



Published in final edited form as:

*Depress Anxiety*. 2013 September ; 30(9): . doi:10.1002/da.22064.

## RELATIONSHIP BETWEEN SLEEP DISTURBANCE AND DEPRESSION, ANXIETY, AND FUNCTIONING IN COLLEGE STUDENTS

Maren Nyer, Ph.D.<sup>\*</sup>, Amy Farabaugh, Ph.D., Kiki Fehling, B.A., David Soskin, M.D., Daphne Holt, M.D., Ph.D., George I. Papakostas, M.D., Paola Pedrelli, Ph.D., Maurizio Fava, M.D., Angela Pisoni, B.A., Ottavio Vitolo, M.D., and David Mischoulon, M.D., Ph.D.

© 2013 Wiley Periodicals, Inc.

<sup>\*</sup>Correspondence to: Maren Nyer, Depression Clinical & Research Program, Massachusetts General Hospital, 1 Bowdoin Square, 6th Floor, Boston, MA 02114., mnyer@partners.org.

### Conflict of interest

Maren Nyer, Ph.D., reports no financial relationships with commercial interests.

Amy Farabaugh, Ph.D., has received grants from Narsad, Kaplen, as well as a K-23 award through NIMH. She received honoraria for talks at the MGH Academy and the APA. She holds/held stocks Pfizer, Glazo, and Smith Klein.

Kiki Fehling, B.A. reports no financial relationships with commercial interests.

David Soskin, M.D. has received research support from Harvard Medical School, Kaplen Fellowship and PharmRx. He has received honoraria for speaking and/or consulting with MGH Psychiatry Academy/Primedia and ClearView Healthcare Partners. Daphne Holt, MD, PhD reports no financial relationships with commercial interests.

George Papakostas, M.D., has served as a consult for Abbott, BMS, Brainsway, Cephalon, Dey Pharmaceuticals, Eli Lilly, Otsuka, PAMLAB, Ridge Diagnostics, Takeda, and Theracos. He receives honoraria from the above companies, in addition to Astra Zeneca, GSK, Lundbeck, Pfizer and Roche. He has received grants from Astra Zeneca, BMS, Forest, NIMH, PAMLAB, Pfizer, Ridge Diagnostics and Sunovion.

Paola Pedrelli, PhD reports no financial relationships with commercial interests.

Maurizio Fava, M.D., has received research support from Abbot; Alkermes; Aspect Systems; AstraZeneca; BioResearch; BrainCells; BMS; CeNeRx; Cephalon; Clinical Trials Solutions; Clintara; Covance; Covidien; Eli Lilly; ElMindA; EnVivo; Euthymics; Forest; Ganeden; GSK; Icon; i3 Innovus/Ingenix; J&J; Lichtwer; Lorex; NARSAD; NCCAM; NIDA; NIMH; Novartis; Organon; PamLab; Pfizer; Pharmavite<sup>®</sup>; Photothera; Roche; RCT Logic; Sanofi-Aventis; Shire; Solvay; Synthelabo; Wyeth-Ayerst. He has served as a consult for Abbott; Affectis; Alkermes; Amarin; Aspect; A-Z; Auspex; Bayer; Best Practice Project Management; BioMarin; Biovail; BrainCells; BMS; CeNeRx; Cephalon Clinical Trials Solutions; CNS Response; Compellis; Cypress; DiagnoSearch Life Sciences; Dinippon Sumitomo; Dov; Edgemont; Eisai; Eli Lilly; EnVivo; ePharmaSolutions; EPIX; Euthymics; Fabre-Kramer; Forest; GenOmind; GSK; Grunenthal; i3 Innovus/Ingenix; Janssen; Jazz; J&J R&D; Knoll; Labopharm; Lorex; Lundbeck; MedA-vante; Merck; MSI Methylation Sciences; Naurex; NeuralStem;Neuronetics; NextWave; Novartis; Nutrition 21; Orexigen; Organon; Otsuka; PamLab; Pfizer; PharmaStar; Pharmavite<sup>®</sup>; PharmRx; Precision Human Biolaboratory; Prexa; Puretech Ventures; PsychoGenics; Psylin; Rexahn; Ridge; Roche; RCT Logic; Sanofi-Aventis; Sepracor; Servier; Schering-Plough; Solvay; Somaxon; Somerset; Sunovion; Supernus; Synthelabo; Takeda; Tal Medical; Tetragenex; TransForm; Transcept; Vanda. He has received honoraria for speaking and/or publishing with Adamed, Co.; Advanced Meeting Partners; APA; ASCP; A-Z; Belvoir Media Group; Boehringer Ingelheim GmbH; BMS; Cephalon; CME Institute/Physicians Postgraduate Press, Inc.; Eli Lilly; Forest; GSK; Imedex; MGH Psychiatry Academy/Primedia; MGH Psychiatry Academy/Reed Elsevier; Novartis; Organon; Pfizer; PharmaStar; United BioSource; Wyeth-Ayerst. He has a minority share in equity holdings at Compellis. He has patents for Sequential Parallel Comparison Design (SPCD) and patent application for a combination of azapirones and bupropion in Major Depressive Disorder (MDD) for research and licensing of SPCD with RCT Logic. He receives copyright royalties for the MGH Cognitive & Physical Functioning Questionnaire (CPFQ), Sexual Functioning Inventory (SFI), Antidepressant Treatment Response Questionnaire (ATRQ), Discontinuation-Emergent Signs & Symptoms (DESS), and SAFER; Lippincott, Williams & Wilkins; Wolkers Kluwer; and World Scientific Publishing Co. Pte. Ltd.

