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Topographic and sex-related differences in sleep spindles in major depressive disorder: A high-density EEG investigation

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Abstract

Background—Sleep spindles are believed to mediate several sleep-related functions including maintaining disconnection from the external environment during sleep, cortical development, and sleep-dependent memory consolidation. Prior studies that have examined sleep spindles in major depressive disorder (MDD) have not demonstrated consistent differences relative to control subjects, which may be due to sex-related variation and limited spatial resolution of spindle detection. Thus, this study sought to characterize sleep spindles in MDD using high-density electroencephalography (hdEEG) to examine the topography of sleep spindles across the cortex in MDD, as well as sex-related variation in spindle topography in the disorder.

Methods—All-night hdEEG recordings were collected in 30 unipolar MDD participants (19 women) and 30 age and sex-matched controls. Topography of sleep spindle density, amplitude, duration, and integrated spindle activity (ISA) were assessed to determine group differences. Spindle parameters were compared between MDD and controls, including analysis stratified by sex.

Results—As a group, MDD subjects demonstrated significant increases in frontal and parietal spindle density and ISA compared to controls. When stratified by sex, MDD women demonstrated increases in frontal and parietal spindle density, amplitude, duration, and ISA; whereas MDD men demonstrated either no differences or decreases in spindle parameters.

Limitations—Given the number of male subjects, this study may be underpowered to detect differences in spindle parameters in male MDD participants.

Conclusions—This study demonstrates topographic and sex-related differences in sleep spindles in MDD. Further research is warranted to investigate the role of sleep spindles and sex in the pathophysiology of MDD.

Keywords

Sleep spindles; Major depressive disorder; High-density EEG

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Conflict of interest

Dr. Plante has owned stock in Pfizer, and has received honoraria from Oakstone Medical Publishing and royalties from Cambridge University Press. Dr. Peterson has received unrelated research support from Sanofi-Aventis. Dr. Tononi has consulted for Sanofi-Aventis and Takeda, and he is currently the David P. White Chair in Sleep Medicine at the University of Wisconsin–Madison, endowed by Phillips Respironics. Dr. Tononi has also received unrelated research support from Phillips Respironics. Dr. Benca has consulted for Merck and Sanofi-Aventis. All other authors declare they have no conflicts of interest.

1. Introduction

Sleep spindles are waxing-waning oscillations (11–15 Hz) that are hallmarks of electroencephalographic (EEG) non-rapid eye movement (NREM) sleep. Although the functional role of sleep spindles remains unclear, there is evidence they are involved in a number of domains including maintaining disconnection from the external environment during sleep (Steriade, 2003), cortical development (Khazipov et al., 2004), and sleep-dependent memory consolidation (Fogel and Smith, 2011). Sleep spindles are heterogeneous in both frequency and location, with fast spindles (13–15 Hz) occurring predominantly in central and parietal regions, whereas slow spindles (11–13 Hz) are more prominent frontally (Anderer et al., 2001; Schabus et al., 2007). Furthermore, the importance of cortical topography in the evaluation of sleep spindle activity is underscored by recent evidence that spindles may occur and be regulated locally (Andrillon et al., 2011; Nir et al., 2011).

Major depressive disorder (MDD) is associated with both decrements in subjective and objective quality of sleep (Benca et al., 1992; Peterson and Benca, 2006; Steiger and Kimura, 2010) and sleep-dependent memory consolidation (Dresler et al., 2010; Dresler et al., 2011), and thus it is not surprising that previous investigations have examined the role of sleep spindles in the disorder. Results have not been consistent among prior studies, with no difference (Goetz et al., 1983; Reynolds et al., 1985) or reductions (de Maertelaer et al., 1987; Lopez et al., 2010) in spindle activity reported in MDD. However, comparison of results across studies is difficult as ages and sexes of subjects have varied widely among studies. Also, prior investigations have typically utilized standard EEG montages in which only one or a few EEG channels were used to detect sleep spindles, and thus topographic differences in spindle activity between groups could not be distinguished. Prior studies have also predominantly evaluated spindle density (number of spindles/unit time), and have not computed other parameters to examine spindle morphology in MDD such as amplitude and duration.

