JCSM
Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Subjective and Objective Measures of Hypersomnolence Demonstrate Divergent Associations with Depression among Participants in the Wisconsin Sleep Cohort Study

David T. Plante, MD[1]; Laurel A. Finn, MS[2]; Erika W. Hagen, PhD[2]; Emmanuel Mignot, MD, PhD[3]; Paul E. Peppard, PhD[2]

[1]Department of Psychiatry, School of Medicine and Public Health, University of Wisconsin-Madison, Madison, WI; [2]Department of Population Health Sciences, School of Medicine and Public Health, University of Wisconsin–Madison, Madison, WI; [3]Stanford University Center for Sleep Sciences, Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Palo Alto, CA

Study Objectives: To examine associations of depression with habitual sleep duration, daytime sleepiness, and objective sleep propensity in a nonclinical population.

Methods: Data from adults participating in the Wisconsin Sleep Cohort Study were utilized in analyses. There were 1,287 adults (3,324 observations) who were used in the analysis of subjective hypersomnolence measures; 1,155 adults (2,981 observations) were used in the analysis of objective sleep propensity assessed by the multiple sleep latency test (MSLT). Repeated-measures logistic regression estimated associations between presence of depression (defined as modified Zung Self-Rating Depression Scale ≥ 50 or use of antidepressant medications) and three primary hypersomnolence measures: subjective excessive daytime sleepiness (Epworth Sleepiness Scale [ESS] ≥ 11), self-reported sleep duration ≥ 9 h/d, and objective sleep propensity (MSLT mean sleep latency < 8 min).

Results: After adjusting for age, sex, body mass index, chronic medical conditions, sedative hypnotic medication use, caffeine, tobacco, and alcohol use, sleep disordered breathing, as well as insomnia and sleep duration when appropriate, estimated odd ratios (95% confidence interval) for depression were: 1.56 (1.31,1.86) for ESS ≥ 11; 2.01 (1.49, 2.72) for habitual sleep time ≥ 9 h; and 0.76 (0.63–0.92) for MSLT mean sleep latency < 8 min.

Conclusions: Our results demonstrate divergent associations between subjective and objective symptoms of hypersomnolence and depression, with subjective sleepiness and excessive sleep duration associated with increased odds of depression, but objective sleep propensity as measured by the MSLT associated with decreased odds of depression. Further research is indicated to explain this paradox and the impact of different hypersomnolence measures on the course of mood disorders.

Commentary: A commentary on this article appears in this issue on page 467.

Keywords: cohort, depression, hypersomnolence, mood disorders, multiple sleep latency test, sleepiness

Citation: Plante DT, Finn LA, Hagen EW, Mignot E, Peppard PE. Subjective and objective measures of hypersomnolence demonstrate divergent associations with depression among participants in the Wisconsin Sleep Cohort study. *J Clin Sleep Med* 2016;12(4):571–578.

INTRODUCTION

Depression is a major global public health problem and is projected to carry an even greater burden of disease worldwide in the coming decades.[1,2] Sleep disturbance is commonly comorbid with mood disorders, and plays an important role in the pathogenesis, assessment, and treatment of depression in children and adults.[3,4] Both insomnia, defined as difficulty initiating and/or maintaining sleep despite adequate opportunity, and hypersomnolence, defined as excessive daytime sleepiness (EDS) and/or excessive sleep duration, are types of sleep disturbance that commonly occur as a principal component of depressive illness.[5] Although a sizeable amount of literature has examined the role of insomnia in depression,[6] relatively little research has explored the role of hypersomnolence in mood disorders.[7–9]

Estimates of the prevalence of hypersomnolence among those with depression vary widely from 9% to 76%, likely due to different criteria used to define hypersomnolence among studies.[7,10] Nonetheless, hypersomnolence plays a key role in the course of depressive illness, as it is a highly treatment-resistant symptom,[11,12] predicts the risk of incident depression[13–15] and depressive relapse,[7,16] and is associated with increased risk of suicide.[17,18] Thus, further research that examines the basis of

BRIEF SUMMARY

Current Knowledge/Study Rationale: Hypersomnolence plays a significant role in the course of mood disorders, but a reliable objective measure to quantify sleepiness in these patients remains elusive. Because prior studies that have examined objective sleep propensity using the multiple sleep latency test (MSLT) in depressed patients have had limited statistical power, this investigation examined associations between depression and subjective and objective hypersomnolence measures in a large epidemiological cohort study.

