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# EEG spectral analysis of nighttime sleep and daytime MSLTs and neurocognitive evaluations in subjects with co-morbid insomnia and OSA

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## Abstract

**Background** Chronic insomnia and obstructive sleep apnea commonly co-occur. Few studies have explored the neurophysiological and neurocognitive characteristics of COMISA, which could help guide improving treatment diagnostic tools and determining novel therapeutic targets. This study aims to explore the neurophysiological and neurocognitive characteristics of COMISA using electroencephalographic (EEG) spectral analysis and subjective and objective neurocognitive measurements.

**Methods** Participants were from our community recruited OSA-insomnia-COMISA cohort with 206 included for our current analysis including 74 chronic insomniacs (CIs), 55 OSA patients and 77 COMISA patients. Standard polysomnography (PSG) and multiple sleep latency tests (MSLTs) were recorded and used to obtain relative EEG spectral power in each sleep stage during PSG and each session during MSLTs. A series of subjective and objective neurocognitive tests were conducted to evaluate executive function, attention, retrospective and prospective memory and meta-cognition.

**Results** In PSG and MSLTs, COMISA patients showed combined EEG power characteristics of both CIs and OSA. Specifically, COMISA patients exhibited similar EEG spectral characteristics to CIs, with decreased delta and increased alpha and beta power in NREM sleep stages, and increased beta power in REM and MSLTs. Similar to the EEG spectral power profile of OSA, COMISA patients showed increased delta power in REM and MSLTs. Compared to OSA patients, COMISA patients exhibited worse subjectively measured attention and meta-cognition related to negative beliefs about uncontrollability and danger of worry (NEG), which were positively associated with ISI scores.

**Conclusions** The EEG spectral power characteristics of COMISA patients in overnight PSG and daytime MSLT appear to be the manifestation of elements of both CIs and OSA. However, the neurocognitive features of COMISA patients in subjectively measured attention and NEG meta-cognition were primarily affected by chronic insomnia.

**Keywords** COMISA, Spectral analysis, Neurocognition, Neurophysiology, Polysomnography, Multiple sleep latency test

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## Background

Insomnia and obstructive sleep apnea (OSA) are the two most prevalent sleep disorders [1, 2] They commonly co-occur [3] with about 30-40% of insomnia patients fulfilling criteria for OSA, and 30-50% of OSA patients reporting insomnia symptoms [4–6]. In 1973, Guilleminault et al. first described the co-occurrence of OSA and insomnia [7], and in 2017 Sweetman et al. coined the term "comorbid insomnia and sleep apnea (COMISA)" [3]. Subsequently, research on COMISA has been increasing [8], with explorations of its prevalence, clinical characteristics, consequences and treatment modalities [4, 5, 8–21]. However, less research has explored the neurophysiological and neurocognitive characteristics of COMISA, which could help guide improving treatment diagnostic tools and determining novel therapeutic targets for this common, yet complex and debilitating condition.

Electroencephalogram (EEG) recordings from overnight polysomnography (PSG) and daytime multiple sleep latency tests (MSLTs) can be quantitatively analyzed by EEG power spectral analysis (PSA) to reveal variations in brain activity. EEG PSA based on overnight PSG has been widely used to explore the neurophysiological characteristics of sleep disorders such as CI, OSA, etc [22, 23]. Although MSLTs are not a routine assessment tool for insomnia disorder, previous studies have used multiple sleep latency (MSL) and EEG data obtained from MSLTs for PSA analysis to assess daytime arousal levels, and found that patients with insomnia disorder exhibited daytime physiological (prolonged MSL) and cortical hyperarousal (increased EEG beta power) [24–28]. Therefore, considering that COMISA is a comorbidity of insomnia disorder and OSA, PSA performed on both overnight PSG and next day MSLTs should more comprehensively reveal its neurophysiological characteristics. To our knowledge, only one study has examined the EEG spectral power of COMISA patients. This study reported that EEG power in a COMISA group was not different from that in an insomnia group, but was significantly higher than that in an OSA group [29]. In this study, insomnia was defined by answers to questions about the presence or absence of insomnia related symptoms, not diagnosis by a physician. Furthermore, the researchers summed power values for all frequency bands rather than calculating EEG power in individual frequency bands. This is important as EEG activity in different frequency ranges is associated with specific functions [30–32]. Thus, to date, no one has applied EEG PSA in patients with a physician determined diagnosis of COMISA to explore its utility in determining disease specific neurophysiological characteristics.

Both insomnia and OSA commonly impair neurocognitive function with deficits in attention, memory and executive functioning [33, 34]. Individuals with COMISA could experience the detrimental effects of each disorder and exhibit cumulative deterioration in neurocognitive function, though this has not been well established. To date only three studies have examined neurocognitive impairment in COMISA patients [35–37]; but these studies applied different assessment tools and obtained divergent results. Two earlier studies reported that COMISA patients presented poor memory and attention with prolonged or retained psychomotor reaction times [35, 36] whereas a more recent study found that individuals with COMISA had worse cognitive control, attention and executive functioning but retained memory and had better psychomotor performance compared to patients with either OSA or insomnia [37]. These discrepancies indicate that additional exploration of the neurocognitive characteristics of COMISA is needed to fully understand its effects.

Therefore, the aims of the present study were to explore the neurophysiological and neurocognitive characteristics of COMISA in physician diagnosed patients by applying EEG spectral analyses and a series of objective and subjective neurocognitive assessments. Through correlation analyses, this study explored the contribution of insomnia and OSA to COMISA in neurophysiological and neurocognitive domains, which could add new evidence regarding the pathophysiology of COMISA.

## Materials and methods

### Participants

Subjects were participants in our OSA-insomnia-COMISA cohort. A description of this cohort and a flow chart of how it was established along with subject enrollment are provided in Supplementary Materials (Table S1 and Figure S1). The study was conducted according to the World Medical Association Declaration of Helsinki in 1975, as revised in 1983, and was approved by the Research Ethics Board of West China Hospital of Sichuan University (NO.1481). All subjects provided their informed written consent.

In the current study, subjects were recruited from December 2023 to August 2024. Insomnia disorder was diagnosed based on DSM-V. OSA was diagnosed based on DSM-V criteria: (1) PSG measured apnea-hypopnea index (AHI) ≥ 15 events/h or (2) AHI ≥ 5 events/h combined with either of the following sleep symptoms: (a) nocturnal breathing disturbances (snoring, snorting/gasping, or breathing pauses during sleep); (b) daytime sleepiness, fatigue, or unrefreshing sleep despite sufficient opportunity to sleep that is not better explained by another mental disorder (including a sleep disorder) and is not attributable to another medical condition. The inclusion criteria for CIs were: (1) diagnosis with insomnia disorder and (2) absence of OSA. OSA patients met

the following criteria: (1) diagnosis with OSA and (2) could not be diagnosed with insomnia disorder based on DSM-V. COMISA patients concurrently met the diagnosis criteria for both insomnia disorder and OSA.