A recent investigation utilizing high-density EEG (hdEEG), which has superior spatial resolution compared to standard scalp-level EEG methods, did not demonstrate topographical differences in spindle parameters between depressed and control participants (Ferrarelli et al., 2007). However, in this study nearly half of MDD subjects were in remission, several participants were taking psychotropic medications, subjects were not sex-matched, and all-night sleep spindle measures could not be ascertained as only sleep from the first NREM period was utilized (Ferrarelli et al., 2007). This is potentially problematic as healthy women may have greater sleep spindle activity relative to men (Huupponen et al., 2002). In addition, decrements in sleep spindles in adolescent MDD have been reported to be more prominent in female MDD patients, and be more readily observed in later portions of the night (Lopez et al., 2010).

Thus, the primary aim of this study was to utilize hdEEG to examine all-night sleep spindle topography in MDD using a well-defined cohort of unmedicated, unipolar MDD subjects relative to age and sex-matched control subjects. Based on prior literature, we hypothesized that MDD subjects would demonstrate decrements in sleep spindles relative to controls, and that these decrements would be more pronounced in female MDD participants.

2. Methods

2.1. Participants

Thirty unmedicated MDD participants (19 female) were selected from a larger study on sleep homeostasis in neuropsychiatric disorders, conducted at the University of Wisconsin–

Madison. MDD was diagnosed via the Structured Clinical Interview for DSM-IV Axis I disorders (SCID) (First et al., 2002b). For inclusion, subjects were required to have moderate or worse unipolar depression, defined as a score of 15 or higher on the clinician-administered 17-item Hamilton Rating Scale for Depression (HRSD) (Hamilton, 1960). Subjects had no history of psychosis, active drug/alcohol dependence, or significant neurological/medical condition. Age and sex-matched healthy comparison subjects without current or past psychiatric disorders were evaluated with the non-patient SCID (First et al., 2002a). Subjects with evidence of clinically significant sleep disordered breathing (apnea-hypopnea index > 10/hr) or sleep-related movement disorder (periodic limb movement arousal index > 10/hr) during overnight recording (see below) were excluded.

All subjects provided informed consent and were instructed to maintain regular sleep-wake schedules, avoid napping, and to limit the use of caffeinated and alcoholic beverages for the duration of the study. Adherence was monitored using sleep-logs and actigraphy (Actiwatch, Mini-Mitter, Bend, OR). This study was approved by the Institutional Review Board of the University of Wisconsin-Madison.

2.2. EEG recording and analysis

All subjects underwent overnight in-laboratory hdEEG recordings that utilized a 256 channel system (Electrical Geodesics Inc., Eugene, OR). During hdEEG recordings, additional monitoring with electrooculogram (EOG), sub-mental electromyogram (EMG), electrocardiogram (ECG), bilateral tibial EMG, respiratory inductance plethysmography, pulse oximetry, and a position sensor were utilized for sleep staging and to evaluate for sleep disordered breathing and sleep-related movement disorders. Participants slept undisturbed in the laboratory beginning within 1 h of their usual bedtime. Sleep hdEEG recordings were collected with vertex-referencing, using NetStation software (Electrical Geodesics Inc., Eugene, OR).

EEG signals were sampled at 500 Hz, first-order high-pass filtered in Net Station (0.1 Hz), down sampled to 128 Hz, band-pass filtered (2-way least-squares FIR, 1–40 Hz) in MATLAB (The Math Works Inc., Natick, MA), and average-referenced to the average scalp voltage computed in all channels. Semi-automatic artifact rejection allowed for removal of channels for individual epochs with high-frequency noise or interrupted contact with the scalp. To increase the signal-to-noise ratio, analyses were restricted to channels falling within a plotting radius of 0.57 specified in the topoplot function of the EEGLAB (Delorme and Makeig, 2004) plug-in for MATLAB, resulting in 173 channels overlaying the scalp. A registered polysomnographic technologist scored sleep stages in 30 s epochs using Alice® Sleepware (Philips Respironics, Murrysville, PA) utilizing a mastoid referenced montage according to standard criteria (Iber et al., 2007).

