# Differentiation Across Bipolar Disorder and Major Depressive Disorder by Whole-Night Polysomnographic Findings

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## Abstract

**Background:** There is growing evidence that understanding the role of sleep disturbance in bipolar disorder (BD) and major depressive disorder (MDD) is helpful when studying the high heterogeneity of patients across psychiatric disorders.

**Objective:** The present study was designed to investigate the transdiagnostic role of sleep disturbance measured by polysomnography (PSG) in differentiating from MDD with BD.

**Methods:** A total of 256 patients with MDD and 107 first-episode and never-medicated patients with BD using the *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition, criteria were recruited. All patients completed 1 night of PSG recording, and the changes in objective sleep structure parameters were determined by PSG analysis.

**Results:** We showed that patients with MDD had statistically longer rapid eye movement (REM) latency, a higher percentage of stage N2 sleep, and lower percentages of stage N3 sleep and REM sleep than those with BD after controlling for confounding factors (all $P < .05$). Moreover, using the logistic regression analysis, we identified that REM latency was associated with BD diagnosis among the PSG sleep features. The cutoff value for PSG characteristics to differentiate BD from MDD was 261 in REM latency (sensitivity: 41.4% and specificity: 84.1%).

**Conclusions:** Our findings suggest that PSG-measured sleep abnormalities, such as reduced REM latency, may be a diagnostic differentiating factor between MDD and BD, indicating their roles in identifying homogeneous transdiagnostic subtypes across psychiatric disorders.

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Major depressive disorder (MDD) and bipolar disorder (BD) are among the top 20 causes of disability around the world,[1] with a lifetime prevalence of 16% and 4% in the general population, respectively.[2,3] Some of these disabilities have been reported to be associated with the incorrect or delayed diagnosis and treatment of both disorders.[4,5] In clinical practice, differentiating between MDD and BD at an individual's initial visit is critical, considering that different types of psychotropic drugs are prescribed for MDD and BD.[6] The correct differentiation between MDD and BD with depressive symptoms plays a critical role in their treatment and prognoses. Nonetheless, the differential diagnosis can be a clinical challenge since both MDD and BD patients exhibit depressive symptoms and are unaware of previous or future manic episodes experienced. Thus, objective biological indices are needed.

Accumulating literature has attempted to find potential biomarkers that can identify mental disorders; however, there are still no specific biomarkers that have been identified to distinguish between different psychiatric disorders. Sleeping problems and sleep disorders are common in all age groups and seriously impair public health.[7–10] It has been reported in clinical and epidemiological studies that the majority of people with depressive symptoms experience sleep disturbances such as insomnia, hypersomnia, and excessive sleepiness in approximately 90% of individuals,[11,12] which is a characteristic symptom of MDD.[13] The sleep abnormality in MDD is not an associated symptom or comorbid condition, but rather a core symptom. Approximately 75% of individuals with MDD have difficulty initiating or maintaining sleep, while 50%–60% of young adults experience sleep abnormalities.[14,15]

In addition to being highly prevalent in MDD, disturbed sleep is also very common among patients suffering from BD, with detrimental impacts on quality of life, functioning, symptom burden, and response to

## Clinical Points

- The present study investigated the transdiagnostic role of sleep disturbance measured by 1 night of polysomnography (PSG) in differentiating between patients with MDD and BD.
- Patients with MDD had statistically longer rapid eye movement (REM) latency, a higher percentage of stage N2 sleep, and lower percentages of stage N3 sleep and REM sleep than those with BD.
- REM latency was associated with BD diagnosis among the PSG sleep features. The cutoff value for PSG characteristics to differentiate BD from MDD was 261 in REM latency (sensitivity: 41.4% and specificity: 84.1%).

psychotropic medications.[16] Previous meta-analyses have reported longer sleep latency, fragmentation, and duration and less efficient sleep in patients relative to control subjects.[17–19] Sleep disruption manifests itself differently in different stages of BD. During mania or hypomania, it usually manifests as a decreased need for sleep.[20] During depression, it usually manifests as hypersomnia or excessive sleepiness, sometimes severe insomnia.[20,21]

