SLEEPJ, 2018, 1–10

doi: 10.1093/sleep/zsy056
Advance Access Publication Date: 24 March 2018
Original Article

ORIGINAL ARTICLE

The neurophysiological basis of the discrepancy between objective and subjective sleep during the sleep onset period: an EEG-fMRI study

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Abstract

Subjective perception of sleep is not necessarily consistent with electroencephalography (EEG) indications of sleep. The mismatch between subjective reports and objective measures is often referred to as "sleep state misperception." Previous studies evince that this mismatch is found in both patients with insomnia and in normal sleepers, but the neurophysiological mechanism remains unclear. The aim of the study is to explore the neurophysiological basis of this mechanism, from the perspective of both EEG power and functional magnetic resonance imaging (fMRI) fluctuations. Thirty-six healthy young adults participated in the study. Simultaneous EEG and fMRI recordings were conducted while the participants were trying to fall asleep in an MRI scanner at approximately 9:00 pm. They were awakened after achieving stable N1 or N2 sleep, or after 90 min without falling into stable sleep. Next they were asked to recall their conscious experiences from the moment immediately prior to awakening. Sixty-one instances of scheduled awakenings were collected: 21 of these after having achieved stable stage N2 sleep; 12, during stage N1 sleep; and, 20 during the waking state. Relative to those awakenings without subjective–objective discrepancy (n = 27), these awakenings with discrepancy (n = 14) were associated with lower θ power, as well as higher α, β, and γ power. Moreover, we found that participants who exhibited the discrepancy, compared with those who did not, evinced a higher amplitude of low-frequency fluctuation levels in the prefrontal cortex. These results lend support to the conjecture that the subjective–objective discrepancy is associated with central nervous system hyperarousal.

Statement of Significance

The discrepancy between subjective sleep perception and objective measures of sleep has been reported commonly in normal sleepers; it is also a clinical feature of some patients with insomnia. The underlying mechanism of this phenomenon, however, has not been well studied. This research is the first simultaneous EEG and fMRI attempt to investigate the neurophysiological mechanisms associated with this discrepancy. Results suggest that subjective–objective difference can be explained, in part, by reference to general hyperarousal of the brain, especially along the fronto-parietal pathway that is related to executive control.

Key words: functional brain imaging; EEG spectral analysis; sleep state misperception; hyperarousal

Submitted: 1 June, 2017; **Revised:** 26 February, 2018

Introduction

Sleep is an altered state during which volition and consciousness are partially or completely absent. This state can be described from the first person perspective of subjective experience, and also from the third person perspective of operational definitions and objective measures. The polysomnographic definition of sleep, characterized by specific electrophysiological measures, is often considered to be the gold standard for research in sleep science. In daily life, however, we characterize sleep in a way that reflects subjective perception. Previous studies have shown that the subjective perception of sleep can be related to the awareness of environmental stimuli as well as to the exercise of self-control over thought processes, both of which decrease as participants fall "more deeply" asleep [1, 2]. Intuitively it might seem that the conscious experience of sleep should correspond to the objective measures of sleep. Data accumulated in recent years, however, suggest that this assumption is erroneous. Discrepancies between subjective sleep perception and objective sleep measurements have been reported in other studies [3, 4]. Indeed, in our previous work, we collected subjective and objective data concerning the sleep experiences of 20 young participants and found that 55 percent of the participants who were awakened during EEG-defined stage-2 sleep reported that they had been sleepless [5].

