0 = male, 1 = female)	0.17	(0.07)	0.015	0.37	(0.07)	0.0001
College graduate‖	0.43	(0.07)	0.0001	0.27	(0.08)	0.0006
Post-college graduate‖	0.57	(0.08)	0.0001	0.29	(0.09)	0.0015

* Results from multiple regression analysis. Adding variables medication use, health history, and alcohol consumption to the model did not affect the relationship between LogAHI and either psychomotor efficiency or memory factor scores.
† ln (AHI + 1).
‡ β is the regression coefficient of the variable.
§ SE is the standard error of β.
‖ Compared with high school graduate or less.

reported uncontrollable sleepiness that interfered with everyday life was significantly associated with decrease in psychomotor efficiency score, independent of SDB and covariates (coefficient of uncontrollable sleepiness interferes with everyday life = −0.24, p = 0.005) (Table 9). Self-reported daytime sleepiness and fatigue were negatively associated with psychomotor efficiency, but the associations were not statistically significant. Self-reported fatigue was significantly associated with increase in memory score, independent of SDB and covariates (coefficient of fatigue = 0.18, p = 0.016); however, self-reported daytime sleepiness and uncontrollable sleepiness that interferes with everyday life were not significantly associated with memory.

There were no significant interactions of LogAHI with age, gender, educational status, or self-reported sleepiness and fatigue in their relationship with neuropsychological factor scores.

Several covariates, independent of LogAHI, age, gender, and educational status, were associated with the neuropsychological factors. The use of ACE inhibitors and hypnosedatives was significantly associated with decrease in psychomotor efficiency score (coefficient of ACE inhibitor = −0.60, p = 0.003 and coefficient of hypnosedatives = −0.43, p = 0.038). Having a history of epileptic seizures was also significantly associated with decrease in psychomotor efficiency score (coefficient of epileptic seizure = −0.66, p = 0.005). Greater average drinks per week and alcohol taken 24 h prior to testing were both significantly associated with decrease in "memory" score (coefficient of drink per week = −0.01, p = 0.031 and coefficient of alcohol taken 24 h prior to testing = −0.20, p = 0.015).

TABLE 7

MEAN NEUROPSYCHOLOGICAL FACTOR SCORES* BY SDB CATEGORIES

		Psychomotor Efficiency		Memory	
Variable	n	Mean* ± SEM	p Value	Mean ± SEM	p Value
Apnea-Hypopnea Index (AHI)					
< 5	642	0.038 ± 0.036	0.035	0.021 ± 0.039	0.279
⩾ 5	199	−0.123 ± 0.066		−0.067 ± 0.070	

* Least square mean adjusted to the mean age, and gender and educational status distributions of our sample.

DISCUSSION

The main finding of this study supports the hypothesis that undiagnosed sleep-disordered breathing is associated with neuropsychological deficits, specifically with the neuropsychological domain off psychomotor efficiency. The results suggest that SDB may impair ability to efficiently coordinate fine visuomotor control and information through sustained attention and concentration. The linear association between SDB and deficits in psychomotor efficiency indicates that even the milder range of range of SDB is associated with some impairment.

Our study did not show an association between SDB and deficits in memory. This finding is consistent with results from some (4, 6, 10), but not all (2, 3, 5, 7), previous studies. Since psychometric methods and study designs varied widely between studies, it is difficult to reconcile the conflicting findings. However, in a study using the same memory test as was used in our study, no association between SDB and deficits in memory was found (4). The possibility remains that there is an association between SDB and memory that is too weak to be detected by our tests. These tests are used widely to discriminate memory in clinic patients (19–20), but their sensitivity to very mild memory deficits has not been fully validated.

Our quantification of the relationship between SDB and psychomotor deficits is useful in assessing the clinical significance of mild SDB. Based on comparing regression coefficients for predictors of psychomotor efficiency, we estimate that an AHI of 15 is equivalent to the decrement in psychomotor efficiency associated with 5 additional years of age, or to 50% of the decrement associated with hypnosedative use. Thus, the behavioral morbidity of even mild SDB is not trivial.

Our findings that self-reported sleepiness did not significantly explain the relationship between SDB and deficits in psychomotor performance cast some doubt on self-reported sleepiness as the major intermediate step between SDB and deficits in neuropsychological functioning. As suggested from studies of sleep clinic patients (2, 3, 6, 7), hypoxemia may play a greater role in the relationship between SDB and neuropsychological deficits.

We found a negative association between self-reported uncontrollable sleepiness that affects everyday life with psychomotor efficiency, independent of SDB, age, gender, and educational status. However, this was not seen with either self-reported daytime sleepiness or fatigue.

