Sex Differences in the Relationship Between Depressive Symptoms and Actigraphic Assessments of Sleep and Rest-Activity Rhythms in a Population-Based Sample

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ABSTRACT

Objective: Depression is often associated with disruptions in sleep and circadian rhythms. We aimed to confirm these relationships via actigraphic assessment in a large, population-based sample and test whether sex moderates these relationships.

Methods: A total of 418 participants (age = 35–85 years, mean [standard deviation] = 57.04 [11.47]) completed questionnaires and 1 week of actigraphy, used to calculate sleep and rest-activity statistics including mesor (mean activity level), amplitude (height of rhythm), and acrophase (time of day that rhythm peaks).

Results: Depressive symptoms, assessed via Center for Epidemiologic Studies Depression Scale, were associated with disrupted sleep and rest-activity rhythms. Furthermore, men demonstrated longer sleep onset latency (SOL, $B = -13.28$, $p < .001$), longer wake time after sleep onset ($B = -6.26$, $p < .01$), lower sleep efficiency ($B = 5.91$, $p < .001$), and lower total sleep time (TST, $B = 33.16$, $p < .001$) than women. Sex moderated the relationship between depression and SOL, TST, mesor, and amplitude; sex-stratified models revealed that higher depression scores were associated with greater SOL ($B = 1.05$, $p < .001$) and less TST ($B = -0.87$, $p < .10$) for women with higher depressive symptoms, but lower mesor ($B = -1.75$, $p < .01$) and amplitude ($B = -1.94$, $p < .01$) for men with higher depressive symptoms.

Conclusions: Depressive symptoms were related to disrupted sleep continuity and rest-activity rhythms in this population-based sample; however, these relationships differed by sex. Women with greater depressive symptoms exhibited difficulty with sleep continuity, whereas men with greater depressive symptoms demonstrated disruption throughout the 24-hour rhythm.

Key words: actigraphy, depression, rest-activity rhythms, sex differences, sleep continuity.

INTRODUCTION

Disturbances in the sleep-wake cycle and rest-activity rhythms are consistently associated with unipolar depression as risk factors for developing depression, symptoms during episodes, and lingering symptoms after remission that predict recurrence (1–3). Depressed individuals demonstrate disrupted circadian and rest-activity rhythms, including delayed melatonin secretion (4), diurnal mood variation with worse mood in the morning and delayed activity peak (5,6), and less robust and stable rest-activity rhythms (7–9). Sleep difficulties in depression are characterized most frequently by insomnia but also by hypersomnia in some individuals (10). Overall, disruptions include reduced total sleep time (TST), lower sleep efficiency, longer time to fall asleep, more awakenings during the night, shorter rapid eye movement (REM) sleep latency, and prolonged first REM sleep period duration (11,12).

The relationship between depression and impaired sleep and rest-activity patterns may vary by sex. Women in general experience greater lifetime incidence of depression (13,14) and higher insomnia rates than men (15). However, studies of sleep and activity patterns in depressed individuals present mixed findings. Some actigraphy studies demonstrated that men had shorter sleep duration, more sleep fragmentation, and less stability in rest-activity rhythms for several days than women (7,16,17), whereas polysomnographic findings indicated that men generally had longer TST and more slow wave and REM sleep but longer sleep latencies than women, although effect sizes were small (18). One study that focused on sex differences in depressive symptom severity found that among other symptoms, depressed women reported more sleep complaints than depressed men (19). Considering the important role that sleep and activity level play in precipitating and maintaining depressive symptoms, it is possible that the sex differences associated with depression, sleep, and activity level may lead to differences in the relationship between depression and sleep and rest-activity rhythms.

In this study, we assessed the relationship between depressive symptoms and disturbances in sleep and rest-activity rhythms in

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CES-D = Center for Epidemiologic Studies Depression Scale, **MIDUS** = Midlife in the United States, **PSQI** = Pittsburgh Sleep Quality Index, **REM** = rapid eye movement, **SE** = sleep efficiency, **SOL** = sleep onset latency, **TST** = total sleep time, **WASO** = wake time after sleep onset

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a large, population-based sample using actigraphy, whereas previous research has often considered single-sex, medical, or depressed samples (2,3,6,8). We hypothesized that higher depression scores would be related to more disrupted sleep continuity and rest-activity rhythms. We further examined the role of sex in moderating the relationship between depressive symptoms and sleep and rest-activity rhythms. Because most studies have indicated that women are more vulnerable to developing depression and depressed women have more significant sleep disruptions such as insomnia, we expected that sleep continuity and rest-activity disturbances would be more severe in women with higher levels of depressive symptoms than men with higher levels of depressive symptoms.