Angela Pisoni, BA reports no financial relationships with commercial interests.

Ottavio Vitolo, M.D., has received research support from Harvard Neurodiscovery Center and Harvard Medical School, Dupont-Warren Fellowship, Harvard Psychiatry Department, Clinical Investigator Training Program, Beth Israel Deaconess Medical Center and Harvard Medical School which was in part funded with an unrestricted grant from Pfizer, Inc. and Merck & Co., Inc. He has pending patents with Ginkgolide compounds, compositions, extracts and uses thereof, methods for treating mild cognitive impairment, and ATF4 as a therapeutic target in Alzheimer's disease and other neurological disorders.

David Mischoulon, M.D., Ph.D., has received research support from the Bowman Family Foundation, Bristol-Myers Squibb Co., Cederoth, FisherWallace, Ganeden, Lichtwer Pharma, and Nordic Naturals. He has received honoraria for consulting, speaking, and writing from PamLab, Bristol-Myers Squibb Co., Nordic Naturals. He has received royalties from Back Bay Scientific for PMS Escape, and from Lippincott Williams & Wilkins for published book "Natural Medications for Psychiatric Disorders: Considering the Alternatives." No payment has exceeded \$10,000.

Depression Clinical & Research Program, Massachusetts General Hospital, Boston, Massachusetts

## Abstract

**Background**—Sleep disturbance (SD) has complex associations with depression, both preceding and following the onset and recurrence of depression. We hypothesized that students with depressive symptoms with SD would demonstrate a greater burden of comorbid psychiatric symptoms and functional impairment compared to students with depressive symptoms without SD.

**Methods**—During a mental health screening, 287 undergraduate students endorsed symptoms of depression (Beck Depression Inventory [BDI]  $\geq 13$ ) and filled out the following self-report measures: demographic questionnaire, BDI, Anxiety Symptom Questionnaire—intensity and frequency (ASQ), Beck Hopelessness Scale (BHS), Beck Anxiety Inventory (BAI), Quality of Life Enjoyment and Satisfaction Questionnaire (QLESQ), and the Massachusetts General Hospital Cognitive and Physical Functioning Questionnaire (CPFQ). SD was measured using the BDI sleep item #16 dichotomized (score 0: no SD; or score > 0: some SD).

**Results**—Students with depressive symptoms and SD ( $n = 220$ ), compared to those without SD ( $n = 67$ ), endorsed significantly more intense and frequent anxiety and poorer cognitive and physical functioning. Students with depressive symptoms with and without SD did not significantly differ in depressive severity, hopelessness, or quality of life.

**Conclusions**—College students with depressive symptoms with SD may experience a greater burden of comorbid anxiety symptoms and hyperarousal, and may have impairments in functioning, compared to students with depressive symptoms without SD. These findings require replication. *Depression and Anxiety* 00:1–8, 2013.

## Keywords

sleep; depression; anxiety; hopelessness; functioning; quality of life; college students; mental health screening; hyperarousal

## INTRODUCTION

Sleep disturbance (SD) has complex associations with depression. SD, which could include over- or under-sleep, as well as disturbed sleep is a common physical symptom in major depressive disorder (MDD) and one criterion used for a DSM-IV-based diagnosis of depression.<sup>[1]</sup> Different depressive symptoms, such as SD, may vary in regard to the amount of associated adverse impact they have on functioning, treatment response, and outcome.<sup>[2]</sup> SD is a risk factor for the onset of depressive episodes<sup>[3]</sup> and also considered to be a prodromal symptom of MDD.<sup>[4]</sup> For example, a recent meta-analysis of 21 studies found that nondepressed individuals with insomnia have a twofold risk of developing depression compared to those without SD.<sup>[5]</sup> In other cases, SD is a frequent residual symptom of MDD.<sup>[6]</sup> Though not found to be true in all studies, <sup>[2]</sup> SD has been shown to predict a depressive.<sup>[7, 8]</sup>

In the college student population, SD is common, though the prevalence rate appears variable, perhaps in part due to methodological differences. Nardoff et al.,<sup>[9]</sup> in a sample of 583 students, found that 13% reported clinically significant symptoms of insomnia over the past 2 weeks (on the Insomnia Severity Index [ISI]). Gaultney<sup>[10]</sup> found that 27% ( $n = 500$ ) of a large-scale sample of college students ( $N = 1,845$ ) were at risk for SD (using the SLEEP-50, an instrument validated for college students, measuring sleep characteristics<sup>[11]</sup>). Other studies have reported a much greater prevalence of SD. In a large study ( $N = 1,125$ ),

the Pittsburgh Sleep Quality Index (PSQI) categorized over 60% of college students as poor-quality sleepers.<sup>[12]</sup> Lastly, Singleton<sup>[13]</sup> found that of the 236 students who completed interview surveys, 79% reported bedtimes after midnight and only 24% reported getting adequate sleep at night (i.e., at least 8.4 hrs). Furthermore, there may be a cohort effect with recent generations of college students exhibiting even higher rates of self-reported dissatisfaction with their sleep.<sup>[14]</sup>