Recently, sleep disturbance has attracted considerable interest as a biomarker of mental disorders.[22–24] Considering that sleep abnormalities are highly comorbid with most mental disorders, there is a growing interest that it could be developed as a transdiagnostic marker.[25,26] Prior literature revealed significant differences between individuals with BD and MDD in terms of objective and subjective measures of sleep architecture. For example, among individuals with MDD who showed similar severity of clinical symptoms as BD subjects, sleep disturbances were worse than in individuals with BD.[27] In addition, MDD patients exhibited significantly worse sleep quality than BD patients. A previous systematic review and meta-analysis demonstrated that the prevalence of obstructive sleep apnea was higher in MDD subjects (36.6%) than in BD subjects (24.5%).[28] In addition, there were significant differences in circadian rhythm characteristics between patients with MDD and BD, with MDD patients having lower morning alertness than BD patients. On the Composite Scale of Morningness items corresponding with morning preference and evening tiredness factors, patients with MDD scored higher than subjects with BD, suggesting that MDD patients were subjectively fatigued in the morning.[29]

Some literature supports the hypothesis that sleep disorders are related to the etiology of certain psychiatric disorders.[30,31] Some of the field's leading researchers have hypothesized that sleep fundamentally impacts psychiatric disorders.[32] However, accumulating clinical studies have reported the heterogeneity of sleep phenotypes in mental disorders.[33–35] Sleep is composed of 2 stages: (1) nonrapid eye movement (NREM) and (2) rapid eye movement (REM) sleep. NREM also includes 3 phases, N1, N2, and N3, each of which is a progressively deeper sleep.[36] Each stage of sleep includes changes in muscle activity, brain wave pattern, and eye movement.[37,38] Alterations that occur in the sleep structure may be confirmed objectively with the help of polysomnography (PSG), particularly the duration and latency of 3 sleep phases.[39–41] PSG can be used to collect the recording of electrophysiological signals, such as electroencephalogram (EEG), muscle activity electromyogram (EMG), respiration, and blood oxygenation during all-night sleep. The data are processed and analyzed to the architecture of sleep, respiratory events, arterial oxygen saturation, snoring, body position, and electrocardiogram (ECG). Therefore, it is a useful tool to investigate the structure of sleep and may be an inherent biomarker to help identify the different psychiatric disorders.

In this study, we examined the sleep structure in patients with MDD and those with BD using PSG. We sought to assess whether the sleep characteristics examined by PSG in individuals with MDD differed from those with BD. We then further used logistic regression analyses to identify domains that differentiated MDD from BD, taking into account potential correlates, such as gender, age, and body mass index (BMI). In addition, with regard to the clinical transdiagnostic utility of distinguishing between BD and MDD, we determined the appropriate cutoff values for sleep parameters.