2.3. Spindle detection and analysis

Spindle detection and analysis was performed similar to prior studies in our laboratory utilizing a customized spindle detection algorithm in MATLAB (Ferrarelli et al., 2007, 2010). NREM epochs were initially filtered between 11 and 15 Hz, and rectified filtered signals were used as time series for each channel. Spindle detection occurred whenever the mean signal amplitude of each channel exceeded an upper threshold that was set at six times the mean amplitude for each channel. The peak amplitude for each spindle was defined as the local maximum above the upper threshold. The beginning and end of the spindle were defined as the points at which the amplitude of the time series dropped below a lower threshold, which was defined as two times the mean amplitude of the channel signal, occurring 0.25 s from the peak. To characterize spindles in the slow (11–13 Hz) and fast

(13–15 Hz) ranges, detected spindles with a frequency falling within these ranges were grouped together.

For all detected spindles, four parameters were investigated: spindle density, duration, maximal amplitude, and integrated spindle activity (ISA). The number of detected spindles divided by NREM sleep duration defined spindle density; ISA was determined by integrating the absolute amplitude values of each spindle divided by NREM sleep duration (Ferrarelli et al., 2007, 2010). To examine topographic differences in slow and fast spindles, spindle parameters were also calculated from NREM data filtered from 11–13 Hz and 13–15 Hz, respectively.

2.4. Statistics

To evaluate the primary outcome measure of topographic differences in all-night sleep spindle parameters in MDD versus control subjects, unpaired two-tailed *t*-tests were used. Given previous reports of sex-related differences in sleep spindles among both healthy and MDD subjects (Huupponen et al., 2002; Lopez et al., 2010), and reported differences in spindle parameters related to age (Feinberg et al., 1967; Guazzelli et al., 1986; Nicolas et al., 2001; Wei et al., 1999), analyses between MDD and healthy controls stratified by sex were also performed to maintain age-matching of subjects. Slow (11–13 Hz) and fast (13–15 Hz) spindles were also evaluated separately given different topographical distributions and likely involvement of different thalamo-cortical circuits (Ferrarelli et al., 2010; Schabus et al., 2007). Statistical non-parametric mapping with suprathreshold cluster tests (STCT) was applied to topographical hEEG data to correct for multiple comparisons (Nichols and Holmes, 2002). Sleep architecture measures were compared using unpaired two-tailed *t*-tests. Statistical relationship between spindle parameters and depression severity were assessed using linear regression. To limit spurious findings due to multiple comparisons, topographic correlations were limited to regions and spindle parameters significantly different between groups. Statistical analyses were performed using MATLAB and STATISTICA (StatSoft Inc., Tulsa, OK).

3. Results

MDD subjects ($n=30$; 19 female) were young to middle aged mean 26.0 ± 9.1 ; range 18 to 53 years) with moderate depression (mean HRSD 18.6 ± 2.7 ; range 15 to 25) (Table 1). One MDD subject (female) required a repeat night in the laboratory be utilized for analysis due to technical problems with the recording. Overall, MDD subjects demonstrated significantly less total sleep time (TST; 377.5 min. vs. 412.7 min; $P=0.02$) than controls. When stratified by sex, MDD men showed significantly greater arousal index (AI; 12.6/hr vs. 7.4/hr, $P=0.04$) and lower sleep efficiency (82.8% vs. 90.1% $P=0.02$) than matched male controls. There were no other significant differences among polysomnographic variables between MDD and controls either unstratified or stratified by sex (Table 1).

Analysis of whole range (11–15 Hz) sleep spindle parameters demonstrated increased right centroparietal spindle density, as well as left frontal and right centroparietal ISA, in MDD relative to controls, without differences in spindle amplitude or duration (Fig. 1). When stratified by sex, MDD women exhibited prominent increases in all spindle parameters relative to matched controls, including increased bilateral centroparietal spindle density, increased frontal amplitude, right centroparietal spindle duration, and bilateral frontal and parieto-occipital ISA (Fig. 1). Conversely, MDD men had lower left parietal spindle density and lower left parietal, right frontal, and occipital spindle duration, without significant differences in amplitude or ISA relative to matched healthy controls (Fig. 1).

MDD subjects showed a left frontal and right parietal increase in ISA of slow (11–13 Hz) spindles, without differences in spindle density, amplitude or duration (Fig. 2). When stratified by sex, MDD women demonstrated prominent increases in slow spindle density in bilateral frontal regions, as well as bilateral frontal increases in amplitude, centroparietal increases in duration, and bilateral frontal and parietal ISA relative to matched controls (Fig. 2). MDD men conversely demonstrated lateral (left and right) parietal decreases in slow spindle density and duration, as well as decreased slow spindle duration in occipital and right frontal regions, without differences in ISA or amplitude, relative to matched controls (Fig. 2).