The following types of SD have been reported in the college population: difficulty falling or staying asleep,<sup>[15–19]</sup> daytime sleepiness,<sup>[15, 19, 20]</sup> poor sleep quality,<sup>[15]</sup> and other general sleep problems.<sup>[15, 17, 21]</sup> In turn, among college students, SD has been associated with a wide variety of functional and psychiatric domains, including suicidal ideation,<sup>[9]</sup> irritability,<sup>[22]</sup> poor physical health,<sup>[12]</sup> academic difficulties,<sup>[10]</sup> substance use,<sup>[15]</sup> and poor mental health.<sup>[16, 23, 24]</sup> In an early study by Vollrath et al.,<sup>[25]</sup> a cross-sectional sample of young adults with continued insomnia demonstrated greater levels of major depression, generalized anxiety, panic, and phobias. Similarly, Taylor et al.<sup>[16]</sup> found that individuals with insomnia, compared to those without, scored higher on somatization, obsessive compulsive, depression, anxiety, and psychic distress. In a study of 136 college students, poor sleepers experienced greater daytime functional impairments.<sup>[26]</sup> Finally, Lund et al.<sup>[12]</sup> also found that students with sleep difficulties had more physical and psychological health problems.

Given the overlap between SD and depression, the interface between the two deserves further characterization. In some cases, if sleep problems are addressed, depressive symptoms may improve. In fact, some depressive symptoms may be secondary to poor sleep (e.g., daytime tiredness or poor concentration). We examined whether students with significant depressive symptoms with and without SD differed across psychiatric and functional domains. Our primary hypothesis was that students with significant depressive symptoms with SD would have a greater psychiatric symptom burden and functional impairment compared to those students with depressive symptoms without SD. We based these hypotheses on previous literature demonstrating a relationship between SD and greater psychiatric burden—i.e., symptoms of anxiety and psychological distress<sup>[16, 25]</sup> and daytime functional impairment.<sup>[26, 27]</sup>

## METHODS

We report on data from a subsample of 287 students from a larger parent study conducted at undergraduate colleges in the United States by the Depression Clinical and Research Program (DCRP) of the Massachusetts General Hospital (MGH) Department of Psychiatry (original study results reported in Farabaugh et al.<sup>[28]</sup>). For a brief summary, we conducted mental health screenings at several universities. At each school, we spent two consecutive days in heavily trafficked areas at a table, offering students a \$10 gift certificate to their university bookstore for completing a packet of self-report measures. Undergraduate college students voluntarily participated in the mental health screening and signed consent forms approved by the MGH Institutional Review Board (IRB). Students endorsing significant symptoms of depression, as measured by a score of 13 or greater on the Beck Depression Inventory (BDI<sup>[29]</sup>), were included in this study. This study was conducted over several years and scales differed throughout the course of the study. As such, the total sample sizes for the scales are inconsistent.

Self-report measures completed by students included

- *Demographics Questionnaire* (unpublished; available upon request): This four-page questionnaire asked students about demographic domains such as age, current grade point average (GPA), marital status, living situation, ethnicity, family

socioeconomic status (SES), and school year. Other than age and GPA, the demographic information was collected categorically.

- *The BDI*: The BDI sleep item (#16) was excluded from the BDI total score, as this item was used as the grouping variable (independent variable). BDI sleep item (BDI #16): this selected item assessed SD and included four response choices: 0 = *I can sleep as well as usual*; 1 = *I don't sleep as well as I used to*; 2 = *I wake up 1–2 hr earlier than usual and find it hard to get back to sleep*; and 3 = *I wake up several hours earlier than I used to and cannot get back to sleep*. For this study, students were assigned to one of the two sleep groups based on their responses to this item. Group 1 represented students with no SD (response of 0 on BDI #16), and group 2 represented students with at least some SD (response of 1, 2, or 3 on BDI #16).
- *The Anxiety Symptom Questionnaire—intensity and frequency scale (ASQ<sup>[30, 31]</sup>)* was also completed. The ASQ is a 17-item questionnaire that asks about the frequency and intensity of somatic and psychological symptoms of anxiety; including worrying, trouble relaxing, insomnia, and functional impairment. Participants separately rated the intensity and frequency of each symptom on a scale of 0–10, from “none” to “frequently.” Higher total scores indicate greater anxiety.
- *The Beck Hopelessness Scale (BHS<sup>[32]</sup>)* was used to assess hopelessness. The BHS is a 20-item questionnaire that asks respondents to answer true or false statements. Each statement reflects a positive or negative attitude regarding the future. Higher scores indicate greater hopelessness.
- *Quality of Life Enjoyment and Satisfaction Questionnaire—Short Form (QLESQ<sup>[33]</sup>)*: The QLESQ—Short Form asks about physical health, general feelings of well-being, work satisfaction, leisure activities, social relationships, and life satisfaction over the past week. Participants are asked to rate their answers on a scale of 1–5, from “very poor” to “very good.” Answers in the “very good” range indicate greater satisfaction with life. A quality-of-life index score for the QLESQ—Short Form is calculated by averaging the scores of all 16 items, with higher scores indicating higher quality of life.
- *The Beck Anxiety Inventory (BAI<sup>[34]</sup>)* is a 21-item scale measuring the severity of self-reported anxiety. It includes descriptive statements of anxiety symptoms rated on a 4-point scale as follows: 0 = *not at all*; 1 = *mildly, it did not bother me much*; 2 = *moderately, it was very unpleasant, but I could stand it*; and 3 = *severely, I could barely stand it*. Higher total scores indicate greater anxiety.
- *The Massachusetts General Hospital Cognitive and Physical Functioning Questionnaire (CPFQ<sup>[35]</sup>)* is a 7-item questionnaire for assessment of cognitive and physical functioning. Higher overall scores indicate greater cognitive and physical dysfunction.