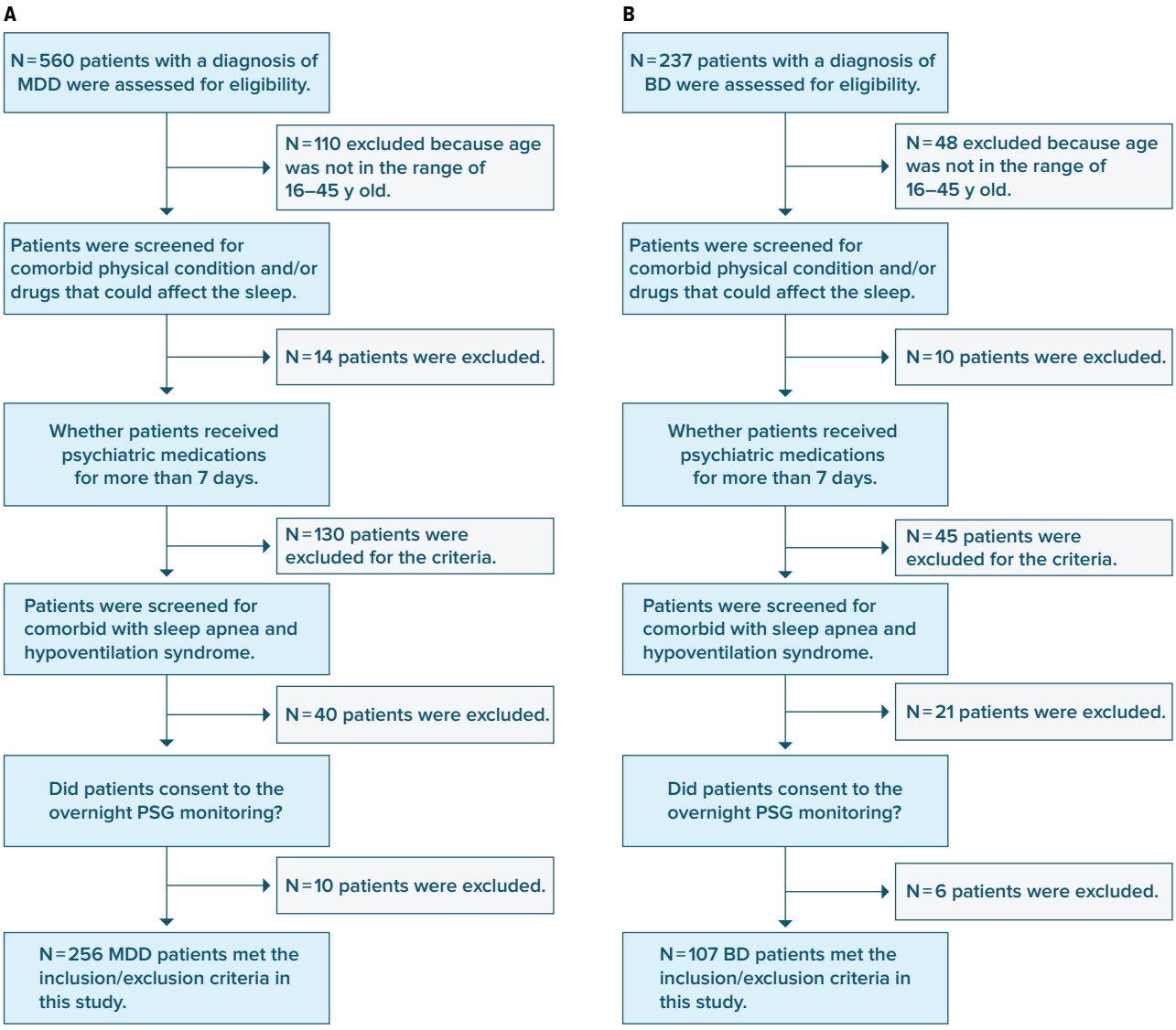
## METHODS

### Patients

A total of 256 patients with MDD and 107 patients with BD were recruited from First Hospital at Shanxi Medical University in this study. The flow diagram of the study selection process for patients with MDD and BD is shown in Figure 1. All participants were interviewed by experienced psychiatric specialists using the severe combined immunodeficiency. Inclusion criteria were as follows: (1) age 18–45 years, (2) first episode, (3) a diagnosis of either BD or MDD according to *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition (DSM-IV), criteria, and (4) ability to consent to participate in the present study. Exclusion criteria include: (1) had a history of substance abuse, (2) suffered from any severe physical illness, (3) had a diagnosis of organic mental disorders, (4) had psychiatric comorbidities with other *DSM-IV-TR* axis I or axis II disorders (eg, anxiety and attention-deficit/hyperactivity disorder), (5) had the comorbid physical condition and/or drugs that could affect the sleep, and (6) were pregnant or breastfeeding.

Figure 1.

**Flow Diagrams of the Study Selection Process for Patients With (A) Major Depressive Disorder (MDD) and (B) Bipolar Disorder (BD)**




Abbreviation: PSG = polysomnography.

All recruited patients had no history of psychiatric medication on admission. However, due to the limited access to the full overnight PSG recording system, some patients had received psychotropic medication while waiting for the overnight PSG testing. Psychotropic drugs include anxiolytics, hypnotics, antidepressants, and mood stabilizers. Of all 363 patients, 255 were treated with benzodiazepines, and 139 received olanzapine. In addition, 20 patients in the MDD group were treated with sertraline (50 mg/d), and 9 patients in the BD group were treated with extended-release sodium valproate (0.5 g/d). The duration of medication exposure was less than 6 days, and the mean treatment period with psychotropic medication was 2.4 days. There were no significant differences in demographic variables (age, years of education, BMI, and duration of illness) or sleep structure parameters (all $P > .05$). All drugs were stopped the day before the overnight PSG.