Study Impact: Results demonstrated subjective daytime sleepiness and increased habitual sleep duration were associated with an increased odds of depression, but increased sleep propensity on the MSLT was associated with reduced odds of depression. These findings underscore the limitations of the MSLT as a measure of sleepiness in mood disorders.

hypersomnolence in mood disorders is required so that these findings can be meaningfully applied to alter the course of depressive illness.

One of the largest barriers faced in the study of hypersomnolence in depression is the absence of an objective measure that can reliably quantify sleepiness in depressed persons. The multiple sleep latency test (MSLT), considered the gold standard measure of excessive sleepiness,[19] has previously failed to segregate hypersomnolent depressed patients from healthy individuals or demonstrate consistent pathologic sleep propensity relative to other disorders associated with excessive sleepiness.[20–23] However, these prior studies have used variable criteria to define hypersomnolence, and have had limited statistical power due to relatively small sample sizes.

The primary aim of this investigation was to examine the associations between depression and hypersomnolence, assessed using objective and subjective measures, in a large population-based cohort study. Based on prior literature, we hypothesized there would be a positive association between subjective hypersomnolence and depressive symptomology, but no clinically meaningful association between depressive symptoms and objectively measured sleepiness derived by the MSLT.

METHODS

Participants

All data were drawn from the ongoing Wisconsin Sleep Cohort (WSC) Study, the methodology of which is described in detail elsewhere.[24–26] Briefly, a cohort of 1,545 individuals had baseline overnight polysomnography (PSG) and were invited for follow-up studies every 4 y. All participants provided informed consent and all study procedures have been approved by the University of Wisconsin-Madison Health Sciences Institutional Review Board. Due to the addition/removal of protocols during the course of the Cohort Study (which has been ongoing since 1988), participant samples utilized in these analyses varied depending on the availability of data. Subjective measures of hypersomnolence were collected at all study visits from 1998–2014; 1,287 subjects provided 3,324 observations for this analysis (46% female, mean age 59 y, range 33–82 y). Objective measures of sleepiness were collected on a targeted subsample of subjects from 1989–2011; 1,155 subjects provided 2,981 observations for this analysis (46% female, mean age 55 y, range 30–78 y).

Subjective Measures of Hypersomnolence

The primary instrument used to assess subjective EDS was the Epworth Sleepiness Scale (ESS).[27] This validated and widely used scale ascertains the self-assessed likelihood of dozing or falling asleep in eight hypothetical situations. The overall ESS score is derived by summing responses, with scores ranging from 0 to 24. Subjects with ESS scores ≥ 11 were characterized as having EDS, consistent with clinically significant excessive sleepiness.[27]

Two additional secondary measures of subjective sleepiness were evaluated. Subjects were asked, "Do you have feelings of excessive daytime sleepiness?" Response options included: 0 = never, 1 = rarely (once a month), 2 = sometimes (2 to 4 times a month), 3 = often (5 to 15 times a month), or 4 = almost always (16 to 30 times a month). Additionally, an affirmative response to the question, "Many people have periods of low energy or fatigue, but, during a typical day do you experience excessive sleepiness when it is difficult to fight an uncontrollable urge to fall asleep?" was also evaluated as a measure of excessive sleepiness. These secondary measures are henceforth referred to as EDS frequency and EDS urge, respectively.