This difference between subjective and EEG-defined sleep seems to be related to alterations in the central nervous system (CNS). A recent study found that among good sleepers the difference is associated with subjective reports of presleep cognitive arousal [6]. The difference between subjective sleep reports and objective measurements of sleep has not only been reported from healthy participants, it has been found to be even more significant among patients with insomnia, and is often referred to as "sleep state misperception" (SSM). Perlis et al. hypothesized that the discrepancy between objective and subjective sleep in insomnia is associated with elevated CNS activity, "hyperarousal" [7]. Support for this hypothesis derives from the finding that patients with insomnia have more high-frequency EEG activity than do normal controls [8–11]. In addition, it has been shown that increased high frequency EEG activity is associated with an increase in the difference between subjective and objective measures of sleep: for example, Perlis et al. discovered that patients with insomnia exhibit higher β and γ activity during NREM sleep than do normal sleepers, and differences between sleep diary reports of total sleep time (TST) and EEG-defined TST are associated with differences in β activity power [12]. What is more, an event-related potentials (ERPs) study showed that, relative to normal sleepers, patients with insomnia have elevated N1 and reduced P2 during the first 5 min of continuous stage-2 sleep [13]. This finding suggests that, relative to good sleepers, patients with insomnia have enhanced attention and reduced inhibitory processes during sleep. Thus, it appears to be the case that patients with insomnia exhibit hyperarousal that correlates with enhanced attention and reduced inhibition during the initial phase of sleep. This state of hyperarousal, it seems, might modulate the subjective perception of sleep.

Although previous studies support that conjecture that the discrepancy between subjective reports and objective measures is associated with elevated CNS activity, evidence adduced on behalf of this hypothesis has been based upon neural electrophysiological studies that do not indicate which brain regions might be playing a distinctive role. In short, we have learned much about temporal parameters, but have no direct evidence concerning spatial parameters. To compensate for this gap in our understanding of the difference between subjective report and objective measures, use of neuroimaging techniques with greater spatial resolution is required.

Recently, Kay and colleagues reported that patients with insomnia who exhibit greater subjective–objective sleep discrepancy—discrepancy between sleep diary reports and polysomnography (PSG) sleep onset latency—differed with respect to glucose metabolism in the insula and the left anterior cingulate cortex (ACC) during NREM sleep [14]. This finding is consistent with the hyperarousal hypothesis. Although Kay et al. correlated brain activity with the discrepancy between subjective and objective measures across the whole night of sleep, they did not show specifically what the brain is doing when the discrepancy occurs.

Therefore, our investigation of normal sleepers incorporated scheduled awakenings to assess subjective sleep perception during EEG-defined sleep while recording simultaneous EEG and MRI. The focus on normal sleepers was chosen because of the difficulty patients with insomnia encounter when trying to fall asleep after being awakened. But given that SSM is found both in healthy participants and in patient populations, our findings may also help us to shed new light on insomnia.

More specifically, the amplitude of low-frequency (0.01–0.08 Hz) fMRI fluctuations (ALFFs) is used as a measure of spontaneous arousal level. fMRI has been used to investigate spontaneous, intrinsic neuronal processes during the brain's "resting" state by neuroscientists for more than a decade. A previous study reported that during the resting state, low-frequency (0.01–0.08 Hz) fMRI fluctuations within the sensorimotor network spontaneously synchronize [15]. Subsequent studies have also suggested that the ALFFs of fMRI signals are related to spontaneous, intrinsic neuronal activity [16–19].

Zang et al. developed the means for measuring ALFF [20]—the integral of the square root of the power spectrum in a given frequency range—and have suggested that it can be used as an index of the regional intensity of intrinsic, spontaneous fluctuations. This index is now widely used in fMRI resting state studies [20–22]. Because ALFF reflects fluctuating levels of the brain's spontaneous activity, it might be well suited to serve as a hemodynamic proxy for hyperarousal phenomenon. Prior studies have found increases in the fluctuation level of the BOLD signal in several cortical areas during sleep onset period [23, 24]. Sämann et al. found that normal sleepers exhibit higher normalized spectral power of the default mode network (DMN) during the sleep onset period [25]. Consistent with the hyperarousal conjecture, we speculate that the population with subjective–objective mismatched sleep exhibits elevated levels of spontaneous activity, as measured by ALFF, especially in the brain regions included within the DMN.

In short, we hypothesize that objective ALFF variation in specific brain regions is associated with both subjective sleep perception and EEG spectral indices. Furthermore, in order to better understand the underlying mechanisms associated with sleep perception, we compare the activity of sleeping brains that exhibit the subjective–objective mismatch to those that do not. Operationally, the subjective–objective mismatch is here defined as when participants report they were not asleep, but online EEG data indicate that they were in fact asleep.