METHODS

Participants

Participants were 440 individuals who completed the Biomarker Project, a subsample from the MIDUS II (Midlife in the United States) survey. MIDUS is a longitudinal, national survey that included a population-based sample of 7108 adults aged 25 to 75 years at study started in 1995. Of this sample, a geographic subset (*n* = 1255) participated in the Biomarker Project, which included several physiological assessments described elsewhere (20). Relevant to the current study, actigraphy was completed by 440 participants living near Madison and Milwaukee, Wisconsin, along with other self-reported and interview measures. The participants were removed from the present analyses if they were nightshift workers (*n* = 5) or if they had poor actigraphy compliance, defined as having less than 5-day (71%) usable data (*n* = 17). The final sample was 418 participants. This subsample of the Biomarker Project differs from the larger MIDUS sample at study started as follows: older age as expected with a longitudinal cohort (*t*(5916) = 3.2, *p* = .001), more female representation (60% versus 54%), and more nonwhite representation due to intentional recruitment of African Americans living in an urban center (Milwaukee, Wis) with the larger Biomarker Project (32% versus 19%); however, this subsample did not differ from the larger sample in terms of educational level.

Procedure

Participants provided informed consent and underwent procedures described elsewhere (20). Relevant to this study, the participants completed a phone interview, physical examination, questionnaires, and 1-week of actigraphy. The University of Wisconsin Health Sciences Institutional Review Board approved the study procedures.

Measures

The participants provided demographic (i.e., age, sex, race) and socioeconomic (i.e., education level) information via phone interview and reported whether they exercised at least 20 minutes three times per week and currently smoked cigarettes. Height and weight were collected during an in-person physical examination to calculate body mass index.

The participants also completed the Center for Epidemiologic Studies Depression Scale (CES-D) (21) and Pittsburgh Sleep Quality Index (PSQI, (22)). The CES-D is a 20-item scale that assesses depressive symptoms in the past week; it shows good convergence with other measures of depression and adequate internal consistency (α value was 0.73 in this sample). Scores higher than 16 indicate clinically significant levels of depression (23). Current use of sleep medications was determined via the PSQI medication subscale, which consists of one item assessing whether participants use sleep medications: not at all (0), less than once per week (1), once or twice per week (2), or three or more times per week (3).

Actigraphy

All participants completed 1 week of actigraphy via Mini Mitter Actiwatch-64 along with a sleep diary indicating time that the participants went to sleep and got up the following morning. The participants wore the actigraph continuously on their nondominant wrist for 7 consecutive days and were asked to press the event marker button on the actigraph when attempting sleep and waking up for the day. Data were collected in 30-second epochs and downloaded to Philips Actiware for a total possible number of 20,160

epochs per participant. Rest intervals used to compute sleep statistics were manually defined as indicated in the participant's sleep diary. If a sleep diary value was not available, event markers were used to determine rest intervals, which occurred in setting rest intervals for 28 participants (6.2% of the sample). If event markers were not available, imputations were used (i.e., for weekdays, the average of the other weekdays with at least 3 weekdays needed for imputation; for weekends, the value from the other weekend day), which occurred in setting rest intervals for 22 participants (5.3% of the current sample). In addition, all data were inspected to exclude unusable segments (i.e., when the watch was off wrist by participant report). For the current sample, the mean (M) amount of usable epochs was 18,201 (standard deviation [SD] = 1,039), so on the mean about 10% of epochs (about 0.7 days) were unusable because of the watch being removed. Then, sleep onset latency (SOL), wake time after sleep onset (WASO), sleep efficiency (SE), and TST were computed by the Actiware program algorithms on the basis of the rest intervals. Data for the sleep indices were aggregated across the 7 days of data collection using mean values.