Usual sleep duration was estimated from the following questions: how many hours of sleep do you usually get in (1) a workday night? (2) a weekend or nonwork night? Daily average sleep duration was calculated as $(5 \times \text{workday sleep} + 2 \times \text{weekend sleep}) / 7$. Habitual sleep time greater than or equal to 9 h per night was considered the primary measure of excessive sleep duration. This cutoff is based on recent population-based estimates, and is congruent with recent nosological standards for hypersomnolence.[5,28]

Objective Measure of Hypersomnolence

The MSLT was conducted over time with two different protocols; a research (R) protocol (n = 1,839 studies) and a clinical (C) protocol (1,142 studies). MSLT studies were conducted on average 3 w after the PSG (R) or the day following the PSG (C). In both protocols, participants went to bed at their habitual bedtime on the night prior to testing. Participants also completed a week-long sleep log prior to their MSLT that was used to calculate total sleep time on the 2 nights preceding testing.

Both MSLT protocols were conducted in accordance with established parameters,[19,29] with modifications consistent with the naturalistic approach of the WSC study. Modifications applicable to all participants included conducting the MSLT even if total sleep time preceding the MSLT was < 6 h, and continuation of typical medications prior to and during the procedure. Four to five nap opportunities took place at 2-h intervals, beginning 1.5 h after awakening from overnight recordings (C) or at 10:00 (R). Sleep onset latency (SOL) for each nap was defined as the time from the start of the recording to the first 30-sec epoch of scored sleep. In the research protocol, participants were awoken immediately after sleep onset was established and the nap trial ended. In the clinical protocol, participants were allowed to sleep for 15 min after sleep onset during naps to assess for sleep onset rapid eye movement (REM) periods. Mean SOL across the first four naps was calculated for each participant, with mean SOL < 8 min indicating EDS in these analyses.[30]

Outcome: Depression

Participants completed the 20-item Zung Self-Rating Depression Scale on the evening of the overnight polysomnography study.[31,32] Scores on this instrument range from 25 to 100, with scores 50 to 59 suggestive of mild depression, and 60 or above indicative of moderate or worse depression. As described previously,[33] instructions for completion of the scale were modified from the original verbiage ("how have you been feeling in the past few days,") to "please read each of the following statements and place an X in the box which best describes how you feel in general from day to day." For these analyses, two sleep related items ("I have trouble sleeping through the night"

and "I get tired for no reason") were omitted to avoid the possibility of a built-in association between sleep related symptoms and depression; this modified Zung score was rescaled to have a 25–100 range to be consistent with the original scale. Use of antidepressant medications (selective serotonin reuptake inhibitors, tricyclic antidepressants, and monoamine oxidase inhibitors) was evaluated via interview and questionnaires. Consistent with prior studies, a score of 50 or greater on the modified Zung scale or the use of antidepressant medication was utilized as the principal operational definition of depression for our analyses.[26]

Covariates

Age, sex, body mass index (BMI; kg/m^2), variables from a self-administered health questionnaire, and overnight PSG were examined as possible covariates and potential interaction factors.

From the questionnaire data, we defined variables for chronic medical conditions (coronary artery disease, congestive heart failure, angina, hypertension, stroke, diabetes, asthma, emphysema, thyroid condition, epilepsy, arthritis, or back pain), sedative hypnotic medication use, caffeine consumption (zero, one to two, three to four, or five or more caffeinated beverages per day), tobacco use (current, past, or never), alcohol consumption (two or more drinks of beer, wine, or hard liquor per day versus less), and insomnia (reporting at least one of four insomnia complaints at least five times per month: difficulty falling asleep, waking repeatedly, waking too early in the morning, waking at night and inability to go back to sleep). Habitual sleep duration (as previously defined) was additionally included as a covariate for subjective measures of daytime sleepiness. The sleep time 2 nights prior to the MSLT were included as covariates for the objective measure of sleepiness.