Methods

Participants

Thirty-six volunteers (15 males and 21 females) participated in this study. Inclusion criteria were as follows: (1) between 20 and 35 years of age; (2) no current or past major medical or psychiatric illnesses, or sleep disorders; (3) no current use of prescribed or recreational drugs that might affect sleep; and (4) not shift-workers or those who do not adhere to a regular sleep–wake schedule. Informed consent was obtained from each participant, and the experiment was carried out in compliance with ethical standards established by the Institutional Review Board (IRB permit number: NTU-REC: 201309EM030).

Procedure

Participants were screened through a clinical interview and a package of questionnaires, which includes Beck Depression Inventory-II (BDI-II) [26], Beck Anxiety Inventory (BAI) [27], and Insomnia Severity Inventory (ISI) [28]. Simultaneous EEG and fMRI recordings were conducted while the participants were trying to fall asleep in an MRI scanner at approximately 9:00 pm. Participants were instructed to close their eyes, relax and try to sleep in the MRI scanner. The MRI scanning room was kept dark. The EEGs were recorded using a 32-channel MR-compatible system (BrainAmp MR plus, Brain Product, Germany). The recording montage included the following: 25 EEG channels positioned according to the international 10/20 systems; two reference channels (A1, A2); two electrooculography (EOG) channels; one electrocardiogram (ECG) channel; and two electromyography (EMG) channels. Built-in impedance for each electrode was 5 kΩ and the electrode-skin impedance was kept below 5 kΩ, using abrasive electrode paste (Abralyt HiCl). Online EEG processing was performed with commercial software (BrainVision RecView, Brain Product, Germany), to remove both the gradient and the ballistocardiogram (BCG) artifacts, for real-time monitoring that enabled identification of sleep stages.

The EEG signal was synchronized with the MR trigger and recorded using BrainVision Recorder (Brain Product, Germany) with a 5 kHz sampling rate and a 0.1 μV voltage resolution. A low-pass and a high-pass filter were set at 250 Hz and 0.0159 Hz, respectively, with an additional 60 Hz notch filter. MRI data were acquired using a 3T Siemens MAGNETOM Skyra system (Erlangen, Germany) using a 20-channel head/neck coil. High-resolution T1-weighted anatomical images (3D-MPRAGE with 256 × 256 × 192 matrix size, 1 mm^3 isotropic cube, flip angle [FA] = 9° repeat time [TR] = 2400 ms, echo time [TE] = 2.27 ms, and inverse time [TI] = 900 ms) were acquired prior to functional scans for geometric localization. Head motion was minimized using customized cushions. Functional scans were subsequently acquired using a single-shot, gradient-recalled echo planar imaging (EPI) sequence (TR/TE/FA = 2400 ms/30 ms/84°, field of view = 220 mm, matrix size = 64 × 64, 32 slices with 3.4 mm thickness) aligned along the AC-PC line, allowing whole-brain coverage.

According to real-time sleep staging, participants were awakened at stable stage N1 or N2 sleep (three consecutive epochs), or after 90 min of remaining in the scanner having failed to achieve a stable sleep pattern. Because it is difficult to fall into stable sleep in the MRI scanner, we allowed 30 min for the participants to try to enter the N2 stage. If they failed to enter the N2 stage within 30 min, we woke them up after three consecutive epochs of N1. As such, the order of N1 and N2 awakening was not counterbalanced. After the first awakening, they were encouraged to fall asleep, for a second time (Figure 1).

Sleep stages were determined according to the American Academy of Sleep Medicine (AASM) guidelines [29]. N1 sleep was defined as the first 30 s epoch in which EEG α activity decreased to less than 50 percent. N2 sleep was defined by the appearance of K-complex or sleep spindle. The participants were then interviewed and asked to report their recall of conscious experiences that immediately preceded awakening. Of particular relevance to this research were questions about perceptual experience, thought processes, and self-control. Questions included the following: sleep perception ("Did you fall asleep?" either yes or no), perceived depth of sleep ("How deep was your sleep?" on a scale of 0–100), experiences of sensation and perception, thought processes, orientations and involvements, emotional experiences, and levels of consciousness [5].