## STATISTICAL ANALYSES

For all measures, descriptive statistics were performed for the entire sample of students with depressive symptoms ( $n = 287$ ), as well as for students with ( $n = 220$ ) and without ( $n = 67$ ) SD. We conducted a series of ANOVA analyses and dichotomized the BDI sleep item (#16), indicating the absence or presence of SD (zero vs. nonzero score on BDI item #16, respectively) over the past week. Depression severity was derived from the total BDI score minus BDI sleep item (#16). The dependent variables included both psychiatric (i.e., BDI total [excluding the sleep item], BHS total, ASQ intensity total, ASQ frequency total, and BAI total) and functional domains (i.e., QLESQ total and CPFQ total).

For exploratory analyses, we examined individual items of the CPFQ, as this questionnaire covers a range of functional domains (Bonferroni correction  $P < .05/7$ ). We also examined whether hyper-arousal was significantly more common in the group with SD. To do so, we selected three items from the different measures that indicated possible hyperarousal (BAI item #4: “unable to relax”; ASQ frequency and intensity item #6: “trouble relaxing”; ASQ frequency and intensity item #15: “feeling restless, keyed up, or on edge”). We ran the same series of ANOVAs as above using these items as the dependent variables (Bonferroni correction,  $P < .05/5$ ). Statistical analyses were performed using SPSS Version 19.  $P$ -values were set at .05 for our a priori or primary hypotheses and a Bonferroni correction was used separately for each of the exploratory analyses (Bonferroni correction: CPFQ items  $P < .05/7$ ; hyperarousal items  $P < .05/5$ ).

## RESULTS

There were no statistically significant differences in demographic characteristics, including age, gender distribution, and self-reported GPA, between students with and without SD ( $P > .05$ ; Table 1). For the total sample, the mean BDI total score was  $19.43 \pm 6.67$  and the mean BDI total score minus the BDI sleep item (#16) score was  $18.34 \pm 6.44$ . The mean BDI total scores minus the BDI sleep item (#16) are listed in Table 3 (with SD:  $M(SD) = 18.45(6.85)$ ; without SD =  $18.00(4.85)$ ). Table 2 illustrates the frequency of students' responses on the BDI sleep item.

Table 3 summarizes the results from the ANOVAs comparing students with and without SD across the various psychiatric and functional outcomes. Students with SD endorsed significantly more intense anxiety on both subscales of the ASQ (intensity and frequency,  $P < .01$ ), but there were no statistically significant differences in BAI total scores. Students with SD endorsed significantly greater deficits in cognitive and physical functioning (CPFQ;  $P < .01$ ) compared to those without SD. There were no statistically significant differences in overall depression severity per BDI total score minus BDI #16, hopelessness per BHS total score, and quality of life per QLESQ total score (Table 3).

When we analyzed the individual items on the CPFQ, correcting for multiple comparisons, one of the seven individual CPFQ items demonstrated significant differences between those with and without SD (Table 3), with higher scores on the CPFQ individual items indicating greater functional impairment. Students with depressive symptoms and SD demonstrated greater impairment to remember/recall information over the past month.

As a post hoc analysis, we examined whether items suggestive of hyperarousal on the anxiety scales were greater in those students with depressive symptoms and SD. We selected items from the BAI and ASQ that assessed aspects of hyperarousal and conducted follow-up ANOVAs with the same methodology as our previous analyses, again correcting for multiple comparisons. Mean scores for the hyperarousal items were greater in the students with SD compared to those without for the ASQ #6 intensity: “trouble relaxing” ( $P < .01$ ). Results are summarized in Table 4.

## DISCUSSION

This study suggests that the presence of SD, not measured as a separate disorder from depressive symptoms, in college students with depressive symptoms characterizes a subgroup that may have more anxiety and cognitive and physical impairment. On self-report measures students with depressive symptoms and SD had greater anxiety (both intensity and frequency totals on the ASQ) and more impaired cognitive and physical functioning (on CPFQ), compared to students without SD. When we examined individual CPFQ items,

remembering and recall of information was significantly worse in students with SD compared to those without SD (Table 3), which may have implications for academic performance. Despite the results not reaching statistical significance, there may be a trend for students with depressive symptoms and SD to have more hyperarousal compared to those without SD.

Interestingly, students with SD did not score significantly higher on the BAI as a whole, despite scoring significantly higher on the ASQ, both in frequency and intensity totals (Table 3). One possible explanation is that the wide confidence interval, large standard deviation, and small sample size for BAI responses ( $n = 55$ ) compared to the ASQ ( $n = 145$  for intensity and  $n = 143$  for frequency) limited the ability to detect statistically significant differences. Nonetheless, students with SD scored approximately five points greater on the BAI, compared to students without SD, which may be clinically meaningful and is consistent with the ASQ findings.