Patients voluntarily participated in the present study and gave written informed consent. This study was approved by the Ethics Committee of First Hospital of Shanxi Medical University. Our study was designed in compliance with the Declaration of Helsinki.

## PSG Acquisition

The sleep-specific electrode array consists of 2 surface electromyogram (sEMG) (electrodes 1 and 2), 2 electro-oculogram (EOG) (electrodes 3 and 4), and 4 forehead

EEG electrodes (electrodes 5–8). All-night sleep recordings were performed using an overnight PSG (Compumedics, Australia) in a quiet room. The electrode array includes a skin adhesive film for easy and stable attachment to the skin. PSG recordings were performed continuously for 8 hours according to the patient's habitual bedtime between 9:00 PM and 11:00 PM until waking up the next day.[42] Each patient underwent an all-night PSG in accordance with the 2007 guidelines of the American Academy of Sleep Medicine (AASM).[43]

The patient follows the instructions to perform the corresponding actions to collect signals. The operator records the basic parameters of the patient's physiological indicators and determines whether the electrodes are placed in the correct position. At the same time, the equipment is checked to ensure that it is in normal working condition, and biological calibration is carried out before the start of monitoring. Various physiological signals, including EEG, EOG, ECG, nasal airflow, chest and abdominal movement, pulse oximetry, and snoring were recorded.

### Sleep Data Analysis

The data were transferred to a laptop computer for postprocessing using a wireless recording system. Sleep stage scoring was according to the AASM rules.[43,44] We divided an overnight sleep into the following stages: wakefulness, NREM phase 1 (N1), non-REM phase 2 (N2), non-REM phase 3 (N3, also known as slow wave sleep), and REM phase (R). Sleep structure parameters were calculated according to the guidelines of AASM, including sleep latency, R latency, sleep efficiency, and percentage of time spent in N1, N2, N3, and R stages. The values of the percentage of stages N1, N2, N3, and R in the total sleep time in the sleep structure were 2%–5%, 45%–55%, 15%–20%, and 20%–25%, respectively.

### Data Analysis

The data were analyzed using the SPSS for Windows version 21.0. The categorical demographic variable was described as the percentage with the number of patients and was compared using the $\chi^2$ test between the BD group and MDD patient group. The numeric variable was described as mean ± SD and was analyzed by the unpaired *t* tests between groups. Nonnormally distributed numeric data were described as median and interquartile ranges and compared by the Kruskal-Wallis test. After the group comparisons between MDD and BD, those variables with $P > .1$ were excluded from our final analysis. Moreover, the least absolute shrinkage and selection operator (LASSO) regression analysis was used to exclude the covariate variables.

Multivariable logistic regression analysis was conducted to determine the predictive values of the sleep structure parameters in the transdiagnosis of BD and MDD. In the models of the diagnosis of BD vs MDD, the independent variables included age, sex, and sleep structure parameters.

Performances were determined by the area under the receiver operating characteristic (ROC) curve. The ROC curve capable of distinguishing between MDD and BD was constructed on the basis of the findings from the multivariable logistic regression analyses. Sensitivity/specificity was then determined based on the ROC curve, and subsequently, the optimal cutoff values for distinguishing MDD from BD were established. *P* values < .05 were set as a statistical significance in this study.

## RESULTS

### Demographic and Clinical Data of Patients with BD and MDD

The demographic and clinical data of participants are shown in Table 1. Among the patients with BD, 77% (N = 398) were diagnosed with bipolar I disorder. No significant difference was observed in age and sex between patients with BD or MDD (all $P > .05$). However, we found significant differences in education years, BMI, and duration of illness between the 2 groups ($P < .05$). Patients with BD exhibited significantly higher BMI and longer disease duration than those with MDD.