During the overnight PSG, we assessed sleep disordered breathing. A 16-channel recording system (Grass Heritage PSG Digital Sleep System; Grass Technologies, West Warwick, RI) recorded electroencephalogram, electromyogram, and electrooculogram for sleep staging.[34] Sleep disordered breathing was assessed using data acquired from a pulse oximeter (Ohmeda Biox 3740; Englewood, CO, USA), oronasal thermistor (ProTec; Hendersonville, TN, USA), nasal pressure transducer (Validyne Engineering Corp., Northridge, CA, USA), and calibrated thoracic/abdominal respiratory inductance plethysmography (Respitrace, Ambulatory Monitoring, Ardsley, NY, USA). Cessation of airflow for 10 sec or more defined an apnea event. A discernable reduction in the amplitude of summed thoracic and abdominal respiratory inductance plethysmography that was associated with reduction in oxyhemoglobin saturation of 4% or more defined a hypopnea event. The apnea-hypopnea index (AHI) was derived as the mean number of apneas plus hypopneas per hour, and was utilized to define the severity of sleep disordered breathing, according to standard cutpoints (absent [AHI < 5], mild [AHI 5 ≤ 15], or moderate or worse [AHI ≥ 15]).[33] Note that between 1988 and 2000, sleep studies were scored using a paper-based system; since 2000, studies have been scored on a computer. All statistical modeling adjusts for the scoring changes; this removes instrumentation-related influences on sleep disordered breathing assessments after the year 2000.

Statistics

All data were analyzed with SAS software (SAS Institute Inc., Cary, NC) and two-sided p values of less than 0.05 were considered to indicate statistical significance.

The primary goal of the study was to estimate the association of depression with subjective and objective hypersomnolence. Zung scale scores were not modeled as outcomes because the common use of antidepressant medication in this cohort likely obscures underlying Zung levels in those who use medications, therefore biasing associations. Thus, we used the binary definition previously described for all analyses.

For all statistical modeling, repeated-measures logistic regression was used. Repeated- measures analysis allows for the efficient use of multiple studies per person by adjusting for within-subject correlation of observations, and for computing robust standard errors for hypothesis testing and computing confidence intervals. All models examining hypersomnolence and depression included age, sex, BMI, smoking status, alcohol use, caffeine use, chronic conditions, insomnia, sedative drugs, and sleep disordered breathing as potential confounders. MSLT models also included terms for the self-reported total sleep time the 2 nights prior to testing. Subjective sleepiness models (ESS, EDS urge, and EDS frequency) additionally included a term for habitual sleep duration.

Interactions between insomnia and hypersomnolence variables were tested for statistical significance. We examined these interactions because: (1) there are well-described relationships between insomnia and depression[6]; (2) insomnia has been associated with complaints of EDS in epidemiologic studies[35]; and (3) patients with insomnia may complain of daytime sleepiness as a consequence of their sleep disturbances.[36]

Sensitivity analyses with variable definitions of hypersomnolence were conducted to corroborate findings from primary analyses. For subjective hypersomnolence measures, self-reported excessive total sleep time was additionally analyzed using a cutpoint of greater than or equal to 10 h per night, which has been utilized in other studies and nosological definitions of excessive sleep duration.[30,37,38] Objective EDS on the MSLT was additionally analyzed using a mean sleep latency cutpoint less than 10 min, which represents a gray area for excessive objective sleep propensity.[39]

RESULTS

Descriptive data for the subjective and objective hypersomnolence samples are presented in **Tables 1** and **2**, respectively.

Results of the logistic regression modeling of the relationship between the hypersomnolence variables and depression are presented in **Table 3**. Among the hypersomnolence measures of interest, subjective and objective measures demonstrated divergent associations with depression. Elevated ESS score and excessive sleep duration were associated with 1.56-fold (95% confidence interval [CI] 1.31–1.86) and 2.01-fold (95% CI 1.49–2.72) increased odds of depression, respectively

Table 1—Descriptive characteristics of the sample included in the analysis of subjective hypersomnolence measures and depression, n = 3,324 studies from 1,287 participants.