In addition, the raw actigraphy data were converted to 1-minute epochs and exported to SAS 9.3 (SAS Institute Inc). A traditional cosinor analysis was used to simultaneously fit 12- and 24-hour rhythms to epoch-by-epoch activity counts averaged by the minute over the 24-hour period for all days (24). This model yields three statistics that describe an individual's rest-activity rhythm. Mesor refers to the intercept of the model or the mean activity level for a participant, considering the cosine model. Amplitude indicates the difference between the peak or trough and the mean of the circadian rhythm wave, providing a measure of the height of the rhythm. Finally, acrophase indexes the time of day that the peak of the rhythm occurs.

Statistical Analyses

Multiple linear regression was used to test for main effects of depressive symptoms and sex in their association with sleep and rest-activity rhythm variables. We added an interaction term to test whether sex moderated the relationship between depressive symptoms and sleep and rest-activity rhythm variables. For all regression models, the depression score was treated as a continuous variable and all independent variables were centered at their mean (sex: women = 0.5, men = −0.5). In each model, we adjusted for age, race, education level, smoker status, exercise, body mass index, and use of sleep medications. We further explored all models where the interaction between depressive symptoms and sex was significant at a *p* value of less than .10 by running sex-stratified simple regressions to test for a main effect of depressive symptoms because they relate to the sleep or rest-activity rhythm variable. All reported regression weights refer to unstandardized coefficients.

RESULTS

Participant characteristics are provided in Table 1. There were significant differences between men and women for race (χ^2 [1, *N* = 418] = 9.27, *p* = .002), with women more likely to identify as nonwhite than men. No other sex differences emerged, including no sex differences in CES-D scores (*t*(412) = .19, *p* = .85), with 17.5% of men and 15.9% of women scoring higher than the clinical significance cutoff. Unadjusted correlations between depressive symptoms and sleep and rest-activity indices revealed significant relationships between higher levels of depressive symptoms and longer SOL, greater WASO, lower SE, and later acrophase (all *r* = ±0.2–0.3, *p* < .01). Higher levels of depressive symptoms demonstrated trending relationships with less TST and lower amplitude (both *r* = −0.1, *p* = .07). There was no significant relationship between depressive symptoms and mesor at the bivariate level (*r* = −0.01, *p* = .8).

Multiple regression models are reported in Table 2, and all models are adjusted for the aforementioned covariates. Depressive symptoms were significantly associated with the sleep and rest-activity rhythm variables SOL, SE, and acrophase, indicating that higher depression scores were related to longer time to fall sleep, less efficient sleep, and a more delayed rest-activity pattern (model 1). Sex was a significant main effect, independent of depressive symptoms, for

SOL, WASO, SE, and TST with men demonstrating longer SOL, longer WASO, lower SE, and lower TST than women (model 2).

Sex moderated the relationship between depressive symptoms and SOL, TST, mesor, and amplitude (model 3). Because sex was a significant moderator for these variables, these models were run as sex-stratified simple regressions (Table 3). To visualize these findings, Figure 1 depicts the means for SOL, TST, mesor, and amplitude for men and women scoring higher or lower than the CES-D cutoff score for clinically significant levels of depression. For the sleep continuity variables, higher depression scores were associated with greater SOL and less TST (trend, $p = .095$) for women, whereas these relationships were nonsignificant in men. Independent-samples t tests confirmed that women with high depressive symptoms showed greater SOL ($t(236) = -5.92$, $p < .001$) and less TST ($t(236) = 3.20$, $p = .002$) than women with low depressive symptoms but did not differ in SOL or TST as compared with men either with high depressive symptoms (SOL, $t(58) = -.59$, $p = .56$; TST, $t(58) = .23$, $p = .82$) or low depressive symptoms (for TST only, $t(160) = .34$, $p = .74$; SOL marginally higher among women with high depressive symptoms, $t(160) = 1.91$, $p = .058$). In contrast, for the rest-activity rhythm variables, higher depression scores were associated with lower mesor and lower amplitude for men, with no significant main effects among women. Follow-up independent t tests confirmed that men with high depression scores demonstrated lower amplitude than women with low depression scores ($t(239) = 2.71$, $p = .007$), women with high depression scores ($t(67) = -1.81$, $p = .075$), and men with low depression scores ($t(164) = 2.70$, $p = .008$), with mesor trending in the same direction.