### Comparisons of Sleep Structure and Sleep Efficiency Between Patients with BD and MDD

We found statistically significant differences in REM latency, stages N2%, N3%, and REM% between MDD and BD patients (all $P < .05$) (Table 1). Patients with MDD had statistically longer REM latency and higher N2%, lower N3%, and REM% than those with BD (all $P < .05$). Due to the significant difference in disease duration and BMI, we reanalyzed after controlling for these confounding factors and found the differences remained significant. However, no significant differences were observed in other sleep structure parameters.

We also analyzed the influence of family history on sleep structure and sleep efficiency between the patients with and without family history and found no significant differences between MDD patients with and without family history, as well as between BD patients with and without family history (all $P > .05$).

LASSO regression was performed to select independent variables to eliminate colinear or redundant variables. The results showed that the mean squared error was minimized when 5 characteristics (BMI, disease duration, REM latency, stages N2%, and REM%) were maintained. Therefore, in this LASSO model, BMI, disease duration of illness, REM latency, stage N3%, and stage REM% were identified.

Table 1.
**Comparisons Between Patients With BD and MDD**

| | BD (n = 107) | MDD (n = 256) | Statistical difference | *P* |
|---|---|---|---|---|
| **Age, y** | 22.0 (19.0, 29.0) | 23.0 (17.0, 34.0) | −0.53 | .59 |
| **Gender, male/female** | 40/60 | 86/137 | 0.2 | .63 |
| **Education years, mean (*P*25, *P*75)** | 12.0 (11.0, 16.0) | 12.0 (10.0, 15.0) | −2.1 | **.03** |
| **BMI, mean (*P*25, *P*75)** | 23.6 (21.5, 27.5) | 22.2 (19.5, 25.4) | −3.3 | **.001** |
| **Duration of illness,[a] mean (*P*25, *P*75)** | 3.0 (2.0, 6.0) | 2.0 (0.9, 2.00) | −3.9 | **<.001** |
| **Lifetime suicidality (%)** | 36 (33.6) | 79 (30.9) | 0.27 | .60 |
| **Lifetime psychosis (%)** | 54 (50.5) | 26 (10.2) | 71.4 | **<.001** |
| **Sleep time, mean (*P*25, *P*75)** | 494.0 (443.0, 537.5) | 495.3 (451.3, 534.0) | −0.1 | .90 |
| **Bedtime, mean (*P*25, *P*75)** | 529.0 (474.0, 562.5) | 534.5 (487.5, 567.3) | −0.5 | .61 |
| **Sleep efficiency, mean (*P*25, *P*75)** | 95.1 (91.2, 97.3) | 94.8 (91.4, 97.1) | −0.03 | .97 |
| **Wakefulness, mean (*P*25, *P*75)** | 12.0 (3.5, 28.0) | 12.5 (6.0, 27.0) | −0.6 | .52 |
| **Wake, mean (*P*25, *P*75)** | 2.00 (1.00, 5.00) | 2.0 (1.0, 5.0) | −0.1 | .92 |
| **Sleep latency, mean (*P*25, *P*75)** | 7.5 (3.5, 17.0) | 8.5 (4.5,17.5) | −0.7 | .49 |
| **REM latency, mean (*P*25, *P*75)** | 176.5 (106.0, 238.5) | 236.3 (152.5, 313.4) | −4.2 | **<.001** |
| **N1%, mean (*P*25, *P*75)** | 4.6 (2.1, 8.5) | 4.3 (2.4, 7.8) | −0.4 | .66 |
| **N2%, mean (*P*25, *P*75)** | 76.0 (67.0, 84.8) | 81.1 (71.8, 88.6) | −3.1 | **.02** |
| **N3%, mean (*P*25, *P*75)** | 5.7 (0.0, 13.6) | 1.6 (0.0, 11.0) | −2.6 | **.01** |
| **REM%, mean (*P*25, *P*75)** | 10.7 (5.6, 14.6) | 8.3 (4.4, 12.3) | −2.4 | **.01** |

[a]Duration of illness is defined as the time after the onset of a psychiatric disorder according to the *DSM* criteria.
Abbreviations: BD = bipolar disorder, BMI = body mass index, *DSM* = *Diagnostic and Statistical Manual of Mental Disorders*, MDD = major depressive disorder, REM = rapid eye movement.