	ESS		
Characteristic	**≥ 11**	**< 11**	**TOTAL**
n (%)	1,032 (31)	2,292 (69)	3,324
Male sex, n (%)	608 (59)	1,193 (52)	1,801 (54)
Age in years, mean (SD)	58 (9)	59 (9)	59 (9)
BMI in kg/m^2, mean (SD)	32 (8)	31 (7)	32 (7)
Chronic condition, n (%)	710 (69)	1,437 (63)	2,147 (65)
Sedative medication, n (%)	67 (6)	163 (7)	230 (7)
Depression, n (%)	335 (32)	527 (23)	1,032 (31)
≥ 5 Caffeinated drinks, n (%)	183 (18)	347 (15)	530 (16)
Current smoker, n (%)	101 (10)	229 (10)	33 (10)
≥ 14 Alcoholic drinks per week, n (%)	43 (4)	150 (7)	193 (6)
Sleep disordered breathing (AHI ≥ 15), n (%)	222 (22)	371 (17)	593 (18)
Insomnia, n (%)	547 (53)	1,050 (46)	1,597 (48)
Self-reported habitual sleep time in hours, mean (SD)	7 (1)	7 (1)	7 (1)

BMI, body mass index; ESS, Epworth Sleepiness Scale; SD, standard deviation.

Table 2—Descriptive characteristics of the sample included in the analysis of the multiple sleep latency test (objective hypersomnolence measure) and depression, n = 2,981 studies from 1,155 participants.

	MSLT		
Characteristic	**MSL < 8**	**MSL ≥ 8**	**TOTAL**
n (%)	1,019 (34)	1,962 (66)	2,981
Male sex, n (%)	625 (61)	997 (51)	1,622 (54)
Age in years, mean (SD)	53 (9)	56 (9)	55 (9)
BMI in kg/m^2, mean (SD)	32 (7)	31 (7)	32 (7)
Chronic condition, n (%)	551 (54)	1,129 (58)	1,680 (56)
Sedative medication, n (%)	26 (3)	128 (7)	154 (5)
Depression, n (%)	196 (19)	520 (27)	716 (24)
≥ 5 Caffeinated drinks, n (%)	227 (22)	339 (17)	566 (19)
Current smoker, n (%)	146 (14)	232 (12)	378 (13)
≥ 14 Alcoholic drinks per week, n (%)	64 (6)	104 (5)	168 (6)
Sleep disordered breathing (AHI ≥ 15), n (%)	190 (19)	302 (16)	492 (17)
Insomnia, n (%)*	235 (42)	758 (51)	993 (49)
Total sleep time in minutes the night before the MSLT, mean (SD)	413 (64)	430 (67)	424 (66)
Total sleep time in minutes 2 nights before the MSLT, mean (SD)	424 (74)	455 (78)	444 (78)

*Sample for the insomnia variable is reduced by 941 due to the addition of this question in 1998. BMI, body mass index; MSL, mean sleep latency; MSLT, multiple sleep latency test; SD, standard deviation.

($p < 0.0001$ for both associations). Secondary measures of subjective sleepiness additionally corroborated the association between somnolence and depression (**Table 3**). A dose-response relationship was observed such that increasing frequency of subjective sleepiness was associated with increased odds of depression, with nearly three times greater odds of depression if excessive sleepiness was experienced most days per month (**Table 3**). Use of a more stringent definition of excessive sleep time (≥ 10 h) was also associated with greater odds of depression (odds ratio [OR]: 2.6, 95% CI 1.2–5.7, $p = 0.014$).