DISCUSSION

Depressive symptoms were associated with disrupted sleep continuity and rest-activity rhythms in this population-based sample; however, the relationship with depressive symptoms differed by sex. Women with higher depression scores demonstrated more sleep disruption than less depressed women, particularly with a longer time to fall asleep and less total time to fall asleep. This is consistent with previous research indicating worse self-reported sleep problems among depressed women (19). In contrast, rest-activity rhythms were less robust (i.e., lower mesor and amplitude) among men with higher depression scores, indicating more disruption in the full 24-hour cycle. Polysomnographic studies similarly suggest that sex moderates the relationship between depression and sleep; specifically, depressed women show increased slow wave activity, whereas depressed men show no change or decreased slow wave activity (25,26). It has been suggested that women may require more sleep than men (17), which in turn could make sleep more vulnerable to disruption by psychological disorders such as depression. Furthermore, because women report more frequent insomnia than men (15), it is possible that sleep disruption plays a more causal role in developing depression for women. In either case, our study provides additional support that sleep is an area of particular vulnerability for women with greater depressive symptoms.

Importantly, regardless of depression symptom severity, we found that men showed worse actigraphic sleep continuity than women on all measures, replicating previous actigraphic findings (16,17). It is possible that this contributed to a floor effect, making it more difficult to detect a relationship between depressive symptoms and sleep disruption in men. Considering this finding in the context of rest-activity rhythms being less robust in men with greater

TABLE 1. Sample Descriptive Characteristics

	Overall		Men		Women	
	M (SD; Range)	n (%)	M (SD; Range)	n (%)	M (SD; Range)	n (%)
Age	57.0 (11.5; 35–85)		58.2 (11.6; 37–85)		56.3 (11.3; 35–84)	
Sex (% female)		252 (60.3)				
Race						
White		284 (67.9)		127 (76.5)		157 (62.3)
Black and/or African American		88 (21.1)		27 (16.3)		61 (24.2)
Native American or Alaska Native		1 (0.2)		0 (0)		1 (0.4)
Asian		2 (0.5)		1 (0.6)		1 (0.4)
Multiracial		38 (9.1)		9 (5.4)		29 (11.5)
Other		4 (1.0)		2 (1.2)		2 (0.8)
Do not know		1 (0.2)		0 (0)		1 (0.4)
Years of education	14.6 (2.7; 8–21)		14.8 (2.7; 7.5–22)		14.4 (2.8; 7.5–22)	
Body mass index	30.6 (7.1; 17.1–65.1)		30.0 (5.7; 20.5–49.8)		31.0 (7.9; 17.1–65.1)	
Exercise (% current exerciser)		300 (71.8)		121 (72.9)		179 (71)
Smoker status (% current smoker)		61 (14.6)		30 (18.1)		31 (12.3)
PSQI-Sleep medications						
Not during the past month		316 (75.6)		134 (80.7)		182 (72.2)
Less than once a week		32 (7.6)		9 (5.4)		23 (9.1)
Once or twice a week		15 (3.6)		3 (1.8)		12 (4.8)
Three or more times a week		55 (13.2)		20 (12.0)		35 (13.9)
CES-D	8.9 (8.3; 0–54)		9.0 (8.6; 0–54)		8.9 (8.1; 0–37)	

M (SD) = mean (standard deviation); PSQI = Pittsburgh Sleep Quality Index; CES-D = Center for Epidemiologic Studies Depression Scale.

TABLE 2. Multiple Regressions With Actigraphic Sleep Continuity and Rest-Activity Variables