Our findings suggest that there may be an association between SD and hyperarousal in those with significant symptoms of depression (Tables 3 and 4). Although the case-control design cannot establish causality, it is possible that SD may be reflective of a general level of hyperarousal during the day. Recent evidence suggests that hyperarousal may represent a common factor linking insomnia and fear-based anxiety disorders.<sup>[36, 37]</sup> Consistent with this hypothesis, a large study ( $n = 1,125$ ) of college students found that tension and stress accounted for 24% of the variance in the Pittsburgh Sleep Quality Index (PSQI), whereas exercise, alcohol, caffeine, and consistency of sleep schedule were not significant predictors of the PSQI score.<sup>[13]</sup>

Our findings also suggest that cognitive impairment, even in a population with significant depressive symptoms, may be associated specifically with SD rather than with depression per se. For example, Moo-Estrella et al.<sup>[20]</sup> found that students with depressive symptoms and sleepiness had more perceived difficulties in academic performance relative to those without sleepiness. In nondepressed college populations, students classified as poor-quality sleepers endorsed more problems with physical and psychological health.<sup>[13]</sup> Another study found that “sleepier” college students and those with “later sleep schedules” had lower GPAs.<sup>[14]</sup> Finally, college students with insomnia symptoms have demonstrated significantly higher rates of comorbid health conditions, such as hypertension, and more psychiatric symptoms, compared to subjects without insomnia.<sup>[17]</sup>

Surprisingly, our study did not find an association between SD and depression severity. This is in contrast to findings from Taylor et al.,<sup>[16]</sup> who observed a relationship between insomnia and depressive symptoms in a general group of undergraduate students. Likewise, Moo-Estrella et al.<sup>[20]</sup> found a relationship between sleepiness and the presence of depressive symptoms in a college population. We may not have found a relationship between depressive severity and SD in part because we only looked at individuals with BDI  $\geq 13$ , potentially limiting the statistical power. These were also students who were willing to volunteer for a mental health screening and thus we may not have captured those with the full range of depressive symptoms.

Our study has several limitations. First, we used only the BDI sleep item (#16) as a sleep measure. The study would be strengthened by the use of other validated sleep instruments, as well as more objective measures of sleep quality. Second, due to the study’s case-control design, a causal relationship between SD and psychological symptoms and functional impairment cannot be determined. Finally, our selected population of college students may limit the generalizability of the results. Replication in other populations and also in different

samples of the college students is warranted to ensure the current findings are not sample specific.

Our findings suggest that poor sleep in college students with symptoms of depression should be a target of therapeutic intervention both proactively and as a residual depressive symptom. SD represents an under-diagnosed and undertreated problem: multiple studies have demonstrated that providers frequently fail to ask about insomnia and that there is a paucity of specialists trained in sleep medicine.<sup>[38–40]</sup> To our knowledge, there have been no prospective psychopharmacological treatment studies targeting insomnia in college students with depressive symptoms, though the adult literature suggests that the use of the benzodiazapine receptor agonist, eszopiclone, can accelerate and increase rates of recovery from depression,<sup>[41]</sup> again suggesting a pathophysiological overlap between depression and insomnia. In another study by the same group, the shorter acting benzodiazapine agonist, zolpidem, did not separate from placebo on measures of response,<sup>[42]</sup> yet showed significant beneficial effects on cognitive and physical functioning, as measured by the CPFQ, which may be applicable to the SD subgroup with greater functional impairment captured in the present study. The need to target SD in college students is also underscored by increasing rates of prescriptions for serotonergic antidepressants,<sup>[43]</sup> since common side effects of these medications include insomnia and cognitive symptoms.<sup>[6]</sup> Finally, the abundance of environmental factors contributing to insomnia in college students, may provide further support for disseminating empirically validated forms of cognitive and behavioral therapy to target sleep.<sup>[44]</sup>

In summary, we have shown that college students who have depressive symptoms and SD may experience a greater burden of anxiety, hyperarousal, and impairments in functioning, compared to students with depressive symptoms and no SD. These findings warrant replication in other populations.

## Acknowledgments

Contract grant sponsor: The Jed Foundation.

## References

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 4. Washington, DC: American Psychiatric Association; 1994.
2. Yang H, Sinicropi-Yao L, Chuzi S, et al. Residual sleep disturbance and risk of relapse during the continuation/maintenance phase treatment of major depressive disorder with the selective serotonin reuptake inhibitor fluoxetine. *Ann Gen Psychiatry*. 2010; 9:52–56.
3. Breslau N, Roth T, Rosenthal L, Andreski P. Sleep disturbance and psychiatric disorders: a longitudinal epidemiological study of young adults. *Biol Psychiatry*. 1996; 30:411–418. [PubMed: 8679786]
4. Fava GA, Grandi S, Canestrari R, Molnar G. Prodromal symptoms in primary major depressive disorder. *J Affect Disord*. 1990; 19:149–52. [PubMed: 2142701]
5. Baglioni C, Battagliese G, Feige B, et al. Insomnia as a predictor of depression: a meta-analytic evaluation of longitudinal epidemiological studies. *J Affect Disord*. 2011; 135:10–19. [PubMed: 21300408]
6. Nierenberg AA, Keefe BR, Leslie VC, et al. Residual symptoms in depressed patients who respond acutely to fluoxetine. *J Clin Psychiatry*. 1999; 60:221–225. [PubMed: 10221281]
7. Perlis ML, Giles DE, Buysse DJ, Tu X, Kupfer DJ. Self-reported sleep disturbance as a prodromal symptom in recurrent depression. *J Affect Disord*. 1997; 42:209–212. [PubMed: 9105962]
8. Manber R, Chambers AS. Insomnia and depression: a multifaceted interplay. *Curr Psychiatry Rep*. 2009; 11:437–442. [PubMed: 19909664]