When interactions between hypersomnolence measures and insomnia were examined, a significant insomnia*habitual sleep time interaction was observed ($p = 0.044$). Subsequent analysis demonstrated that excessive sleep duration was significantly associated with depression in those with insomnia (OR 2.73, 95% CI 1.86–3.99, $p < 0.0001$), but not significantly in those without insomnia (OR 1.45, 95% CI 0.89–2.35, $p = 0.13$). There were no other significant interactions between insomnia and other primary or secondary subjective or objective hypersomnolence measures in the principal analysis.

Given the lack of an interaction between insomnia and MSLT-derived excessive sleepiness, as well as the loss of power associated with inclusion of insomnia as a covariate because these questions were not included in the WSC study until 1998, logistic modeling for objective hypersomnia (mean sleep latency < 8 min) was performed without including insomnia as a

Table 3—Results of repeated measures logistic modeling of the relationship between hypersomnolence measures and depression.

Primary Hypersomnolence Measures	Odds Ratio	95% CI	p value
Epworth Sleepiness Scale ≥ 11 (vs. < 11) [a]	1.56	1.31,1.86	< 0.0001
Self-report habitual sleep time ≥ 9 h (vs. < 9)	2.01	1.49,2.72	< 0.0001
Mean sleep latency from MSLT < 8 min (vs. ≥ 8) [b]	0.76	0.63,0.92	0.004
Secondary Hypersomnolence Measures			
Excessive daytime sleepiness-frequency (vs. Never) [a]			
Rarely	0.99	0.77,1.27	0.927
Sometimes	1.60	1.23,2.08	0.0005
Often	2.38	1.77,3.19	< 0.0001
Almost always	2.92	2.00,4.25	< 0.0001
EDS-urge yes (vs. no) [a]	1.65	1.38,1.98	< 0.0001

Model adjusted for age, sex, body mass index, smoking status, alcohol use, caffeine use, chronic conditions, insomnia, sedative drugs, and sleep disordered breathing. [a] Additionally adjusted for self-reported habitual sleep time. [b] Additionally adjusted for minutes of sleep the 2 nights prior to the multiple sleep latency test (MSLT) and not adjusted for insomnia due to the loss of sample size and the lack of confounding.

covariate. Objective sleep propensity was associated with lower odds of depression (OR: 0.76, 95% CI 0.63–0.92, p = 0.004). To be sure the type of MSLT protocol did not affect our findings, we stratified the data on protocol type and found that standardized (beta) coefficients for MSLT data collected using clinical and research protocols were nearly identical and did not warrant stratification (−0.23 and −0.25, respectively). Similar results were obtained using the more liberal definition of objective sleepiness of mean sleep latency < 10 min (OR: 0.84, 95% CI 0.70, 0.99, p = 0.039). Congruent findings were also observed among a smaller sample (2,040 observations; 996 participants), in which insomnia data were available and thus were included as a covariate (OR 0.78; 95% CI 0.63–0.97, p = 0.022).

DISCUSSION

Our findings indicate divergent associations between subjective and objective measures of hypersomnolence with depression. Specifically, both self-reported EDS and habitual sleep duration were associated with increased odds of depressive symptoms, but conversely, excessive sleep propensity, as measured by the MSLT, was associated with reduced likelihood of depression. To our knowledge, this is the first large epidemiologic study that has examined associations between depression and sleepiness quantified by the MSLT. Our findings corroborate previous literature on hypersomnolence in depressive illness, and underscore the limitations of the MSLT in the assessment of sleepiness in mood disorders.

Several prior investigations have similarly demonstrated associations between subjective sleepiness and depressive symptoms. Among outpatients with depressive disorders, increased ESS scores have been associated with more severe depressive symptomatology and suicidal ideation.[40] Also, elevated ESS scores have been associated with increased likelihood of both current and lifetime history of depressive disorders in a large cohort of women, who were carefully assessed for psychiatric disorders using the Structured Clinical Interview for DSM-IV Disorders.[41] However, these investigations were unable to control for sleep disordered breathing, which is frequently associated with both depressive symptoms and EDS.[42] The importance of controlling for sleep apnea in epidemiologic studies of sleepiness in mood disorders is highlighted by recent data that has demonstrated associations of both self-reported depressive symptoms and sleep disordered breathing with EDS.[35] Prior data from the Penn State Cohort study, which had PSG data to objectively quantify both the presence and severity of sleep disordered breathing, demonstrated that self-reported excessive sleepiness was more strongly associated with depression than sleep disordered breathing.[43] Our findings further extend this literature through the use of multiple questions to assess daytime sleepiness that provide convergent validity, as well as validated measures of both excessive sleepiness and depressive symptomatology, enhancing face validity of the study.