### Correlations of These Identified Sleep Parameters

Correlation analysis was performed to explore the associations between these significant independent variables. Associations were observed between N3% and REM latency ($r = -0.14$ and $P = .009$), N2% ($r = -0.75$ and $P < .001$), and REM% ($r = 0.14$ and $P = .007$). In addition, we also found significant correlations between REM latency and stage N2% ($r = 0.22$ and $P < .001$) and a correlation between REM% and N2% ($r = -0.61$ and $P < .001$) (Table 2).

### Identifying Contributing PSG Characteristics for the Classification of BD and MDD

The independent variables selected by the LASSO algorithm were entered into the logistic regression analyses, and the dependent variable was MDD vs BD. We found that, among the several independent variables in the models, using MDD as a reference, BMI, disease duration, and REM latency were identified as the determining features differentiating MDD from BD (Nagelkerke $R^2 = 0.13$) (Table 3). BMI and disease duration were the protective factors for BD (risk factors for MDD) (odds ratio [OR] = 1.068, 95% CI, 1.016–1.123 for BMI; OR = 1.106, 95% CI, 1.023–1.196), while REM latency was the risk factors for BD (OR = 0.997, 95% CI, 0.995–0.999). Namely, the higher in BMI and longer disease duration, the higher the risk of being diagnosed with MDD (and the lower the risk of being diagnosed with BD). While the longer REM latency, the more likely a person was to be diagnosed with MDD (and the less likely to be diagnosed with BD).

Next, we constructed the ROC curve (c-index) of the regression model to identify MDD and BD, 95% CI, and the calibration curve. The ROC curve revealed an AUC of 0.64 (95% CI, 0.58–0.70, $P < .001$) of REM latency in identifying MDD and BD (Figure 2). We found that the logistic regression model identified MDD and BD within a threshold value of 20%–60% for a higher overall net benefit, indicating that the regression model had a better clinical usefulness Table 4. According to the ROC curve, the best cutoff value for the REM latency to distinguish BD from MDD was 261 (sensitivity: 41.4% and specificity: 84.1%).

## DISCUSSION

Sleep accounts for one-third of human life and plays a fundamental role in maintaining neuronal circuitry and helps maintain overall health.[45,46] We found that (1) patients with MDD had statistically a longer REM latency, a higher percentage of stage N2 sleep, and lower percentages of N3 sleep and REM sleep than those with BD; (2) among these sleep parameters, REM latency was a determining factor in differentiating BD and MDD.

Sleep quality and time spent in each sleep phase may be different in patients with MDD and BD, after controlling for age and gender. REM sleep contributes to maintaining neuronal homeostasis in the brain, because disruption of REM sleep affects brain excitability, synaptic pruning, and neurogenesis, while REM sleep deprivation

Table 2.

## Correlations Between Sleep Parameters in Patients With MDD and BD

| | | BMI | Disease duration | REM latency | N2% | N3% | REM% |
|---|---|---|---|---|---|---|---|
| **BMI** | *r* | 1 | 0.091 | −0.086 | −0.105* | 0.035 | 0.053 |
| | *P* | | .083 | .102 | .046 | .500 | .311 |
| **Disease duration** | *r* | 0.091 | 1 | −0.120* | −0.003 | −0.050 | 0.008 |
| | *P* | .083 | | .022 | .952 | .338 | .885 |
| **REM latency** | *r* | −0.086 | −0.120* | 1 | 0.219** | −0.138** | −0.265** |
| | *P* | .102 | .022 | | .000 | .009 | .000 |
| **N2%** | *r* | −0.105* | −0.003 | 0.219** | 1 | −0.754** | −0.613** |
| | *P* | .046 | .952 | .000 | | .000 | .000 |
| **N3%** | *r* | 0.035 | −0.050 | −0.138** | −0.754** | 1 | 0.142** |
| | *P* | .500 | .338 | .009 | .000 | | .007 |
| **REM%** | *r* | 0.053 | 0.008 | −0.265** | −0.613** | 0.142** | 1 |
| | *P* | .311 | .885 | .000 | .000 | .007 | |

*$P < .05$; **$P < .01$.
Abbreviations: BD = bipolar disorder, BMI = body mass index, MDD = major depressive disorder, REM = rapid eye movement.