For all participants, we excluded subjects who: (1) were under 18 or over 60 years old; (2) had a sleep onset rapid eye movement period (SOREMP) during either PSG or MSLT; (3) had other sleep disorders based on subjective self-report and objective PSG and MSLT measurements; (4) had incomplete PSG or MSLT EEG data; (5) or had a current diagnosis of psychiatric or neurological disorders or severe physical diseases.

#### Sample size calculation

Based on our pre-experiment results for relative beta power, at least 192 subjects were required to complete the study protocol with a minimum of 72 CIs, 48 OSA and 72 COMISA patients. This provided for power of 90%, $\alpha = 0.05$ with 3 groups (group means = 4.24 3.19 4.45, standard deviation = 1.956, group allocation pattern: 1.5, 1.0, 1.5). To improve the ability of exploring potential differences in EEG spectral power among three groups, our final sample included 74 CIs, 55 OSA and 77 COMISA patients from our OSA-insomnia-COMISA cohort.

#### Polysomnography and multiple sleep latency tests

All subjects underwent one overnight PSG in the sleep laboratory. Subjects were continuously monitored with six EEG channels, bilateral electrooculography (EOG), submental and anterior tibialis electromyography (EMG) and respiratory signals. The sleep parameters and respiratory records were scored according to American Academy of Sleep Medicine (AASM) Manual for scoring of Sleep and Associated Events (version 2.4) by a senior technician who was blind to subject group [38]. The morning after PSG, all subjects reported subjective total sleep time (TST) for the PSG night and the average TST of the past month.

Daytime EEG data were obtained from five MSLTs which were performed on the day immediately after the overnight PSG recording based on AASM practice parameters for clinical use of the MSLT [39]. Each MSLT was comprised of 20-minute nap opportunities with an interval of 2 h (09:00, 11:00, 13:00,15:00 and 17:00). A sleep technician continuously monitored overnight PSG and each MSLT recording to ensure data quality.

#### Spectral analysis

EEG PSA was performed using a paid commercial offline software package (Synwing EEG analysis software) written in Python and developed by Synwing Technologies Co. Ltd. This package has been validated and used in several previously published papers [28, 40–42]. Before preprocessing, all records were scanned and checked manually to ensure data quality. EEG signals were sampled at 500 Hz and were filtered between 0.5 and 40 Hz via an infinite impulse response (IIR) filter. Visual inspection was used to identify artifacts; EEG recordings contaminated by body movements and other various artifacts (including EMG, etc.) were then manually excluded. Accepted artifact-free EEG data were used for PSA, in which 50% overlapping 5-s epochs were weighted with a Hanning window and subjected to a Fast Fourier transform algorithm (FFT) using Welch's method. EEG spectra for each artifact-free 5-s epoch were then aligned with 30-s visually scored sleep stages including non-rapid eye movement sleep (NREM) stage 1 (N1), NREM stage 2 (N2), NREM stage 3 (N3), NREM and rapid eye movement sleep (REM). Considered more sensitive with higher stability than absolute power when performing group comparisons [42, 43], we calculated relative power across the following bands: delta (0.5–4.0 Hz), theta (4.0–8.0 Hz), alpha (8.0–13.0 Hz), sigma (13.0–16.0 Hz), and beta (16.0–30.0 Hz) [28, 42, 44, 45].

We calculated relative power in N1, N2, N3, NREM, REM, overnight total (the sum of NREM and REM), each MSLT session and daytime total (sum of five MSLT sessions) on central electrode placements (C3 or C4 channel, with C4 as an alternative channel). Because previous studies suggest that logarithmic transformation of EEG spectral power values tend to have a normal distribution [46–48], relative power values shown in the results and used for statistical analyses were log transformed.

#### Questionnaires and neurocognitive assessments

On the PSG recording night, several questionnaires were used to evaluate sleep, depression and anxiety related symptoms including the insomnia severity index (ISI), Pittsburgh sleep quality index (PSQI), morningness-eveningness questionnaire (MEQ-19), pre-sleep arousal scale (PSAS), dysfunctional belief and attitudes about sleep (DBAS-16), patients health questionnaire-9 (PHQ-9), and general anxiety disorder-7 questionnaire (GAD-7). ISI was used to evaluate insomnia severity from the severity of initial, middle and late insomnia, sleep satisfaction, interference of insomnia with daytime functioning, noticeability of sleep problems by others, and distress about sleep difficulties, in which total scores of 0–7 indicate absence of insomnia, 8–14 sub-threshold insomnia, 15–20 moderate insomnia, and 22–28 severe insomnia [49]. PSQI, a widely used self-report questionnaire, was used to assess sleep quality and screen for insomnia and other sleep disorders with total scores lower than 5 indicating good sleep quality and total scores higher than 5 indicating poor sleep quality and existing sleep disturbance [50]. The MEQ-19 was used to evaluate circadian rhythm preferences of subjects, in which total scores of 70–86 indicate definite morning type, 65–69 moderate

morning type, 53–64 intermediate type, 47–52 moderate evening type, 16–46 definite evening type [51]. The PSAS was designed to measure cognitive and somatic arousal levels before sleep with higher scores correlated with higher arousal level [52]. The DBAS-16 measures maladaptive thoughts and beliefs that contribute to insomnia and sleep disturbance, in which higher scores indicated more dysfunctional beliefs [53]. The PHQ-9 and GAD-7 are self-report questionnaires designed to screen for and measure the severity of depression and generalized anxiety disorder, respectively. Higher total scores on these questionnaires suggest greater severity [54, 55].

Neurocognitive assessments were conducted during the first MSLT interval to obtain measures of subjective and objective neurocognitive function. Neurocognitive assessments tools included the Wisconsin card sorting test (WCST), Dysexecutive Questionnaire (DEX), perceived deficits questionnaire-depression (PDQ-D), and meta-cognitions questionnaire-30 (MEQ-30). The WCST is a critical tool for evaluating executive functions, particularly cognitive flexibility, abstract reasoning, and the ability to shift mental sets in response to changing environmental contingencies. Reaction time and accuracy were the two primary scoring metrics we considered in our study. Specific information about the WCST is provided in Table S2 and Figure S2. The DEX questionnaire was used to assess behavioral and cognitive manifestations of executive dysfunction in daily life, and higher scores suggest impaired functioning [56]. The PDQ-D is a self-report measure designed to assess subjective cognitive complaints in individuals with depression, and has been used to evaluate cognitive impairment distress in three domains including attention/concentration, retrospective memory and prospective memory, with higher scores indicating more severe subjective cognitive impairment [57]. The MEQ-30 is a self-report tool for assessing metacognitive beliefs, thoughts about how individuals perceive and respond to their own cognitive processes (e.g. worrying, attention, memory etc.). It has been used to evaluate maladaptive metacognitive patterns linked to anxiety, depression and other psychological disorders. In our analysis, we also calculated the scores of five subscales, including cognitive confidence (CC), positive beliefs about worry (POS), cognitive self-consciousness (CSC), negative beliefs about uncontrollability and danger of worry (NEG) and need to control thoughts (NC) [58].