9. Nadorff MR, Nazem S, Fiske A. Insomnia symptoms, nightmares, and suicidal ideation in a college student sample. *Sleep*. 2011; 34:93–8. [PubMed: 21203379]
10. Gaultney JF. The prevalence of sleep disorders in college students: impact on academic performance. *J Am Coll Health*. 2010; 59:91–97. [PubMed: 20864434]
11. Spoomaker V, Verbeeck I, Van Den Bout J, Lip EC. Initial validation of the SLEEP-50 questionnaire. *Behav Sleep Med*. 2005; 3:227–246. [PubMed: 16190812]
12. Lund HG, Reider BD, Whiting AB, Prichard JR. Sleep patterns and predictors of disturbed sleep in a large population of college students. *J Adolesc Health*. 2010; 46:124–132. [PubMed: 20113918]
13. Singleton RA, Wolfson AR. Alcohol consumption, sleep, and academic performance among college students. *J Stud Alcohol Drugs*. 2009; 70:355–363. [PubMed: 19371486]
14. Hicks RA, Fernandez C, Pellegrini RJ. Striking changes in the sleep satisfaction of university students over the last two decades [Abstract]. *Percept Motor Skills*. 2001; 93:660. [PubMed: 11806582]
15. Vail-Smith K, Felts WM, Becker C. Relationship between sleep quality and health risk behaviors in undergraduate college students. *Coll Stud J*. 2009; 43:924–930.
16. Taylor DJ, Gardner CE, Bramoweth AD, et al. Insomnia and mental health in college students. *Behav Sleep Med*. 2011; 9:107–116. [PubMed: 21491233]
17. Buboltz WC, Brown F, Soper B. Sleep habits and patterns of college students: a preliminary study. *J Am Coll Health*. 2011; 50:131–135. [PubMed: 11765249]
18. Brooks PR, Girgenti AA, Mills MJ. Sleep patterns and symptoms of depression in college students. *Coll Stud J*. 2009; 43:464–472.
19. Forquer LM, Camden AE, Gabriau KM, Johnson CM. Sleep patterns of college students at a public university. *J Am Coll Health*. 2008; 56:563–565. [PubMed: 18400669]
20. Moo-Estrella J, Pérez-Benítez H, Solís-Rodríguez F, Arankowsky-Sandoval G. Evaluation of depressive symptoms and sleep alterations in college students. *Arch Med Res*. 2005; 36:393–398. [PubMed: 15950081]
21. Regestein Q, Natarajan V, Pavlova M, Kawasaki S, Gleason R, Koff E. Sleep debt and depression in female college students. *Psychiatry Res*. 2005; 176:34–39. [PubMed: 20079935]
22. Pilcher JJ, Ginter DR, Sadowsky B. Sleep quality versus sleep quantity: relationships between sleep and measures of health, well being and sleepiness in college students. *J Psychosom Res*. 1997; 42:583–596. [PubMed: 9226606]
23. Mellman TA. Sleep and anxiety disorders. *Psychiatr Clin North Am*. 2006; 29:1047–1058. [PubMed: 17118281]
24. Orzech KM, Salafsky DB, Hamilton LA. The state of sleep among college students at a large public university [Abstract]. *J Am Coll Health*. 2011; 59:612–619. [PubMed: 21823956]
25. Vollrath M, Wicki W, Angst J. The Zurich study. VIII. Insomnia: association with depression, anxiety, somatic syndromes, and course of insomnia. *Eur Arch Psychiatry Neurol Sci*. 1989; 239:113–124. [PubMed: 2806334]
26. Alapin I, Fichten CS, Libman E, Creti L, Bailes S, Wright J. How is good and poor sleep in older adults and college students related to daytime sleepiness, fatigue, and ability to concentrate? *J Psychosom Res*. 2000; 49:381–390. [PubMed: 11164064]
27. Ustinov Y, Lichstein KL, Vander Wal GS, Taylor DJ, Riedel BW. Association between report of insomnia and daytime functioning. *Sleep Med*. 2010; 11:65–68. [PubMed: 19783473]
28. Farabaugh A, Bitran S, Nyer M, et al. Depression and suicidal ideation in college students. *Psychopathology*. 2012; 45:228–234.10.1159/000331598 [PubMed: 22627683]
29. Beck A, Ward C, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961; 4:561–571. [PubMed: 13688369]
30. Porter, E.; Keshaviah, A.; Owens, ME.; Fava, M.; Simon, NM.; Pollack, MH. Psychometric properties of the anxiety symptoms questionnaire: a novel self-rated measure of general anxiety symptoms. Poster presented at the 6th world congress of behavioral and cognitive therapies; Boston, MA. 2010.