Our results that demonstrate increased odds of depression with excessive sleep duration are also congruent with other prior cross-sectional investigations. Long self-reported sleep duration has been associated with depression in multiple epidemiologic studies conducted in several countries.[44–46] Moreover, recent population-based data have demonstrated that the likelihood of sleeping ≥ 9 h/d coupled with distress/impairment is 3 to 12 times higher among persons with a mood disorder.[28] Our finding of an interaction between self-reported insomnia and excessive sleep duration suggests that, perhaps, increased habitual sleep time as a symptom of depression is more closely related to excessive time in bed than to sleep duration per se. This interpretation is supported by recent actigraphic data in patients with bipolar disorder.[47] Such findings underscore the need to utilize both objective and subjective measures in the study of hypersomnolence in mood disorders.

As previously discussed, the MSLT, considered the gold standard objective measure for quantifying sleepiness, has failed to segregate hypersomnolent mood disordered patients from healthy persons or demonstrate increased sleep propensity relative to other disorders of excessive sleepiness.[20–23] Our results are thus congruent with prior investigations that have

similarly demonstrated a paradoxical relationship between objective and subjective measures of sleepiness in mood disorders. What is not clear, and what requires further elucidation, is the reason for this divergence between self-reported and externally quantified somnolence.

A common interpretation of discrepant subjective and objective measures of sleepiness in depression is that patients with mood disorders misperceive fatigue as sleepiness. This is a plausible explanation, particularly given the negative cognitive biases and dysfunctional beliefs that are common in mood disorders.[48] Moreover, significant correlations between fatigue severity measures and the ESS have been observed in major depression.[49] However, difficulty segregating a subjective sense of sleepiness from fatigue is not unique to mood disorders. Significant correlations between the fatigue severity index and ESS have been demonstrated in narcolepsy, restless legs syndrome, sleep apnea, and other disorders of hypersomnolence, as well as in healthy individuals.[50] Moreover, prior studies have also demonstrated that patients with obstructive sleep apnea who are objectively sleepy based on MSLT results are more likely to report that they experience fatigue, tiredness, or lack of energy than that they experience sleepiness.[51] Such findings corroborate the clinical challenges of segregating sleepiness from fatigue, because many patients, regardless of their underlying diagnosis, frequently have difficulty discriminating these symptoms, particularly when they co-occur.

The MSLT quantifies the ability to fall asleep on multiple repeated nap opportunities. As such, it measures one particular aspect of sleep propensity, sometimes called "sleepability" [52], but does not quantify other facets of sleepiness such as drowsiness or the ability to maintain vigilance.[53] In fact, results of the MSLT and maintenance of wakefulness test, which measures the ability to maintain vigilance under soporific conditions, can be discordant from one another,[23] highlighting the fact that sleepiness is a multifaceted construct unlikely to be wholly quantified by a single measure. Thus, although many hypersomnolent patients with mood disorders may not demonstrate sleepiness when assessed with the MSLT, it is quite possible that the MSLT is an insufficient tool to quantify sleepiness in this particular population. The limitations of the MSLT as a measure of pathological hypersomnolence are further underscored by the observation that persons with short sleep latencies on the MSLT can simultaneously be devoid of clinically significant subjective sleepiness, as well as the very modest correlations between the MSLT and subjective measures of sleepiness such as the ESS.[52,54]

Regardless of the causes of the discrepant objective and subjective measures of hypersomnolence that may occur in depression, future studies directed toward resolving this apparent paradox may prove a fruitful line of inquiry. The need to develop and validate new tools beyond the MSLT to assess sleepiness is a crucial area for sleep disorders research and clinical care.[55] In many ways, hypersomnolence in mood disorders may prove an ideal model system to test new methods that quantify aspects of sleepiness beyond those assayed by the MSLT.