### Statistical analysis

Analysis of Variance (ANOVA) with post hoc least significant differences (LSD) tests were used to evaluate differences in demographic and clinical characteristics, EEG power during nighttime sleep stages among the CI, OSA and COMISA groups. Analysis of Covariance (ANCOVA) with post hoc LSD tests were applied to assess differences in EEG power during each MSLT with sleep duration, number of sleeps and sleep latency of MSLTs as covariates. For total daytime EEG power, univariate multi-way analyses of variance (multi-way ANOVA) was used to evaluate the effects of groups, MSLT sessions and their interactions on EEG power in all frequency bands, in which sleep duration, number of sleeps and sleep latency of MSLTs were included as covariates in the model. Post hoc LSD tests were used to examine how EEG power changed between groups. ANCOVA with post hoc LSD tests were applied to assess differences in neurocognitive function with known confounders (age, gender and education level) used as covariates. To reveal the clinical factors related to alterations of EEG power and neurocognitive function and further underscore the contribution of insomnia and OSA to COMISA in neurophysiological and neurocognitive domain, Pearson correlation coefficients among EEG power values, cognitive function and insomnia and OSA clinical characteristics were calculated. Statistical analyses were performed using SPSS version 26.0. All statistical tests were 2-sided, and $P$ value and adjusted $P$ value for post hoc comparisons of less than 0.05 were considered statistically significant.

## Results

### Demographics, PSG and MSLT measurements of the participants

A total of 206 participants of were included for analysis: 74 CIs (aged 23 to 59 years old), 55 OSA (aged 20 to 59 years old) and 77 COMISA (aged 23 to 60 years old) patients. Compared to OSA patients, those in the COMISA group were older and had lower BMI. The COMISA group had more male patients and higher BMI when compared with CIs. Education level was comparable across the three group. Patients with COMISA presented higher insomnia severity compared to OSA patients, but lower severity relative to CIs. Compared to OSA patients, COMISA patients and CIs reported shorter subjective TST on the PSG night and over the past month. PSG measured percentage of REM (REM%) and N2 (N2%) were lower and percentage of N1 (N1%) was higher in the COMISA and OSA groups, compared with CIs. Objective TST was shorter and sleep efficiency (SE) was lower in the COMISA and CIs groups compared to OSA. Arousal index (AI), AHI, oxygen desaturation index (ODI), recording time with $SaO_2 < 90\%$ (T90%) in COMISA patients were worse than in CIs, but better than in OSA patients. COMISA and OSA patients exhibited higher ESS but shorter mean sleep latency (MSL) than CIs; however, COMISA patients had prolonged MSL relative to OSA patients. For questionnaires, COMISA and CIs patients reported higher scores in PSQI, PHQ-9

and GAD-7, compared with OSA patients. Demographics and clinical characteristics of all participants are provided in Table 1.

### Comparison of EEG spectral power among CIs, OSA and COMISA groups

For nighttime power among the three groups, compared to OSA patients, delta power was lower in COMISA patients and CIs during N1, NREM sleep stages and overnight recordings, but higher in COMISA and OSA patients than in CIs during REM sleep. Compared to CIs, COMISA patients had lower theta power in REM. COMISA patients and CIs exhibited higher alpha power in N1 and overnight recordings relative to OSA. COMISA and OSA patients showed decreased sigma power in N2 and NREM sleep stages, and had decreased beta power in N1 and REM compared to CIs. However, COMISA patients had higher beta power in NREM and overnight recordings compared with OSA. The results of post hoc LSD corrected comparisons are shown in Fig. 1.

In daytime MSLTs, COMISA patients showed significantly increased delta power in MSLT 1 and daytime recordings compared to CIs. COMISA patients also presented decreased alpha power in daytime recordings compared with OSA patients; and they exhibited decreased sigma power in MSLT 1, MSLT 3 and daytime recordings compared to CIs. Among the three groups, beta power in MSLT 1 and MSLT 2 was lower in COMISA and OSA patients while beta power in daytime recordings was higher in COMISA patients and CIs. Furthermore, COMISA patients presented lower beta power than CIs in daytime recordings. Comparisons of daytime MSLT EEG power for CIs, OSA and COMISA groups are shown in Fig. 2.

### Comparison of neurocognitive function among CIs, OSA and COMISA groups

WCST-RT, WCST-accuracy, DEX, retrospective memory and prospective memory subdomains of the PDQ-D and the MEQ-30 and its subdomains including cognitive confidence (CC), positive beliefs about worry (POS), cognitive self-consciousness (CSC) and need to control thoughts (NC) in COMISA patients were comparable to CIs and OSA patients. Compared to OSA patients, COMISA patients presented higher PDQ-D and attention/concentration of PDQ-D scores. COMISA patients and CIs exhibited similar objective and subjective neurocognitive function in the current assessments (See Table 2).

### Correlations among EEG power, neurocognitive function and disease characteristics

In CIs, overnight spectral power was associated with PSG measured sleep structure parameters and daytime EEG power was related to objective daytime sleepiness. Overnight delta power was negatively associated with sleep onset latency (SOL) and AI, and was positively associated with percentage of N3 (N3%) and ESS. Overnight theta, alpha and sigma power were positively associated with disrupted sleep indicators, such as SOL, wake after sleep onset (WASO) and AI. MSL was negatively associated with daytime delta power but positively related to daytime alpha. Subjective neurocognitive assessments scores were positively associated with insomnia and OSA severity indicators such as ISI and T90%. There were no significant correlations between objective neurocognitive evaluations and most indicators of insomnia and OSA severity.

In OSA patients, overnight and daytime spectral power was associated with OSA severity relevant parameters. AHI, AI, ODI and T90% were positively associated with overnight and daytime delta power, but negatively associated with overnight alpha, daytime theta and sigma power. Subjective neurocognitive assessments scores including PDQ-D, attention/concentration, retrospective memory and prospective memory, were positively related to ESS. WCST accuracy was negatively associated with OSA severity relevant indicators, such as AHI, AI and ODI.