MDD subjects exhibited increased density of fast (13–15 Hz) centroparietal spindles, as well as ISA in frontal and parietal regions (Fig. 3). Relative to controls, MDD subjects also demonstrated decreased duration of fast spindles in bilateral frontal channels, without differences in fast spindle amplitude (Fig. 3). When stratified by sex, MDD women demonstrated significant topographic increases in all parameters for fast spindles relative to matched controls including bilateral parietal spindle density, bilateral frontal and parietal ISA, bilateral frontal amplitude, and right centroparietal duration (Fig. 3). However, MDD males demonstrated no significant differences in fast spindle parameters relative to matched controls.

Among MDD participants, depression severity (HRSD score) did not correlate with spindle density, amplitude, duration, or ISA either globally (average of all channels) or topographically, either stratified or unstratified by sex (data not shown).

4. Discussion

In this study, our findings demonstrated that young to middle aged women with MDD had significant topographic increases in several sleep spindle parameters including density, duration, amplitude, and integrated spindle activity relative to matched controls subjects. In contrast, men with MDD had topographic decreases (or no changes) in spindle parameters relative to matched healthy controls. Strengths of this investigation include age and sex-matching of subjects, which allowed for analyses stratified by sex, lack of confounding psychotropic medications, the evaluation of multiple spindle characteristics, and the use of hdEEG to evaluate the topography of sleep spindle parameters.

This study highlights the importance of cortical topography, type of spindle parameter, and sex in the evaluation of sleep spindles in MDD. In regards to topography, our data suggest that differences in sleep spindles between MDD and healthy controls may occur regionally. Thus, inconsistencies among prior studies that have demonstrated either no difference (Goetz et al., 1983; Reynolds et al., 1985) or reductions (de Maertelaer et al., 1987; Lopez et al., 2010) in spindle activity may have been due to the use of limited EEG derivations (typically 1–2 central or frontal electrodes) in these investigations. The use of hdEEG provides significantly improved spatial resolution, thus allowing local differences in sleep spindles in MDD to be ascertained. Moreover, this investigation highlights the fact that the use of spindle density as a sole measure of spindle activity may underestimate and/or fail to capture regional differences between groups. Differences between MDD and controls in spindle density, amplitude, and duration occurred in different cortical regions in our study, suggesting that both incidence and morphology of sleep spindles may vary topographically. In many instances, ISA, which quantifies the power of detected sleep spindles and thus accounts for density, amplitude, and duration, demonstrated the most robust between group differences, suggesting this parameter may be a more sensitive measure in the evaluation of sleep spindles in depression.

In regards to the importance of sex on sleep spindles in MDD, our results suggest that differences in spindle parameters relative to healthy controls differ between male and female MDD subjects. Moreover, because spindle parameters in this study were largely increased in women, but decreased or unchanged in men with MDD, conflicting results of prior studies may have been related to different proportions of male and female participants. It is noteworthy that one of the two prior investigations that demonstrated decreased spindle activity in depression examined a cohort that was exclusively male (de Maertelaer et al., 1987). The other study that has demonstrated a reduction in sleep spindles in MDD (Lopez et al., 2010) utilized subjects with roughly equivalent numbers of male and female participants, however, because this study examined children and adolescents (age range 8–15 years), results may not be directly comparable to our investigation, given the sizeable differences in age between study participants.

The cause of increased sleep spindles in women with MDD cannot be determined by this study; however, it is possible that neurohormonal factors may be involved. Healthy women have demonstrated increases in sleep spindles in frontal EEG derivations relative to men (Huupponen et al., 2002). Additionally, sleep spindle activity is greater in the luteal phase of the menstrual cycle (Driver et al., 1996; Ishizuka et al., 1994), during which progesterone is increased relative to the follicular phase. During both the luteal (Hardoy et al., 2006) and follicular (Holsen et al., 2011) phases of the menstrual cycle, women with MDD have demonstrated increased progesterone relative to healthy controls. Sleep spindles are generated by the GABAergic thalamic reticular nucleus (De Gennaro and Ferrara, 2003). Allopregnanolone, which is synthesized in the brain from progesterone by 5α reductase type I and 3α -hydroxysteroid dehydrogenase, is a potent allosteric modulator of GABA action at GABA_A receptors (Belelli and Lambert, 2005; Puia et al., 1990). Notably, both of these enzymes are co-expressed in GABAergic reticular thalamic nuclei neurons (Agis-Balboa et al., 2006). Thus, although speculative, the increase in sleep spindles among MDD women in our study may be related to increased progesterone potentiating the activity of the GABAergic thalamic reticular nucleus. Further research that examines the effects of progesterone on the generation of sleep spindles, and how this may relate to the pathophysiology of MDD in women, is clearly indicated.