Questionnaires

A package of questionnaires was administered to the participants. The BDI-II [26] is a subjective rating scale for depression, which contains a 21-item with four-point Likert scale. The higher scores represents greater severity of depression with a cutoff score of 14 for significant level of depression. The BAI [27] is a 21-item self-rating scale that is developed to measure the level of anxiety. Participants are asked to rate the level of somatic and psychological symptoms of anxiety during the past week on a 4-point scale. A cut-off score of 21 was used to define a significant level of anxiety. The ISI [28] is a 7-item self-rating scale that is designed to measure the severity of insomnia during the last 2 weeks. The suggested ranges for the interpretation of total score are 0–7 as normal sleeper, 8–14 as subthreshold insomnia, and 15–28 as clinical insomnia.

Data Analysis

Sleep stages

The EEG recording data of 5 min before awakening were processed offline to confirm the sleep stages. The EEG data were up-sampled to 50 kHz to avoid the phase shift between EEG and fMRI signals. MR gradient removal and ballistocardiogram artifacts removal were performed with commercial software (BrainVision Analyzer 2, Brain Product, Germany), before spectral filtering (0.5–30 Hz). The gradient artifact was corrected using volume triggers, and the average artifact subtraction technique [30] implemented in Analyzer was used. We also re-referenced the signal from each electrode to the whole brain average and applied independent component analysis (ICA) to subtract the residual ballistocardiographic artifact in EEGLAB [31]. Sleep stages were determined according to the AASM guidelines [29].

Power spectral analysis

Filtered EEG signals between 0.3 and 60 Hz were used for the power spectral analysis (PSA). PSA included the last 5 min of data just prior to awakening, and by computing fast Fourier