	Model 1		Model 2		Model 3	
	B	t	B	t	B	t
Sleep onset latency						
CES-D	0.56	2.82**	0.51	2.59*	0.46	2.34*
Sex			−13.28	−4.44***	−12.99	−4.35***
CES-D by sex					0.66	1.85†
Adjusted R^2		0.02**		0.06***	0.06***	
Wake time after sleep onset						
CES-D	0.28	1.87†	0.26	1.70†	0.24	1.56
Sex			−6.26	−2.70**	−6.14	−2.65**
CES-D by sex					0.27	0.98
Adjusted R^2		0.01†		0.02**	0.02**	
Sleep efficiency						
CES-D	−0.14	−2.23*	−0.12	−1.93†	−0.11	−1.76†
Sex			5.91	6.38**	5.85	6.31***
CES-D by sex					−0.13	−1.21
Adjusted R^2		0.01*		0.09***	0.09***	
Total sleep time						
CES-D	−0.15	−0.34	−0.01	−0.01	0.12	0.28
Sex			33.16	5.20***	32.41	5.10***
CES-D by sex					−1.71	−2.26*
Adjusted R^2		0.00		0.06***	0.07***	
Mesor (mean activity level)						
CES-D	−0.52	−1.14	−0.51	−1.12	−0.66	−1.43
Sex			2.56	0.36	2.85	0.40
CES-D by sex					1.70	2.02*
Adjusted R^2		0.00		0.00	0.01*	
Amplitude (height of the rest-activity rhythm)						
CES-D	−0.74	−1.68†	−0.73	−1.64†	−0.89	−1.98*
Sex			7.06	1.01	7.38	1.06
CES-D by sex					1.86	2.27*
Adjusted R^2		0.003†		0.003†	0.01*	
Acrophase (peak of the rest-activity rhythm)						
CES-D	0.03	2.54*	0.03	2.58*	0.03	2.51*
Sex			0.17	0.89	0.17	0.89
CES-D by sex					0.00	0.19
Adjusted R^2		0.01*		0.01*	0.01*	

CES-D = Center for Epidemiologic Studies Depression Scale.
* $p < .05$.
** $p < .01$.
*** $p < .001$.
† $p < .10$.

depressive symptoms, men presenting with depressive symptoms would likely benefit from comprehensive assessment of the full 24-hour rest-activity pattern, including disruptions in sleep continuity and daytime symptoms such as behavioral withdrawal and decreased physical activity. Supplementing clinical interviews with sleep and daytime activity diaries or actigraphy monitoring may be particularly useful to provide information regarding both nighttime sleep and daytime activity and rest-activity rhythm disruption. In addition, depression interventions could take sex into account with

greater focus on nighttime sleep disruption in women (e.g., cognitive-behavioral interventions for insomnia) and more attention to the 24-hour rhythm for men (e.g., adding behavioral activation and social rhythm strategies to insomnia treatment).

Across the full sample, as expected, depression was associated with greater sleep disruption. However, these findings were significant only for SOL and SE; because SE in part reflects SOL, it is likely that depressed individuals may struggle most with falling asleep. This could result from a more delayed rest-activity and

TABLE 3. Sex-Split Simple Regressions

	Women		Men	
	B	t	B	t
Sleep onset latency				
CES-D	1.05	4.76***	−0.14	−0.39
Adjusted R^2		0.08***		0.00
Total sleep time				
CES-D	−0.87	−1.67†	0.95	1.39
Adjusted R^2		0.01†		0.01
Mesor (mean activity level)				
CES-D	0.48	0.76	−1.75	−2.81**
Adjusted R^2		0.00		0.03**
Amplitude (height of the rest-activity rhythm)				
CES-D	0.25	0.42	−1.94	−2.97**
Adjusted R^2		0.00		0.04**

CES-D = Center for Epidemiologic Studies Depression Scale.
* $p < .05$.
** $p < .01$.
*** $p < .001$.
† $p < .10$.

sleep pattern that can be typical among depressed individuals, found in the present sample (i.e., a significant relationship between later acrophase and higher depressive symptoms) and elsewhere (4,8,9). Depressive symptoms were also related to a less robust overall rhythm (i.e., lower amplitude), consistent with previous studies (8,9).