In COMISA patients, EEG power was significantly associated with both PSG measured sleep structure and OSA severity parameters. Overnight delta power was positively associated with TST, SE, T90% and ESS, but negatively associated with WASO and MSL. Overnight theta, alpha and beta power were positively associated WASO and MSL, and negatively associated with TST, SE, T90% and ESS. Overnight alpha power was negatively related to AI and ODI. Daytime delta power was positively associated with SE, but negatively related to WASO. Subjective and objective neurocognitive assessment results were also significantly associated with insomnia and OSA severity. Subjective neurocognitive assessments scores were positively related to ISI, ESS, AHI and ODI. In contrast to OSA patients, WCST-accuracy was positively related to AHI, AI, T90% and ESS in COMISA patients. Correlations among EEG power, neurocognitive function and disease characteristics were depicted in Fig. 3.

## Discussion

We compared EEG power in overnight sleep and subsequent daytime MSLTs and neurocognitive function in CIs, and OSA and COMISA patients to determine neurophysiological and neurocognitive characteristics in COMISA patients relative to the individual disorders. Our findings indicate that COMISA patients exhibit decreased EEG power in low frequency (delta) and increased EEG power in high frequency (alpha and

**Table 1** Demographics and clinical characteristics in CIs, OSA and COMISA groups

| Variables | CIs (*N* = 74) | OSA (*N* = 55) | COMISA (*N* = 77) | F | *P* |
|---|---|---|---|---|---|
| Demographic characteristics | | | | | |
| Age (y) | 42.15 (9.925) | 38.91 (10.536) | 44.68 (9.355) | 5.462 | **0.005**$^{\&}$ |
| Sex (m/f) | 27/47 | 45/10 | 56/21 | 33.420 | **< 0.001**$^{*\#}$ |
| Education level | | | | | 0.272 |
| Middle school or lower n (%) | 16 (21.6) | 5 (9.1) | 12 (15.6) | | |
| High school n (%) | 16 (21.6) | 12 (21.8) | 22 (28.6) | | |
| College or higher n (%) | 42 (56.8) | 38 (69.1) | 43 (55.8) | | |
| BMI | 22.61 (3.846) | 27.66 (4.332) | 26.23 (4.221) | 25.993 | **< 0.001**$^{*\#\&}$ |
| Insomnia symptoms and severity | | | | | |
| ISI total score | 17.54 (4.761) | 6.69 (3.862) | 15.74 (5.219) | 125.634 | **< 0.001**$^{*\#\&}$ |
| ISI-difficulty falling sleep | 2.19 (1.110) | 0.40 (0.648) | 1.76 (1.082) | 68.726 | **< 0.001**$^{*\#\&}$ |
| ISI-difficulty maintaining sleep | 2.37 (1.078) | 0.51 (0.655) | 1.83 (1.063) | 83.120 | **< 0.001**$^{*\#\&}$ |
| ISI-early morning awakening | 2.06 (1.105) | 0.79 (0.690) | 1.95 (1.057) | 42.199 | **< 0.001**$^{*\&}$ |
| Subjectively reported TST | | | | | |
| TST in PSG night | 307.26 (139.097) | 414.90 (93.633) | 320.35 (134.001) | 12.332 | **< 0.001**$^{*\&}$ |
| TST in past month | 342.11 (109.921) | 428.91 (57.467) | 357.89 (91.336) | 15.479 | **< 0.001**$^{*\&}$ |
| Objective sleep parameters | | | | | |
| SOL (min) | 22.36 (35.378) | 11.14 (14.232) | 15.91 (29.025) | 2.506 | 0.084 |
| TST (min) | 381.92 (89.188) | 433.11 (70.731) | 394.19 (81.984) | 6.491 | **0.002**$^{*\&}$ |
| SE (%) | 78.89 (15.411) | 86.15 (14.455) | 79.56 (15.947) | 4.122 | **0.018**$^{*\&}$ |
| WASO (min) | 75.37 (58.019) | 61.79 (82.263) | 86.02 (71.381) | 1.917 | 0.150 |
| REM (%) | 19.62 (7.953) | 17.03 (6.480) | 16.84 (5.721) | 3.775 | **0.025**$^{*\#}$ |
| N1 (%) | 21.05 (11.753) | 39.21 (19.956) | 36.85 (17.229) | 25.382 | **< 0.001**$^{*\#}$ |
| N2 (%) | 58.23 (11.511) | 42.73 (16.661) | 45.73 (15.975) | 21.315 | **< 0.001**$^{*\#}$ |
| N3 (%) | 1.11 (3.013) | 1.02 (2.556) | 0.59 (1.790) | 0.934 | 0.395 |
| AI (event. hour$^{-1}$) | 14.77 (7.289) | 39.56 (23.137) | 33.09 (18.691) | 38.112 | **< 0.001**$^{*\#\&}$ |
| OSA severity | | | | | |
| AHI (event. hour$^{-1}$) | 6.54 (4.180) | 53.12 (27.143) | 44.12 (21.814) | 109.880 | **< 0.001**$^{*\#\&}$ |
| ODI | 5.084 (4.734) | 51.73 (29.339) | 40.42 (24.738) | 85.978 | **< 0.001**$^{*\#\&}$ |
| T90% | 9.78 (31.304) | 84.64 (78.573) | 53.13 (80.394) | 20.740 | **< 0.001**$^{*\#\&}$ |
| Daytime sleepiness | | | | | |
| ESS | 7.23 (4.714) | 12.09 (5.340) | 10.39 (6.104) | 11.698 | **< 0.001**$^{*\#}$ |
| MSL (min) | 12.93 (4.259) | 9.56 (4.491) | 11.62 (4.472) | 7.401 | **0.001**$^{*\#\&}$ |
| Questionnaires | | | | | |
| PSQI | 11.67 (3.694) | 5.81 (2.525) | 10.80 (3.795) | 43.521 | **< 0.001**$^{*\&}$ |
| MEQ-19 | 51.82 (10.858) | 47.42 (10.031) | 51.32 (9.572) | 2.245 | 0.109 |
| PSAS | 34.99 (11.342) | 29.30 (8.237) | 33.03 (10.089) | 3.614 | **0.029**$^{*}$ |
| DBAS-16 | 38.64 (9.223) | 45.29 (10.669) | 39.58 (8.714) | 7.907 | **0.001**$^{*}$ |
| PHQ-9 | 7.76 (4.881) | 4.88 (4.325) | 7.97 (4.128) | 8.197 | **< 0.001**$^{*\&}$ |
| GAD-7 | 5.93 (4.614) | 3.73 (3.547) | 5.28 (3.999) | 4.081 | **0.018**$^{*\&}$ |