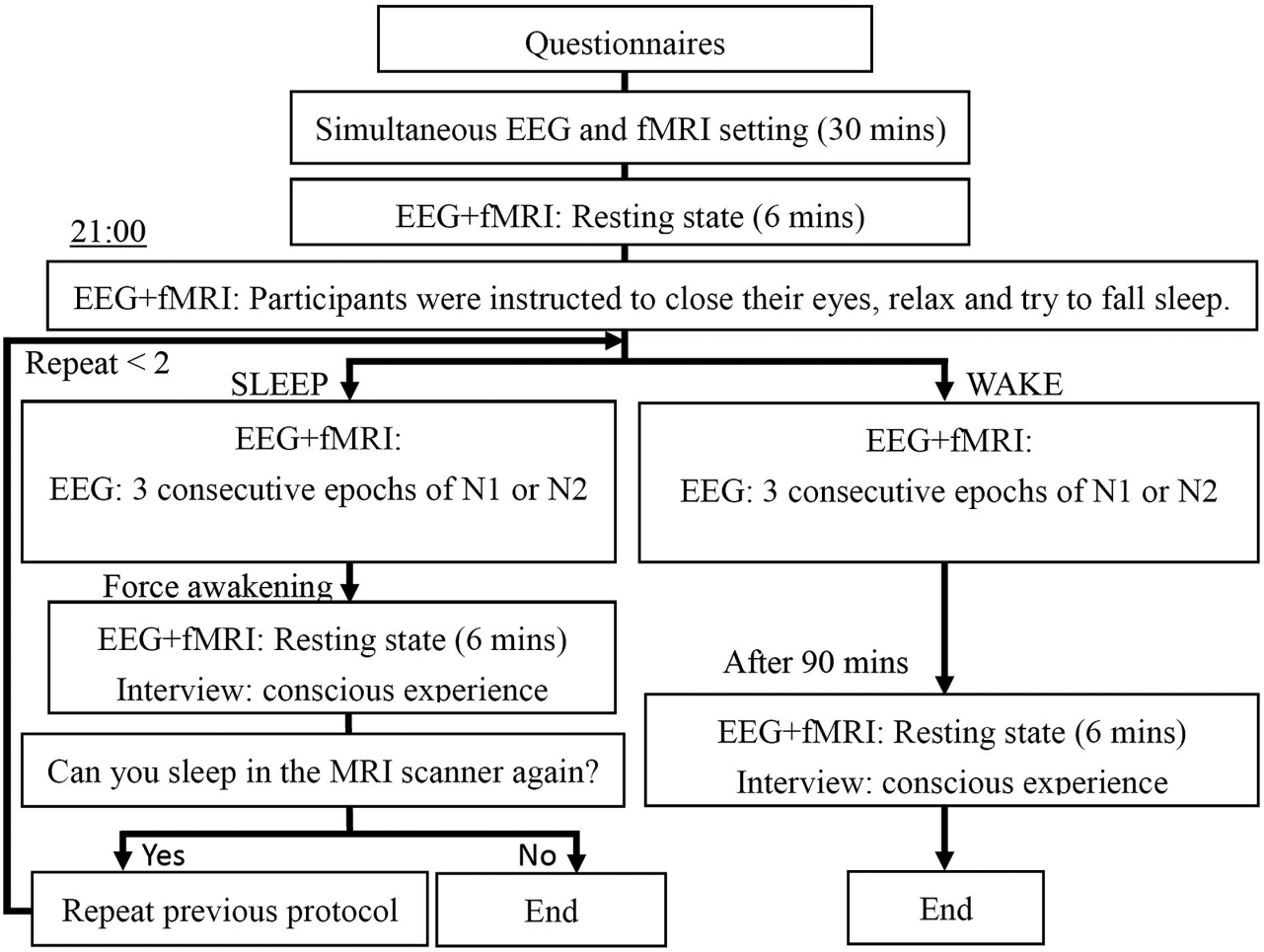

Figure 1. Experimental protocol.

transforms (FFT), was conducted over 25 EEG sites—Fp1, Fp2, F3, F4, C3, C4, P3, P4, O1, O2, F7, F8, T7, T8, P7, P8, Fz, Cz, Pz, POz, Oz, FC1, FC2, CP1, CP2. A1 and A2 were used as references and were not included in the PSA analysis. Frequency bands were defined as δ (0.5–2.5 Hz), θ (2.5–7.5 Hz), α (7.5–12 Hz), σ (12–14 Hz), β (14–35Hz), and γ (35–45 Hz). The independent component analysis was used to subtract the residual ballistocardiographic artifact. Absolute and relative power spectral values were log transformed to normalize the distributions.

Image preprocessing and analysis

For fMRI data, we applied standard preprocessing including motion correction, spatial normalization, smoothing (full width at half maximum = 6 mm), temporal detrending, nuisance covariates regression (head motion, CSF, and white matter signals), and filtering (frequency band ranged from 0.01–0.08 Hz) with MATLAB-based Statistical Parametric Mapping (SPM5; Wellcome Institute of Cognitive Neurology, University College London, London, UK) and REST toolbox [32]. We used linear (first order) detrend instead of the polynomial regression, using the MATLAB command "detrend" for voxel-wise trend removal. The purpose of the CSF and white-matter signal nuisance regressors is to remove sources of spurious or regionally nonspecific variance by regression [33]. The spontaneous low-frequency (0.01–0.08 Hz) fluctuations in fMRI were found to be related in spontaneous brain activities at resting state [15]. Then, the power spectral density of the last 5 min of data before awakening was calculated by FSL [34], with the preprocessed data. The time series were transformed to the frequency domain using FFT to obtain the power spectrum. The power of a given frequency band is proportional to the square of the amplitude of this frequency component in the original time series, and the ALFF is the averaged square root value. The normalized-ALFF (nALFF) index was calculated from the division of ALFF of each voxel by the mean ALFF value within the whole-brain mask. The ALFF index normalized to the entire brain is a standard approach in resting-state fMRI studies [22]. The ALFF value is defined as the averaged square root across 0.01–0.08 Hz of the power spectrum (frequency domain) which was transformed from the time series (time domain) at each voxel. But because the signal intensity of BOLD-fMRI is not quantifiable—the result of complex neurophysiology and hardware calibration—Tsai et al. and others use the ALFF value normalized to the whole brain (relative ALFF) in order to reduce the between-subject variability [35].