31. Pollack, MH.; Jacoby, RJ.; Bentley, KH., et al. Psychometric properties of the anxiety symptoms questionnaire (ASQ) in a college student sample. Poster presented at the 2011 ADAA Annual Conference; New Orleans, LA. 2011.
32. Beck A, Weissman A, Lester D, Trexler L. The measurement of pessimism: the hopelessness scale. *J Consult Clin Psychol.* 1974; 42:861–865. [PubMed: 4436473]
33. Endicott J, Nee J, Harrison W, Blumenthal R. Quality of life enjoyment and satisfaction questionnaire: a new measure. *Psychopharmacol Bull.* 1993; 29(2):321–326. [PubMed: 8290681]
34. Beck, AT.; Steer, RA. *Manual for the Beck Anxiety Inventory.* San Antonio, TX: Psychological Corporation; 1990.
35. Fava M, Iosifescu DV, Pedrelli P, Baer L. Reliability and validity of the Massachusetts General Hospital Cognitive and Physical Functioning Questionnaire. *Psychother Psychosom.* 2009; 78:91–97.10.1159/000201934 [PubMed: 19218827]
36. Dia DA, Harrington D, Silverman WK. An examination of the tripartite model of anxiety and depression in an outpatient sample of adolescents. *J Evid Based Soc Work.* 2010; 7:302–312.10.1080/19371910903178771 [PubMed: 20799129]
37. Fernandez-Mendoza J, Vela-Bueno A, Vgontzas AN, et al. Cognitive-emotional hyperarousal as a premorbid characteristic of individuals vulnerable to insomnia. *Psychosom Med.* 2010; 72:397–403.10.1097/PSY.0b013e3181d75319
38. Hajak G. Evaluation of severe insomnia in the general population—implications for the management of insomnia: the German perspective. *J Psychopharmacol.* 1999; 13(4 Suppl 1):S30. [PubMed: 10667455]
39. Sateia MJ, Doghramji K, Hauri PJ, Morin CM. Evaluation of chronic insomnia. An American academy of sleep medicine review. *Sleep.* 2000; 23:243–308. [PubMed: 10737342]
40. Shochat T, Umphress J, Israel AG, Ancoli-Israel S. Insomnia in primary care patients. *Sleep.* 1999; 22:S359–S365. [PubMed: 10394608]
41. Fava M, McCall WV, Krystal A, et al. Eszopiclone co-administered with fluoxetine in patients with insomnia coexisting with major depressive disorder. *Biol Psychiatry.* 2006; 59:1052–1060.10.1016/j.biopsych.2006.01.016 [PubMed: 16581036]
42. Fava M, Asnis GM, Shrivastava RK, et al. Improved insomnia symptoms and sleep-related next-day functioning in patients with comorbid major depressive disorder and insomnia following concomitant zolpidem extended-release 12.5 mg and escitalopram treatment: a randomized controlled trial. *J Clin Psychiatry.* 2011; 72:914–928.10.4088/JCP.09m05571gry [PubMed: 21208597]
43. Kadison R. Getting an edge—use of stimulants and antidepressants in college. *N Eng J Med.* 2005; 353:1089–1091.10.1056/NEJMp058047
44. Brown FC, Buboltz WC Jr, Soper B. Relationship of sleep hygiene awareness, sleep hygiene practices, and sleep quality in university students. *J Behav Med.* 2002; 28:33–38.10.1080/08964280209596396

TABLE 1

Clinical and demographic variables

	Total sample <i>N</i> = 287			Without <i>SD</i> <i>N</i> = 64			With <i>SD</i> <i>N</i> = 212		
	<i>M</i>	<i>SD</i>	<i>n</i>	<i>M</i>	<i>SD</i>	<i>n</i>	<i>M</i>	<i>SD</i>	<i>n</i>
Age ( <i>n</i> = 269)	19.81	1.87	19.61	1.42	19.87	1.99			
Grade point average ( <i>n</i> = 242)	3.24	0.50	3.29	0.58	3.23	0.47			
Gender ( <i>n</i> = 276)		Percentage	<i>n</i>	Percentage	<i>n</i>	Percentage			
Female	184	64.1	43	64.2	141	64.1			
Male	92	32.1	21	31.3	71	32.3			
School year ( <i>n</i> = 275)		Percentage	<i>n</i>	Percentage	<i>n</i>	Percentage			
Freshman	74	25.8	23	34.3	51	23.2			
Sophomore	73	25.4	14	20.9	59	26.8			
Junior	70	24.4	11	16.4	59	26.8			
Senior	49	17.1	13	19.4	36	16.4			
Other	9	3.1	3	4.7	6	2.7			
Living situation ( <i>n</i> = 112)		Percentage	<i>n</i>	Percentage	<i>n</i>	Percentage			
On campus alone	33	11.5	4	6.0	29	13.2			
On campus with roommates	34	11.8	10	14.9	24	10.9			
Off campus alone	8	2.8	0	0.0	8	3.6			
Off campus with relatives	8	2.8	1	1.5	7	3.2			
Off campus with roommates	29	10.1	8	11.9	21	9.5			
Ethnicity ( <i>n</i> = 249)		Percentage	<i>n</i>	Percentage	<i>n</i>	Percentage			
Black, not of Hispanic origin	22	7.7	3	4.5	19	9.9			
Hispanic	19	6.6	4	6.0	15	7.9			
White, not of Hispanic origin	157	54.7	36	53.7	121	63.4			
American Indian or Alaskan native	1	.3	0	0.0	1	.5			
Asian or Pacific Islander	36	12.5	114	20.9	22	11.5			
Other	14	4.9	1	1.5	13	6.8			
Family socioeconomic status ( <i>n</i> = 101)		Percentage	<i>n</i>	Percentage	<i>n</i>	Percentage			
Low income (<\$24, 999)	6	2.1	2	3.0	4	1.8			
Low-middle income (\$25,000–\$49,000)	13	4.5	2	3.0	11	5.0			
Middle income (\$50,000–\$79,999)	29	10.1	8	11.9	21	9.5			