Table 1-Data expressed as mean (standard deviation) or numbers (%). BMI, mean body index; MSL, mean sleep latency of five multiple sleep latency tests; TST, total sleep time; SE, sleep efficiency; SOL, sleep onset latency; WASO, wake after sleep onset; NREM, time of whole non-rapid eye movement sleep; N1, duration of non-rapid eye movement sleep stage 1; N2, duration of non-rapid eye movement sleep stage 2; N3, duration of non-rapid eye movement sleep stage 3; REM, rapid eye movement sleep time; AI, arousal index; AHI, apnea hypopnea index; ODI, oxygen desaturation index; T90%, recording time with $SaO_2 < 90\%$; ESS, Epworth sleepiness scale; ISI, insomnia severity index; PSQI, Pittsburgh sleep quality index; MEQ-19, morningness-eveningness questionnaire; PSAS, pre-sleep arousal scale; DBAS-16, dysfunctional belief and attitudes about sleep; PHQ-9, patients health questionnaire-9; GAD-7, general anxiety disorder-7. CIs, chronic insomniacs; OSA, obstructive sleep apnea; COMISA, comorbid insomnia and obstructive sleep apnea. Bold font indicated *p* value less than or equal to 0.05; *, statistically significant in post-hoc analysis with least significant difference correction between CIs and OSA; #, statistically significant in post-hoc analysis with least significant difference correction between CIs and COMISA; &, statistically significant in post-hoc analysis with least significant difference correction between OSA and COMISA

beta) bands during NREM sleep stages, and increased EEG power in both low and high frequency bands (delta and beta) in REM and daytime MSLTs. This suggests that COMISA patients have a slowing of EEG activities and 24-hour cortical hyperarousal. In terms of neurocognition, COMISA patients showed more impaired subjectively measured attention/concentration and negative beliefs about uncontrollability and danger of worry but have objective executive function comparable to CIs and OSA alone. Our results describe the

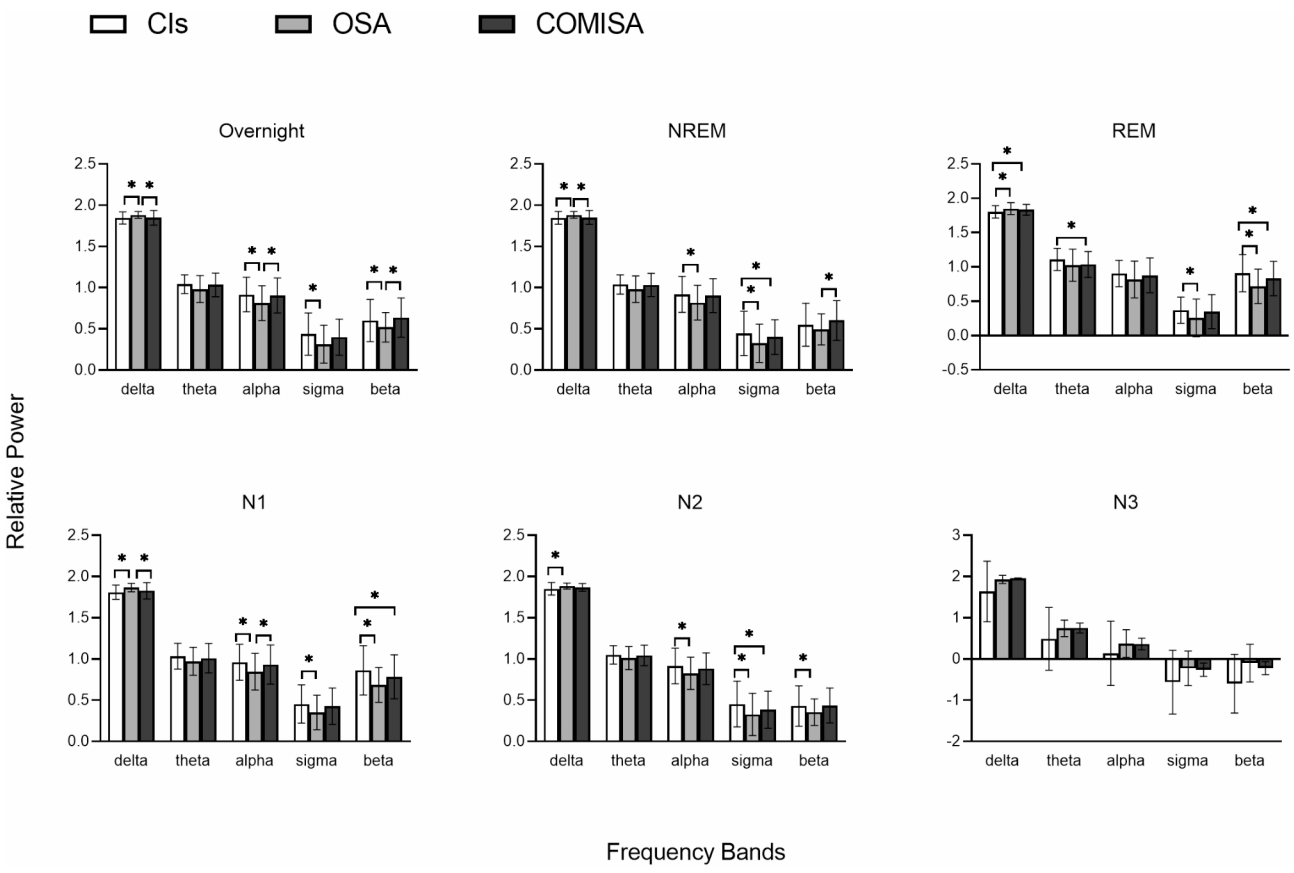


**Fig. 1** Comparison of EEG power for CIs, OSA and COMISA patients during nighttime sleep stages. The power of all frequency bands shown in Fig. 1 was log transformed. NREM: non-rapid eye movement sleep; REM: rapid eye movement sleep; Overnight, including NREM and REM sleep stages; CIs: chronic insomniacs; OSA: obstructive sleep apnea; COMISA: comorbid insomnia and obstructive sleep apnea. Delta: 1–4 Hz; Theta: 4–8 Hz; Alpha: 8–12 Hz; Sigma: 12–15 Hz; Beta: 15–30 Hz. *, adjusted *P* value less than or equal to 0.05

neurophysiological and neurocognitive characteristics of COMISA patients and add new evidence regarding the pathophysiology of COMISA.