We also found differences in the associations of these sleepiness variables and the memory score. Our study showed an unexpected positive association between self-reported fatigue and memory; however, self-reported daytime sleepiness and uncontrollable sleepiness that interferes with everyday life were not significantly associated with memory. A possible explanation for an association between better memory performance and increased fatigue is that report of fatigue may correlate with social and motivational factors that are also related to memory. For example, people who report fatigue due to sleep deprivation may be more likely to be high achieving, upwardly mobile individuals. In addition, intentionally overreporting fatigue might be more prominent in highly motivated achievers who in turn may be better at memory tasks.

These findings suggest that fatigue, sleepiness, and hypersomnolence (uncontrollable sleepiness that affects daily living) are distinct conditions. Roth and colleagues (21) have suggested different types of sleepiness may have different etiologies. For example, fatigue may be an end result of exces-

TABLE 8

THE EFFECT OF SELF-REPORTED SLEEPINESS AND FATIGUE ON THE RELATIONSHIP BETWEEN LogAHI* AND NEUROPSYCHOLOGICAL FACTORS

Model	Independent Variables	Psychomotor Efficiency β†	(SE)‡	p Value	Memory β	(SE)	p Value
I.	LogAHI	−0.16	(0.03)	0.0001	−0.09	(0.03)	0.0041
II.	LogAHI, age, gender, and educational status	−0.07	(0.03)	0.016	−0.03	(0.03)	0.410
III.	Model II plus fatigue	−0.08	(0.03)	0.022	−0.027	(0.03)	0.441
IV.	Model II plus daytime sleepiness	−0.07	(0.03)	0.022	−0.03	(0.03)	0.375
V.	Model II plus uncontrollable sleepiness interferes with everyday life	−0.06	(0.03)	0.048	−0.03	(0.03)	0.402

* ln (AHI + 1).
† β is the regression coefficient of the LogAHI variable.
‡ SE is the standard error of β.

sive energy consumption or prolonged mental activity, sleepiness (with no perceived effect on everyday life) may be due to insufficient sleep, perhaps from voluntary sleep deprivation, and hypersomnolence may be the result of a chronic dyssomnia.

Our findings that sleepiness variables relate differently to neuropsychological outcomes support the view that sleepiness comprises multiple disorders, each of which may have different etiologies.

An important consideration in interpreting our results is measurement validity. The conventional laboratory polysomnography that we used to derive the apnea-hypopnea index is currently accepted as the clinical standard for measuring sleep and respiration. Thus, in addition to providing high-quality data, the use of attended, laboratory-based polysomnography gave SDB measures that are comparable with clinical measures. Furthermore, our use of the previously validated neuropsychological tests (22–24) showed the expected correlations of the tests with age and education (24–25). We also found associations between neuropsychological factors and medical histories consistent with previous findings. We found that those who used hypnosedatives, compared to those who did not, had significantly greater deficits in psychomotor efficiency tasks. Previous studies (26–27) have shown healthy subjects display impairment in psychomotor performance and visuospatial tasks after taking hypnosedatives such as benzodiazepines. Our findings of a significant association between history of epileptic seizures and decreased psychomotor efficiency are consistent with studies showing the tendency for epileptics to have lower scores on motor tasks requiring sustained activity that are scored for speed (28–29). The significant relationship between alcohol use and decreased psychomotor performance level seen in our results has also been reported in previous studies (30–31).

Due to the cross-sectional nature of our study, the direction of causality between SDB and psychomotor deficits cannot be determined from our results. Previous experimental studies (32–35) on neuropsychological outcomes after treatments with nasal continuous positive airway pressure (CPAP) and surgical procedure provide limited support for a causal association between SDB and neuropsychological deficits. All studies reported significant improvements in scores on some neuropsychological tests after treatment. However, three (33–35) of the four studies did not conclude overall that treatment improved neuropsychological deficits. Since psychometric methods and criteria for interpreting the neuropsychological test results varied across studies, it is difficult to assess confidently the findings. Further longitudinal investigation on a population sample is necessary to investigate causality.

In summary, we found that unrecognized, untreated SDB in the general adult population is significantly related to psychomotor deficits but not to memory performance deficits. The dose response relationship between SDB and psychomotor deficits in conjunction with the high prevalence of mild to moderate SDB suggests that a large number of adults in the most productive period of their lives may have some diminished psychomotor performance attributable to SDB.

TABLE 9

RELATIONSHIP BETWEEN SELF-REPORTED SLEEPINESS AND FATIGUE VARIABLES AND NEUROPSYCHOLOGICAL FACTORS

Model	Psychomotor Efficiency β*	(SE)†	p Value	Memory β	(SE)	p Value
Fatigue‡	−0.02	(0.06)	0.79	0.18	(0.08)	0.016
Datime sleepiness‡	−0.13	(0.07)	0.066	0.15	(0.08)	0.053
Uncontrollable sleepiness interferes with everyday life‡	−0.24	(0.09)	0.005	0.14	(0.09)	0.12

* β is the regression coefficient of the sleepiness variable.
† SE is the standard error of β.
‡ Adjusting for LogAHI, gender, age, and educational status.

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