Table 3.

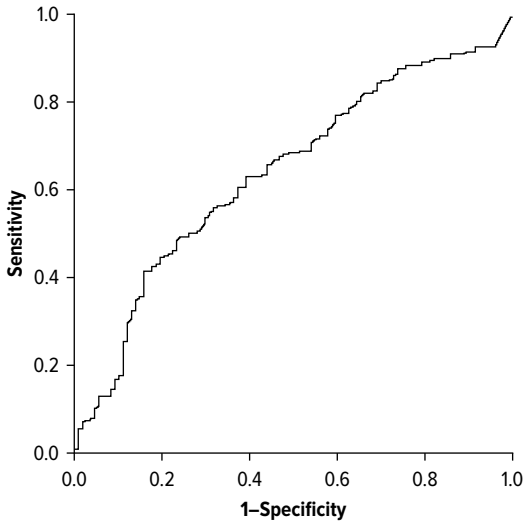
## Multivariable Logistic Regression Analysis by the Backward Elimination Method of the Diagnosis of MDD and BD[a]

| | B | SE | Wald $\chi^2$ | *P* | OR | 95% CI |
|---|---|---|---|---|---|---|
| **BMI** | 0.066 | 0.026 | 6.701 | .010 | 1.068 | 1.016, 1.123 |
| **Disease duration** | 0.101 | 0.040 | 6.477 | .011 | 1.106 | 1.023, 1.196 |
| **REM latency** | −0.003 | 0.001 | 7.071 | .008 | 0.997 | 0.995, 0.999 |
| **N2%** | −0.013 | 0.024 | 0.288 | .592 | 0.987 | 0.941, 1.035 |
| **N3%** | 0.019 | 0.028 | 0.451 | .502 | 1.019 | 0.965, 1.076 |
| **REM%** | 0.009 | 0.031 | 0.078 | .780 | 1.009 | 0.948, 1.073 |

MDD as a reference.
[a]Fit index of this model: $\chi^2 = 35.42$ ($P < .01$); Nagelkerke $R^2 = 0.132$; Hosmer-Lemeshow test: $\chi^2 = 6.824$, $P = 0.556$; sensitivity = 0.74; specificity = 0.58; positive predictive value = 0.94; negative predictive value = 0.21; predictive accuracy = 0.72.
Abbreviations: BD = bipolar disorder, BMI = body mass index, MDD = major depressive disorder, REM = rapid eye movement.

Figure 2.

## Discriminatory Capacity of Sleep Characteristics for Distinguishing Between Patients With Major Depressive Disorder and Bipolar Disorder




can lead to neurodegeneration.[47] The quality and duration of REM sleep have been reported to be associated with mood disorders.[48]

This study for the first time reported that individuals with MDD showed a longer REM latency, a higher percentage of stage N2 sleep, lower percentages of N3 sleep, and REM sleep measured by PSG relative to those with BD. Sleep disturbances are common in mood disorders compared to healthy controls and have been repeatedly reported in both MDD and BD.[35,49–51] MDD is a sleep-circadian phenotype characterized by longer sleep latency, shorter total sleep time, and frequent awakenings after sleep onset.[52–54] BD is characterized by mania episodes of reduced sleep need, depressive episodes of hypersomnia or excessive sleepiness or severe insomnia, and mixed episodes that exhibit both features.[20,21,55–57] Previous studies have shown a close relationship between sleep disturbance and increased risks of BD or MDD.[58,59] However, we further revealed a significant difference in sleep parameters, such as REM latency, and percentages of stage N2, N3, and REM in a large sample size. Our findings are similar to recent meta-analyses of various PSG alterations in neuropsychiatric disorders, suggesting that no two psychiatric disorders had the same sleep characteristics after looking across PSG variables.[60] Thus, the overall changes in PSG characteristics should serve as a fundamental dimension of psychiatric disorders that can be comprehensively assessed as their potential

Table 4.