The spectral analysis performed on EEG data in overnight each sleep stages found delta power decreased in N1, NREM and overnight recordings, but increased delta power in REM sleep. Delta power has been demonstrated as a measure of sleep propensity, which is negatively associated with arousal threshold and physiological arousal [31, 45, 59, 60]. In our correlation analyses, overnight delta power was negatively associated with sleep tendency and depth (SOL and N3%) but was positively related to measures of sleep apnea severity (AHI, AI, ODI, T90%). Decreased delta power in NREM sleep stages suggests that COMISA patients present less sleep intensity and higher physiological arousal level, which may be related to sleep disturbances associated with insomnia symptoms; for instance, prolonged sleep latency, frequent awakenings and shallow sleep depth, etc. In REM sleep, muscle tone reaches its lowest level which contributes to the most severe apnea occurring in REM sleep [61]. Therefore, we propose that increased delta power in COMISA patients during REM is related to frequent apnea/hypopnea events and severe hypoxia they experience. Considering that NREM sleep accounts for 75-80% of total sleep stages and NREM EEG power of COMISA patients is strongly influenced by chronic insomnia [62]; we suggest that decreased delta power in COMISA patients during overnight PSG could attribute to the synthesis of CIs and OSA EEG power characteristics and primarily manifest as the features of chronic insomnia. In daytime MSLTs, COMISA patients exhibited increased delta power, which was also positively associated with nighttime sleep apnea and hypoxia of OSA (AHI, AI, ODI and T90%) and negatively related to SE. The increased delta power in the following daytime MSLTs is the combined results of the sleep breathing, sleep quality and sleep quantity disturbances in COMISA patients.

With respect to EEG power in high frequency bands, COMISA patients exhibited increased beta power in nighttime PSG and daytime MSLTs. Given that beta power has been shown to be associated with sensorimotor and cognitive process [32, 63], increased nighttime

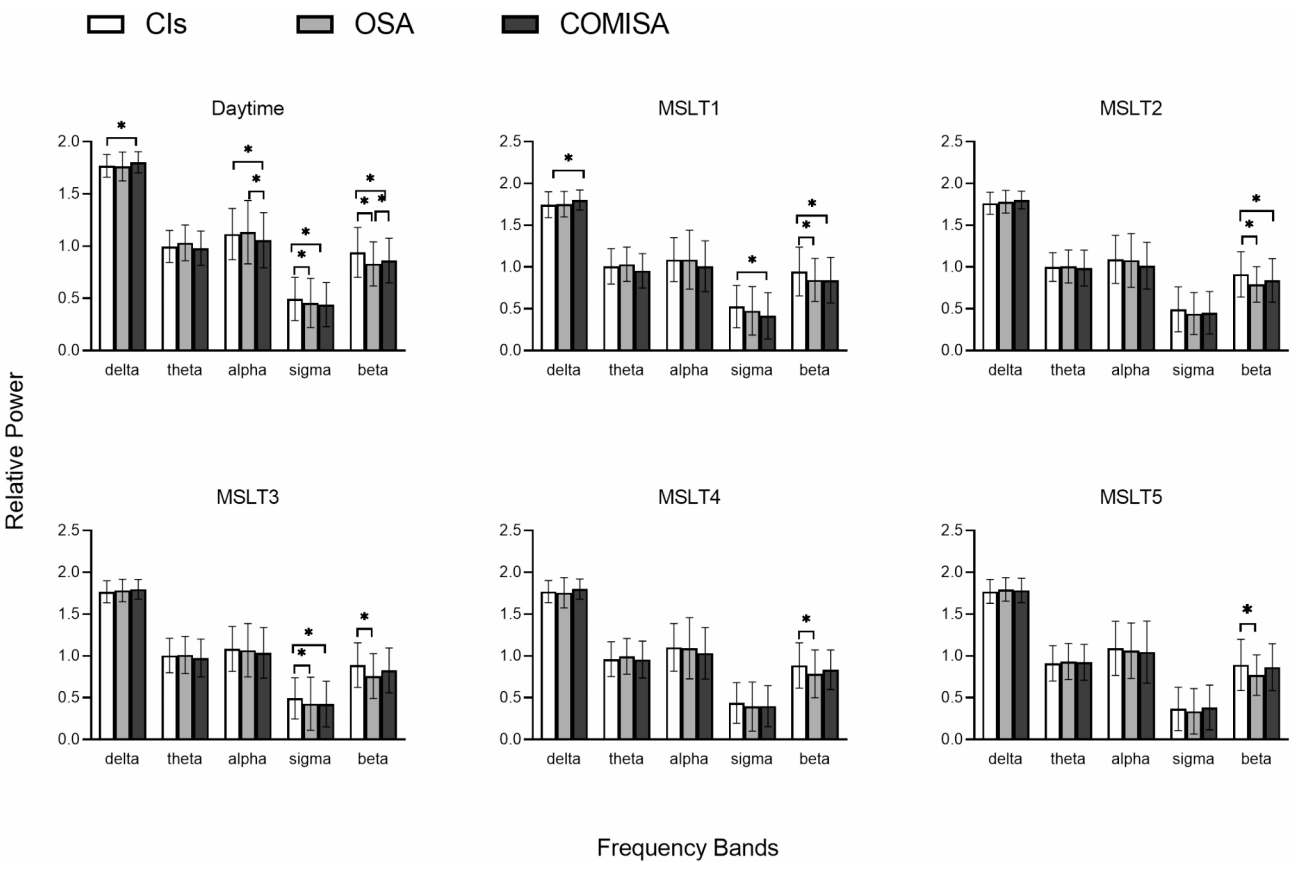


**Fig. 2** Comparision of EEG power for CIs, OSA and COMISA patients during daytime MSLT sessions. The power of all frequency bands shown in Fig. 2 was log transformed. MSLT: multiple sleep latency test; CIs: chronic insomniacs; OSA: obstructive sleep apnea; COMISA: comorbid insomnia and obstructive sleep apnea. Delta: 1–4 Hz; Theta: 4–8 Hz; Alpha: 8–12 Hz: Sigma, 12–15 Hz; Beta: 15–30 Hz. *, adjusted *P* value less than or equal to 0.05