Unlike a study in older women (6), we did not find that depressive symptoms were related to impaired rest-activity rhythms
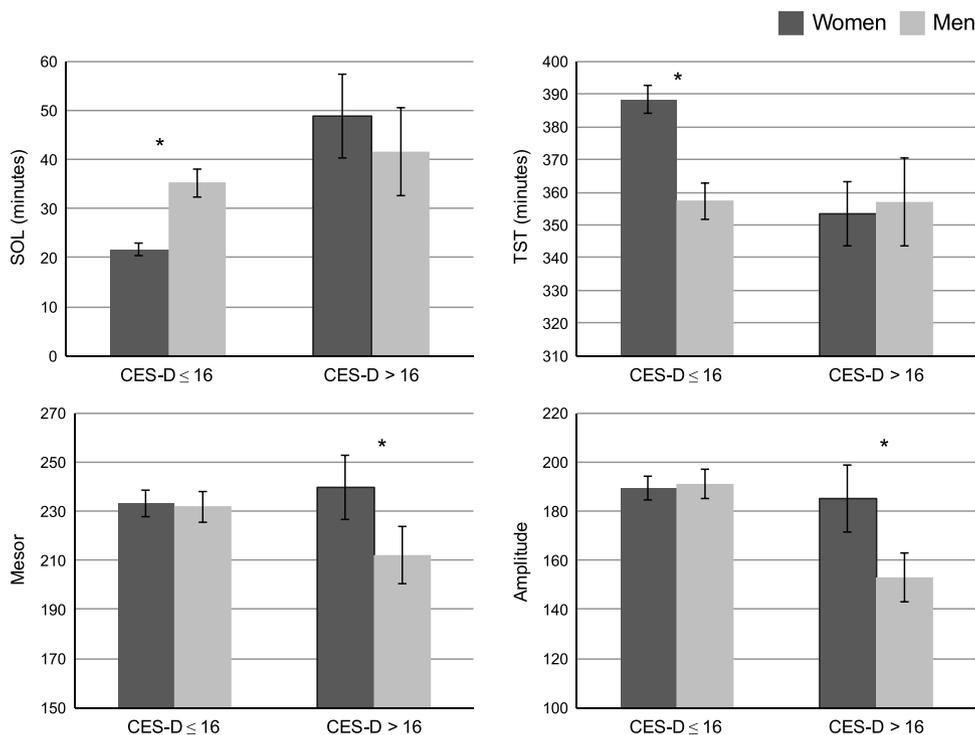

FIGURE 1. Sex moderates the relationships between depression and SOL, TST, mesor (mean activity level), and amplitude (height of the rest-activity rhythm). SOL = sleep onset latency; TST = total sleep time. Asterisk indicates statistically significant contrast. Error bars represent the standard error of the mean. Women with CES-D ≤ 16 (n = 212), M (SD) CES-D score = 6.2 (4.6); women with CES-D > 16 (n = 40), M (SD) CES-D = 24.2 (6.6); men with CES-D ≤ 16 (n = 137), M (SD) CES = 6.0 (4.7); and men with CES-D > 16 (n = 29), M (SD) CES-D = 24.0 (7.4).

among women. However, our sample did not include many women in the age range studied by Maglione and colleagues (i.e., older than 70 years), so it is possible that this relationship does not emerge until late adulthood. Of note, men and women did not differ in depression severity in this sample. Depression rates differ the least between sexes in older populations or children (27), so it is possible that the generally, older age of this sample (M = 56.87 years) contributed to the similar depressive symptom severity between men and women.

Strengths of this study include the large, diverse, population-based sample and continuous recording of 7 days of actigraphic data. Actigraphic indices included more traditional sleep-wake statistics that have the limitation of only being a proxy for sleep and wakefulness because actigraphy cannot distinguish sleep from quiet wakefulness. However, actigraphic indices also included cosinor indices categorizing the rest-activity pattern (i.e., mesor, amplitude, and acrophase), thus producing measures of the full 24-hour period for analysis.

Limitations include the inability to determine causal relationships from this cross-sectional study design. Previous research has observed that sleep and rest-activity rhythm disruption can predict development of depression, whereas current depression is associated with further disruption in these areas (2,3). Furthermore, it is important to note that the effect sizes associated with the reported analyses are small to medium in size (see R^2 reported in Tables 2, 3). Thus, although depression and sex may be related to sleep continuity and rest-activity rhythms, it is likely that other variables not examined in this study also play an important role in determining these relationships. In addition, depressive symptom severity was assessed via self-reported measure, which can be subject to over- or underreporting; future replication using clinical interviews would be useful.

In summary, these findings emphasize the dynamic relationship between depression, sex, and sleep and rest-activity rhythms, pointing to the need for further research on the role of sex in improving assessment and treatment of sleep continuity and rest-activity dysregulation in depression.

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