**Sensitivity, Specificity, and Likelihood Ratio of Sleep Parameters in Differentiating BD From MDD (ROC Curve)**

| REM Latency | Sensitivity | 1–Specificity | Specificity | Youden Index |
|---|---|---|---|---|
| 239.0000 | 0.492 | 0.243 | 0.757 | 0.249 |
| 240.2500 | 0.484 | 0.234 | 0.766 | 0.251 |
| 241.5000 | 0.477 | 0.234 | 0.766 | 0.243 |
| 242.2500 | 0.469 | 0.234 | 0.766 | 0.235 |
| 257.7500 | 0.426 | 0.178 | 0.822 | 0.248 |
| 259.0000 | 0.422 | 0.178 | 0.822 | 0.244 |
| 260.2500 | 0.414 | 0.178 | 0.822 | 0.236 |
| 261.0000 | 0.414 | 0.159 | 0.841 | 0.255 |
| 262.2500 | 0.410 | 0.159 | 0.841 | 0.251 |
| 263.5000 | 0.406 | 0.159 | 0.841 | 0.247 |
| 264.7500 | 0.402 | 0.159 | 0.841 | 0.243 |
| 265.7500 | 0.398 | 0.159 | 0.841 | 0.240 |
| 266.2500 | 0.391 | 0.159 | 0.841 | 0.232 |

Abbreviations: BD = bipolar disorder, MDD = major depressive disorder, ROC = receiver operating characteristic.

disease-specific biomarkers.[61] In particular, our findings were in line with recent analyses that reveal that PSG characteristic alterations can be considered as transdiagnostic sleep features across various psychiatric disorders.[46,62]

Interestingly, we further found that REM latency was a transdiagnostic biomarker between MDD and BD. It is well known that, in contrast to other areas of medicine, mental disorders are still plagued by problems such as the fact that the classification of psychiatric diseases is based on symptoms of overlapping disease entities rather than causal factors. Thus, there is an urgent need to map diagnostic labels from clinically defined symptoms to different biomarkers.[63] Our findings were consistent with other studies showing that sleep abnormality can predict the development of mental disorders (ie, MDD, anxiety, and BD).[64–66] REM latency is the time interval between sleep onset and the first REM episode. Previous studies have shown that decreased REM latency may be a trait marker of disease vulnerability and a biomarker of MDD and depressive episodes in BD.[67] Our study provides further evidence that reduced REM latency may be specific to MDD and different mental diseases are related to different alterations in REM alterations.[68,69] Taken together, our study suggests that specific sleep patterns measured by PSG may best define distinct mental diseases.

The strength of this study is the large sample size. In addition, most patients recruited were never-medicated and first-episode. We also excluded patients with other comorbid neuropsychiatric disorders, thus minimizing or mitigating the potential confounding factors for accurate PSG testing. However, a few limitations should be noted in this study. First, no healthy controls were recruited in our study, so we were unable to compare PSG patterns between patients and controls. Second, this was a cross-sectional study, and we did not perform a second PSG testing after treatment with various antipsychotic drugs. Third, the data in this study were the first PSG recordings from the recruited patients. We did not exclude the first night effects. The effects of first night adaptation to PSG recording in hospitalized patients may have had an impact on the results. Fourth, we did not collect data of smoking status in this study, so we cannot add it as a confounding factor in the regression models. Fifth, our study did not evaluate the symptoms in the participants. Sleep duration, quality, and structure depend on the mood symptoms. For instance, patients with acute mania present a decreased need for sleep, and patients with depression show insomnia or hypersomnia. So, further studies should present the status of participants' mood symptoms, such as the Hamilton Depression Rating Scale, the Montgomery-Asberg Depression Rating Scale, or the Young Mania Rating Scale.

In conclusion, this study revealed the different changes in the overall patterns of PSG parameters between patients with MDD and those with BD. Furthermore, we provide new evidence for the transdiagnostic role of sleep disturbance measured by PSG in distinguishing MDD from BD. Our findings suggest that changes in the PSG profile could be assessed as an underlying dimension and potential disorder-specific biomarkers for psychiatric disorders in future studies. Our findings, if repeated in further studies, may also have a significant clinical implication for the early diagnosis of BD and MDD.

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