**Table 2** Neurocognitive function assessments in CIs, OSA and COMISA groups

| | CIs | OSA | COMISA | F | *P* |
|---|---|---|---|---|---|
| WCST-RT | 3616.74 (1930.098) | 2838.62 (1274.951) | 3599.68 (1548.325) | 2.471 | 0.088* |
| WCST-accuracy | 65.99 (14.799) | 72.51 (13.238) | 64.73 (16.530) | 0.864 | 0.423 |
| DEX | 21.05 (14.662) | 19.23 (10.088) | 22.36 (11.178) | 1.526 | 0.220 |
| PDQ-D | 22.22 (17.181) | 18.91 (13.143) | 25.93 (16.238) | 2.915 | 0.057& |
| Attention/ concentration | 8.13 (6.689) | 6.55 (5.101) | 9.60 (6.233) | 3.725 | **0.026**& |
| Retrospective memory | 10.67 (7.982) | 9.61 (6.358) | 12.56 (7.608) | 2.458 | 0.089 |
| Prospective memory | 3.42 (3.337) | 2.75 (2.669) | 4.01 (3.360) | 1.779 | 0.172 |
| MEQ-30 | 72.39 (16.594) | 67.36 (15.707) | 70.82 (16.612) | 1.988 | 0.140 |
| CC | 13.39 (4.116) | 13.61 (4.363) | 14.33 (3.436) | 0.775 | 0.462 |
| POS | 13.42 (4.143) | 12.68 (4.079) | 12.95 (3.847) | 1.087 | 0.339 |
| CSC | 16.52 (3.871) | 15.30 (3.373) | 15.77 (3.557) | 1.597 | 0.206 |
| NEG | 14.78 (4.913) | 12.23 (4.028) | 14.10 (3.966) | 3.867 | **0.023***& |
| NC | 14.28 (3.601) | 13.48 (3.605) | 13.70 (3.530) | 1.655 | 0.194 |

WCST, Wisconsin card sorting test; RT, reaction time; DEX, dysexecutive questionnaire; PDQ-D, perceived deficits questionnaire-depression; MEQ-30, meta-cognitions questionnaire 30; CC, cognitive confidence; POS, positive beliefs about worry; CSC, cognitive self-consciousness; NEG, negative beliefs about uncontrollability and danger of worry; NC, need to control thoughts. *, statistically significant in post-hoc analysis with least significant difference correction between CIs and OSA; &, statistically significant in post-hoc analysis with least significant difference correction between OSA and COMISA

PSG and daytime MSLT beta in COMISA patients suggests that 24-h cortical hyperarousal could play an important role in the occurrence and progression of the disorder. This hypothesis was supported in the current study, in which overnight beta power was positively related to short TST, low SE, long WASO and high AI. In our current and previous studies, we also found that CIs present 24-h cortical hyperarousal via elevated beta

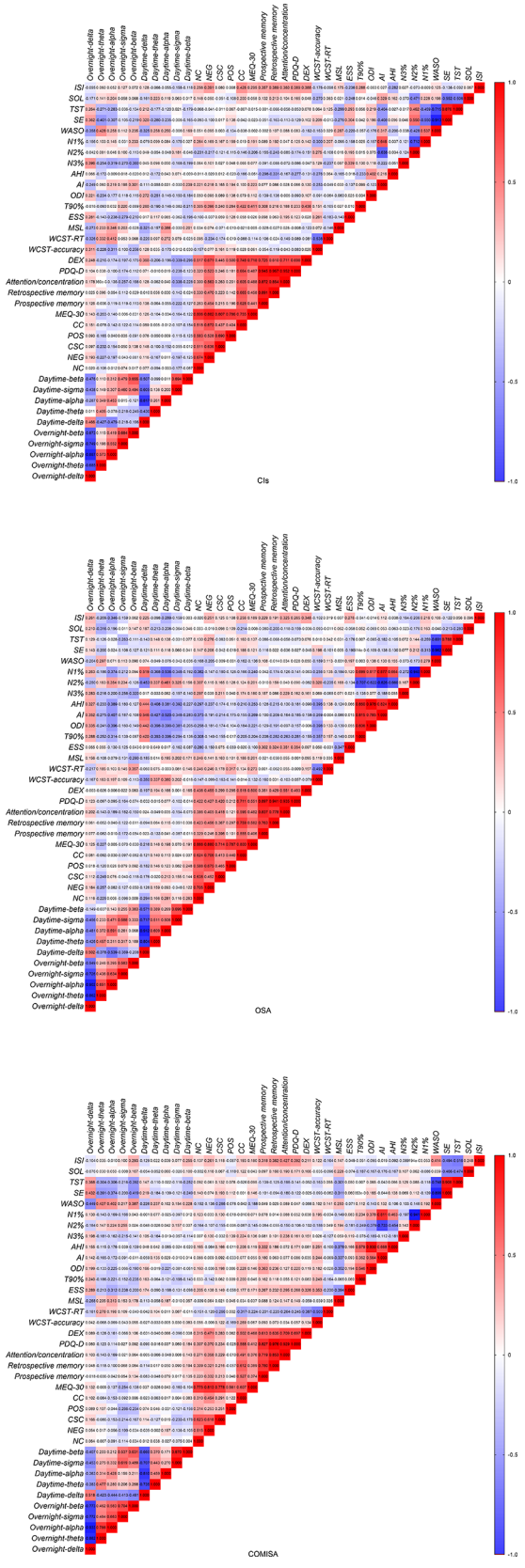


**Fig. 3** Correlations among EEG power, insomnia and OSA severity, PSG parameters and cognitive function

power in nighttime PSG and daytime MSLTs [28]. Therefore, the 24-h cortical hyperarousal in COMISA patients appears to be related to insomnia symptoms including difficulty in falling into and maintaining sleep, shallow sleep or sleep state misperception, which may be caused by failure to fully terminate sensorimotor and cognitive process during sleep initiation and sleep progression [64, 65].

Power in another high frequency band, alpha, increased in nighttime sleep stages but decreased in daytime MSLTs. Alpha synchronization reflects the top-down control of cortical activation and reflects inhibition, which assists neurons in distributed networks to effectively activate common targets cells and helps to form a highly selective activation pattern [30]. Elevated alpha power in COMISA patients during N1 and the overnight PSG can be viewed as activation during the process of falling asleep and sleep maintenance, which reflects impaired regulation of initiating and maintaining sleep in COMISA patients like that found in CIs [66, 67]. This speculation is supported by the finding that higher overnight alpha power was positively correlated with SOL, WASO, and AI, but was negatively correlated with TST and SE. Decreased alpha power in daytime MSLTs was related to insomnia and hypoxia severity (ISI, T90% and ODI) which may reflect decreased restorative functions of sleep and excessive daytime sleepiness, and could be reflected in the positive relationship between daytime alpha and MSL. Taken as whole, we infer that COMISA patients showed combined neurophysiological characteristics of chronic insomnia and OSA based on EEG spectral analysis.