There are limitations of this study that merit discussion. First, we did not have an objective measure of habitual sleep duration and thus our results cannot shed further light on whether there is a discrepancy between objective and subjective measures of sleep duration similar to that observed for excessive sleepiness. Second, our outcome of depression was based in part on a self-reported rating scale, which is less accurate than the gold standard of structured interviews in the assessment of psychiatric disorders. In a similar vein, the insomnia measure utilized as a covariate in analysis was not a validated instrument. Also, this measure was not added to the WSC Cohort study until 1998, thus limiting power for statistical inference regarding interactions of insomnia symptoms with objective measures of sleep propensity. Also, specific data regarding self-assessed sleep latency on MSLT nap opportunities were not readily available, which may have shed light on whether divergent associations between subjective and objective sleepiness with depression observed in this study were related to sleep-state misperception. Finally, despite our best efforts to control for factors that would influence results, there may have been unmeasured and/or unadjusted covariates that could have affected findings. However, the use of PSG to quantify the severity of sleep disordered breathing, as well as detailed assessment of other health-related activities/habits that were included as covariates, limits the likelihood of such confounding substantially altering results.

In conclusion, we have demonstrated divergent associations between subjective and objective measures of hypersomnolence with depression among participants in the WSC Study. Subjective sleepiness and excessive sleep duration were associated with an increased likelihood of depression; however, an objective measure of sleepiness demonstrated an inverse relationship, such that short sleep latencies on the MSLT were associated with decreased likelihood of depressive symptomatology. Further research that probes the underlying cause of these paradoxical findings, and assesses whether subjective and objective measures of hypersomnolence impart divergent risks on the development of mood disorders, are indicated to clarify the clinical significance of these findings.

ABBREVIATIONS

BMI, body mass index
C, clinical protocol
CI, confidence interval
EDS, excessive daytime sleepiness
ESS, Epworth Sleepiness Scale
MSLT, multiple sleep latency test
PSG, polysomnography
R, research protocol
REM, rapid eye movement
SD, standard deviation
SOL, sleep onset latency
WSC, Wisconsin Sleep Cohort

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ACKNOWLEDGMENTS

The authors thank Terry Young, K. Mae Hla, Amanda Rasmuson, Kathryn Pluff, Katherine Stanback, Robin Stubbs, and Mary Sundstrom for their contributions to obtaining funding (TY) and study design and data collection.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication October, 2015
Submitted in final revised form October, 2015
Accepted for publication November, 2015
Address correspondence to: David T. Plante, MD, Wisconsin Psychiatric Institute and Clinics, 6001 Research Park Blvd., Madison, WI 53719; Tel: (608) 262-0130; Fax: (608) 263-0265; Email: dplante@wisc.edu

DISCLOSURE STATEMENT

This was not an industry-supported study. This work was supported by the National Institute of Mental Health (grant K23MH099234), National Heart, Lung, and Blood Institute (grant R01HL62252), National Institute of Aging (grant R01AG14124), National Institute of Neurological Disorders and Stroke (grant NIH-NS23724), the National Center for Research Resources (grant 1UL1RR025011) at the US National Institutes of Health, Brain and Behavior Research Foundation, American Sleep Medicine Foundation, and the University of Wisconsin School of Medicine and Public Health. Dr. Mignot reports grant support, investigational drug/device, and consultancy for Jazz Pharmaceutical, research support from Merck and GSK, and intellectual property rights with ALPCO. All other authors report no financial conflicts of interest.