	Total sample <i>N</i> = 287		Without SD <i>N</i> = 64		With SD <i>N</i> = 212	
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>
Upper-middle income (\$80,000–\$199,999)	41	14.3	6	9.0	35	15.9
Upper income (\$200,000 or more)	12	4.2	5	7.5	7	3.2

*M*, mean; *SD*, sleep disturbance; *SD*, standard deviation. There were no statistically significant differences in demographic information between students with and without sleep disturbance ( $P > .05$  for all comparisons).

**TABLE 2**

Frequencies of responses to Beck Depression Inventory (BDI) sleep item (#16) and level of depressive symptoms

	<i>N</i>	Percentage	BDI score, minus #16 <i>M(SD)</i>
BDI sleep item #16			
(0) I can sleep as well as usual.	67	23.3	18.00 (4.85)
(1) I don't sleep as well as I used to.	145	50.5	17.45 (5.74)
(2) I wake up 1–2 hr earlier than usual and find it hard to get back to sleep.	49	17.1	18.35 (6.75)
(3) I wake up several hours earlier than I used to and cannot get back to sleep.	26	9.1	24.23 (9.69)
Total	287	100	18.35 (6.44)

*M*, mean; *SD*, standard deviation.

TABLE 3

Students with and without sleep disturbance across primary outcome variables

	With SD		Without SD		ANOVA	
	n	M(SD)	n	M(SD)	F	P
BDI total score (minus item #16)	220	18.45 (6.85)	67	18.00 (4.85)	0.250	.617
ASQ intensity total score	107	75.77 (29.08)	38	54.63 (21.13)	16.869	<.001*
ASQ frequency total score	106	71.60 (29.32)	37	54.14 (21.15)	11.093	.001*
QLESQ total score	104	47.53 (9.14)	28	48.54 (8.43)	0.274	.602
BHS total score	74	5.93 (4.10)	21	7.14 (4.13)	1.417	.237
BAI total score	44	18.32 (12.15)	11	13.45 (9.65)	1.417	.224
CPFQ total score	131	22.23 (5.40)	43	19.49 (5.61)	8.203	.005*
CPFQ #1: <i>How has your motivation/interest/enthusiasm been over the past month?</i>	131	3.27 (1.19)	43	3.02 (1.24)	1.332	.250
CPFQ #2: <i>How has your wakefulness/alertness been over the past month?</i>	131	3.46 (1.08)	43	3.05 (.95)	4.952	.027
CPFQ #3: <i>How has your energy been over the past month?</i>	131	3.42 (1.03)	43	3.02 (1.04)	4.913	.028
CPFQ #4: <i>How has your ability to focus/sustain attention been over the past month?</i>	131	3.38 (1.07)	43	2.91 (1.09)	6.320	.013
CPFQ #5: <i>How has your ability to remember/recall information been over the past month?</i>	131	3.05 (1.06)	43	2.47 (1.05)	9.758	.002**
CPFQ #6: <i>How has your ability to find words been over the past month?</i>	131	2.82 (1.06)	43	2.47 (1.08)	3.674	.057
CPFQ #7: <i>How has your sharpness/mental acuity been over the past month?</i>	131	2.83 (.954)	43	2.56 (.854)	2.806	.096

SD, sleep disturbance; M, mean; SD, standard deviation; BDI, Beck Depression Inventory; BHS, Beck Hopelessness Scale; CPFQ, The Massachusetts General Hospital Cognitive and Physical Functioning Questionnaire; QLESQ, Quality of Life Satisfaction Questionnaire—Short Form; ASQ, Anxiety Symptom Questionnaire; BAI, Beck Anxiety Inventory.

\*  $P < .01$ .

\*\* Bonferroni correction,  $P < .007$ .

**TABLE 4**

Students with and without sleep disturbance across hyperarousal items

	With SD		Without SD		ANOVA	
	<i>n</i>	<i>M(SD)</i>	<i>n</i>	<i>M(SD)</i>	<i>F</i>	<i>P</i>
BAI #4: "Unable to relax"	47	1.77 (.96)	12	1.00 (.95)	6.10	.017
ASQ #6 <i>intensity</i> : "Trouble relaxing"	109	5.71 (2.59)	38	3.97 (2.70)	12.40	.001*
ASQ #6 <i>frequency</i> : "Trouble relaxing"	108	5.65 (2.87)	37	4.32 (3.08)	5.68	.019
ASQ #15 <i>intensity</i> : "Feeling restless, keyed up, or on edge"	109	4.26 (2.81)	38	3.11 (2.74)	4.80	.030
ASQ #15 <i>frequency</i> : "Feeling restless, keyed up, or on edge"	109	3.86 (2.73)	37	3.05 (2.84)	2.35	.128

\* Bonferroni correction,  $P < .01$ ; SD, sleep disturbance; *M*, mean; *SD*, standard deviation; ASQ, Anxiety Symptom Questionnaire; BAI, Beck Anxiety Inventory.