It is also plausible that sleep spindles may play a role in impaired memory consolidation in MDD. Recent work in healthy subjects has suggested that sleep spindles, particularly fast spindles, are important in sleep-dependent memory consolidation (Barakat et al., 2011; Bergmann et al., 2012; Nishida and Walker, 2007; Seeck-Hirschner et al., in press; van der Helm et al., 2011), which is thought to be impaired in MDD (Dresler et al., 2010, 2011). Interestingly, our results suggest that there may be differential regulation of sleep spindles in MDD that varies by sex, which may influence spindle-related research in sleep-dependent memory consolidation. This presupposition is supported by recent work in healthy subjects that has demonstrated both a sex and menstrual cycle effect on memory performance following naps, with spindle activity correlating with motor learning in men and women in the luteal, but not follicular phase, of the menstrual cycle (Genzel et al., 2011). In this context, the increase in sleep spindles observed in MDD women in our study may be interpreted as a possible compensatory mechanism to account for impaired memory consolidation. Future work that examines the effects of both sleep spindles and sex hormones in MDD on sleep-dependent memory consolidation may shed further light on the connections between these variables.

Given the cross-sectional design of this study, we are not able to determine whether alterations in sleep spindles in MDD are a state or trait marker for the illness. The lack of a correlation between spindle parameters and depression severity may support the notion that alterations in spindle parameters are a trait marker, however, is also plausible that our MDD

subjects did not have sufficient variability in HRSD scores (e.g., most had relatively moderate depression), to detect a correlation. This study was also not designed to determine the functional significance of specific spindle parameters, and how alterations in a given parameter may be related to specific symptoms in MDD. Thus, future research that compares spindle parameters in remitted and non-remitted depressives (ideally utilizing a longitudinal within-subjects design), evaluates the role of sleep spindle parameters in specific symptom domains, and considers the role of sex and neurohormones in these parameters, may provide deeper insights into this conceptual framework.

5. Limitations

There are limitations of this study that merit discussion. First, the findings of this study must be considered in the context of the ratio of women to men, which was roughly 2:1, approximating the differential prevalence of MDD among women and men in the population (Kessler et al., 1993). Thus, this study may have been underpowered to detect differences in spindle parameters in male MDD participants. In the same vein, findings in the unstratified analysis may not have been demonstrated had the ratio of women to men been proportionate. Subjects also did not have an adaptation night in the laboratory, and thus results may have been affected if first-night effects differentially affected groups. However, it is noteworthy that sigma range activity during NREM sleep (which includes spindle range activity) is stable across nights, and thus spindle parameters may not be as susceptible to first night effects as other sleep EEG waveforms (De Gennaro et al., 2005). Menstrual phase (e.g., luteal vs. follicular) was not ascertained for female subjects, which may be an important uncontrolled covariate (Driver et al., 1996; Ishizuka et al., 1994). Additionally, we did not control for differences in intelligence among subjects, which may have affected results as there is evidence that sleep spindle incidence and/or activity correlates with intelligence quotient (Fogel and Smith, 2011). Finally, subjects were young to middle aged, and thus, results may not be applicable to MDD in geriatric or child/adolescent populations.

In conclusion, here we have demonstrated topographic and sex-related differences in sleep spindle parameters in MDD subjects relative to matched healthy controls. These findings underscore the importance of considering both sex and cortical topography in the study of sleep spindles in mood disorders. Further research is indicated to explore the functional significance of alterations in sleep spindle parameters in MDD, and how these factors may be influenced by sex-related differences in neurobiology.

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Fig. 1.

Topographic whole range (11–15 Hz) spindle parameters in MDD subjects versus healthy controls, both unstratified and stratified by sex. *T*-values plotted for the comparisons between groups (2-tailed, unpaired *t*-test) at each channel with red and blue corresponding to respective increase or decrease ($p < 0.1$) for a given parameter. Green dots denote channels with significant between group differences following statistical non-parametric mapping with suprathreshold cluster test to correct for multiple comparisons. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 2.