COMISA patients showed worse cognitive symptoms than individuals with OSA alone in areas of attention/concentration and NEG using subjective questionnaire tools. Attention/concentration deficits were positively associated with ISI and ESS, which indicated that subjective perceived attention impairments in COMISA may be the result of the combined effects of nighttime sleep disturbance (insomnia) and daytime function impairments (excessive daytime sleepiness). However, COMISA patients reported worse performance in NEG could be attributed to severe insomnia, which is supported by the positive relationship between NEG and ISI and significant group differences between CIs and OSA patients in NEG. However, we could not find differences in executive function using the DEX questionnaire and WCST test. Only one previous study examined executive function in COMISA patients using the Stroop test which found COMISA had worse executive functioning [37]. The control subjects (insomnia, OSA and healthy controls) were from other published studies in which different evaluator and evaluation methods resulted in instability of obtained results. Furthermore, two other earlier studies

only assessed psychomotor vigilance task (PVT) performance in elderly COMISA patients and showed diverse results, in which one study found prolonged PVT reaction time but another proved insignificant vigilance alterations [35, 36]. To our knowledge, we are the first to explore neurocognitive characteristics of COMISA in young-to-middle age adults, and including several cognition domains. We found that COMISA patients had worse subjectively measured attention and NEG relative to OSA, which were highly affected by chronic insomnia. Therefore, the neurocognitive effects of COMISA should be elucidated in future studies containing COMISA patients with a wide age range and including multiple neurocognitive domains.

We conducted a correlation analysis in CIs, OSA and COMISA patients to explore possible differences related to EEG spectral power across diseases. In CIs and OSA, EEG spectral power alterations were differentially correlated with insomnia and OSA severity, with similar changes in the COMISA group (e.g., increased delta power was positively correlated with OSA severity but negatively associated with insomnia severity). These findings further support that the COMISA power spectral profile is a combination of insomnia and OSA features, and that COMISA power spectral profiles may depend on different specific contributions of insomnia and OSA. In addition, correlation analyses were also used to explore possibly related subjective and objective neurocognitive impairments. The results showed that the subjective impairments of COMISA were primarily associated with severe insomnia and daytime sleepiness. However, findings for objective executive function differed. In OSA, WCST accuracy was negatively correlated with OSA severity but was positively related to OSA severity in COMISA. We speculate that the mild-to-moderate apnea and hypoxia (AHI in OSA was higher than COMISA) may not have been sufficient to reduce performance in COMISA patients. This speculation and the possible reasons about the inverse correlations between OSA severity and objective executive function in OSA and COMISA should be further explored in future studies including COMISA subjects with different OSA and insomnia severity levels.

Comparison of PSG measurements and ISI score found that COMISA patients showed greater insomnia severity than OSA patients, but less severity than CIs. Similarly, COMISA patients exhibited more prominent apnea and hypoxia than CIs but showed less severe symptoms than OSA patients. Consistent with a recent study, our results indicate that insomnia and OSA severity of COMISA patients presented an intermediate state of OSA and CI [16]. The scores of PHQ-9 and GAD-7 were higher in COMISA patients and CIs, compared with OSA, which could be confirmed by the bidirectional relationships between insomnia and anxiety and depression in that insomnia contributes to anxiety and depression symptoms, and anxiety and depression symptoms disturb sleep [68–71]. Therefore, we recommend effective insomnia treatments strategies should be provided to COMISA patients for preventing further anxiety and depression disorders.

The current study has some limitations. First, our study lacks sufficient females in the OSA and COMISA groups to assess sex differences. The subjects in the current analysis were continually included as they were recruited into our OSA-insomnia-COMISA cohort, instead of matching basic information among groups (such as by gender, age, etc.), resulting in a limited number of female participants in OSA and COMISA groups. The stability of our findings should be validated in future studies that include sufficient female OSA and COMISA patients; and the features of EEG spectral power in female COMISA patients should be explored in the future studies. Second, gender imbalance among the three groups limits the possibility of generalizing the findings; our suggestive findings will need to be confirmed in a sex-matched sample. Third, given that existing evidence indicates that quantitative EEG outcomes during sleep shows high short-term stability [72], no adaption night was employed. However, potential first night effects cannot be discounted.

## Conclusions

In conclusion, the current study demonstrated that COMISA patients showed reduced delta and enhanced alpha and beta power during NREM sleep stages, increased delta and beta power in REM sleep and daytime MSLTs, and that the spectral characteristics of COMISA include those of combined OSA and insomnia. Neurocognitive function of COMISA was strongly affected by chronic insomnia and patients exhibited worse subjectively measured attention and negative beliefs about uncontrollability and danger of worry, compared to OSA. Our study describes the EEG spectral power and neurocognitive features of COMISA, adding to our knowledge of its neurophysiological and neurocognitive characteristics.

### Abbreviations

| | |
|---|---|
| AHI, | Apnea-hypopneas index |
| ANOVA, | Analysis of Variance |
| AASM, | American Academy of Sleep Medicine |
| BMI, | Body mass index |
| COMISA, | Co-morbid insomnia and obstructive sleep apnea |
| CIs, | Chronic insomniacs |
| DSM-V, | Statistical Manual of Mental Disorder-V |
| EEG, | Electroencephalogram |
| EOG, | Electrooculography |
| EMG, | Electromyography |
| FFT, | Fast Fourier transform |
| PSG, | Polysomnography |
| MSLTs, | Multiple sleep latency tests |
| MANOVA, | Multivariate analyses of variance |

| | |
|---|---|
| NREM, | Non-rapid eye movement |
| N1, | Non-rapid eye movement sleep stage 1 |
| N2, | Non-rapid eye movement sleep stage 2 |
| N3, | Non-rapid eye movement sleep stage 3 |
| OSA, | Obstructive sleep apnea |
| PSA, | Power spectral analysis |
| REM, | Rapid eye movement |
| SWA, | Slow wave activity |
| SOREMP, | Sleep onset rapid eye movement period |
| SOL, | Sleep onset latency |
| SE, | Sleep efficiency |
| TST, | Total sleep time |
| WASO, | Wake after sleep onset |

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12931-025-03193-x.

Supplementary Material 1

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**Author contributions**
XT supervised the study. YS and XT were responsible for conceptualization and methodology. YS, YN, FH, XF and YZ conducted the experiment and analyzed data. YS and XT wrote the original draft of the manuscript. LD, RR and XT edited the manuscript.

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**Data availability**
The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

## Declarations

**Ethics approval and consent to participate**
The study was conducted according to the World Medical Association Declaration of Helsinki in 1975, as revised in 1983, and was approved by the Research Ethics Board of West China Hospital of Sichuan University (NO.1481). All subjects provided their informed written consent.

**Consent for publication**
Written informed consent for publication was obtained from all participants.

**Competing interests**
The authors declare no competing interests.

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