Topographic all-night slow (11–13 Hz) spindle parameters in MDD subjects versus healthy controls, both unstratified and stratified by sex. *T*-values plotted for the comparisons between groups (2-tailed, unpaired *t*-test) at each channel with red and blue corresponding to respective increase or decrease ($p < 0.1$) in a given parameter. Green dots denote channels with significant between group differences following statistical non-parametric mapping with suprathreshold cluster test to correct for multiple comparisons. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Fig. 3.

Topographic all-night fast (13–15 Hz) spindle parameters in MDD subjects versus healthy controls, both unstratified and stratified by sex. *T*-values plotted for the comparisons between groups (2-tailed, unpaired *t*-test) at each channel with red and blue corresponding to respective increase or decrease ($p < 0.1$) in a given parameter. Green dots denote channels with significant between group differences following statistical non-parametric mapping with suprathreshold cluster test to correct for multiple comparisons. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 1

Demographic, polysomnographic, and spindle range activity for MDD and control participants.

	MDD (N=30)	HC (N=30)	P	MDD females (N=19)	HC females (N=19)	P	MDD males (N=11)	HC males (N=11)	P
Age (years)	26.0 (9.1)	25.4 (8.5)	0.79	23.4 (5.6)	23.1 (6.2)	0.89	30.6 (12.1)	29.4 (10.7)	0.81
HRSD-17	18.6 (2.7)	–	–	19.0 (3.0)	–	–	17.9 (1.6)	–	
TST (min)	377.5 (66.3)	412.7 (47.5)	0.02	388.0 (54.1)	419.6 (49.8)	0.09	356.0 (81.7)	400.8 (42.9)	0.12
WASO (min)	42.6 (30.8)	30.2 (20.7)	0.07	37.0 (27.1)	30.7 (20.6)	0.43	52.4 (35.4)	29.4 (21.8)	0.08
AI (#/h)	10.3 (5.5)	7.9 (4.3)	0.07	8.9 (5.2)	8.2 (3.8)	0.61	12.6 (5.5)	7.4 (5.3)	0.04
SE (%)	86.6 (7.9)	89.6 (7.4)	0.14	88.9 (7.1)	89.2 (8.6)	0.89	82.8 (8.1)	90.1 (4.9)	0.02
SOL (min)	15.7 (16.5)	18.6 (24.3)	0.60	12.0 (10.6)	20.6 (28.0)	0.22	22.1 (22.7)	15.0 (16.7)	0.41
N1 (%)	8.0 (5.3)	7.9 (4.7)	0.99	7.34 (5.6)	7.7 (5.0)	0.82	9.0 (5.0)	8.3 (4.2)	0.72
N2 (%)	57.6 (8.2)	60.4 (6.1)	0.14	56.4 (8.7)	60.4 (5.2)	0.10	59.5 (7.2)	60.4 (7.8)	0.79
N3 (%)	16.9 (9.2)	14.8 (7.1)	0.34	20.1 (7.6)	15.9 (6.3)	0.07	11.2 (9.3)	13.0 (8.2)	0.65
REM (%)	18.2 (6.6)	16.9 (5.0)	0.39	16.1 (6.6)	16.0 (5.2)	0.98	22.2 (4.8)	18.4 (4.5)	0.07
REML (min)	127.1 (77.9)	122.2 (69.7)	0.80	151.9 (81.2)	131.1 (71.2)	0.41	80.0 (43.7)	106.7 (67.4)	0.30
SRA ($\mu V^2/Hz$)	1.2 (0.5)	1.1 (0.4)	0.58	1.3 (0.5)	1.1 (0.4)	0.13	0.9 (0.4)	1.1 (0.4)	0.44

MDD, major depressive disorder; HC, healthy control; HRSD-17, Hamilton rating scale for depression (17-item); TST, total sleep time; WASO, wake after sleep onset; AI, arousal index; SE, sleep efficiency; SOL, sleep onset latency; N1/2/3, NREM stage 1/2/3 (% of TST); REM, stage REM (% of TST); REML, REM latency; SRA, global spindle range activity (EEG power in 11–15 Hz range average 173 channels). Values are displayed as mean (standard deviation). *2-tailed, independent samples *t*-tests. Significant differences highlighted in bold.