Statistical analysis

Independent *t*-tests were conducted to compare absolute and relative power, and log-transformed values, as well as ALFF values between the data from awakenings accompanied

by subjective–objective discrepancy and those from awakenings not accompanied by discrepancy. The group-level nALFF analyses were performed across the whole brain using two-sample *t*-tests by SPM8, and the multiple correction of AlphaSim approach with auto-correlation estimations (suggested by AFNI) was applied for multiple comparisons on the group results, leading to the corrected $p < .05$ (uncorrected $p < .001$, cluster size of 62 consecutive voxel) [36]. The voxel-wise analyses were conducted to compare group differences, with the significant difference area serving as prior knowledge for ROI selection. To avoid the double-dipping problem, we conducted the ROI analysis using the AAL template—Automated anatomical labeling [37]—as based upon the results of voxel-wise analyses. The ROI-level analyses were conducted to compare group difference using two-sample *t*-tests by SPSS. To further analyze the correlation between subjective and objective sleep evaluation, we performed Pearson product-moment correlations of subjective ratings on the depth of sleep across δ, θ, α, σ, β, and γ powers, as well as the nALFF value for the data set wherein subjective and objective measures were consistent.

Results

Demographic data

Thirty-six volunteers (15 males and 21 females) participated in this study. Their mean age was 24.5 years, with a standard deviation of 4.0. The demographic data of participants are presented in Table 1. The mean scores of ISI, BDI, and BAI were all below the cut-off points of clinical significant levels.

Sleep data

Sixty-one instances of awakening were collected for this study. Twenty-nine were awakened after entering stable stage N2 sleep; 12, during stage N1 sleep; and 20, during the waking state. We found a moderate positive correlation between sleep stages and subjective perception of depth of sleep for the awakenings without discrepancy ($\rho = .277$; $p = .044$). Instances of awakening from N1 and N2 were included in the analyses and categorized to different types of instances depending on their answer to a short question—"Were you sleeping before being awakened?" Instances in which participants reported "yes" to the question were classified as "without discrepancy" ($n = 27$); those who reported "no" were classified as "with discrepancy" instance ($n = 14$) (Table 2). Percentage of different sleep stages in the last 5 min before awakening were calculated in this study, and we found no group differences among the three states (awake, N1 sleep, and N2 sleep; Figure 2).

EEG PSA results

δ *(0.5–2.5 Hz)*

There was no significant difference between awakenings with and without discrepancy in δ power.

θ *activity (2.5–7.5Hz)*

Log-transformed of absolute θ activity in awakenings with discrepancy was lower than that without discrepancy at Fz ($t = 2.33$, $p = .025$) (Figure 3).

α *Activity (7.5–12 Hz)*

Absolute EEG PSA. Log-transformed of absolute α activity was higher in awakenings with discrepancies than those without discrepancy at FP1, FC1, and FC2 (FP1: $t = -2.14$, $p = .039$; FC1: $t = -2.46$, $p = .019$; FC2: $t = -2.21$, $p = .033$) (Figure 3).

Relative EEG PSA. Relative α activity was found to be higher in awakenings with discrepancy than those without discrepancies at FP1 and P3 (FP1: $t = -2.17$, $p = .048$; P3: $t = -2.33$, $p = .035$). Compared with those without discrepancies, log-transformed of relative α activity was higher in those with discrepancies at FP1, F8, and P7 (FP1: $t = -2.88$, $p = .006$; F8: $t = -2.03$, $p = .049$; P7: $t = -2.18$, $p = .036$) (Figure 3).

Log-transformed of relative α and β activities was also found to be higher in awakenings with discrepancy than those without discrepancies at FP1 (Figure 3).

σ *(12–14 Hz)*

There was no significant difference between awakenings with and without discrepancy in σ power.

β *activity (14–35 Hz)*

Relative EEG PSA. Relative β activity in awakenings with discrepancy was higher than those without discrepancies at P7 ($t = -2.17$, $p = .036$). Log-transformed of relative β activity in awakenings with discrepancies was higher than those without discrepancy at FP1 and P7 (FP1: $t = -2.06$, $p = .047$; P7: $t = -2.38$, $p = .022$) (Figure 3).

γ *activity (35–45 Hz)*

Absolute EEG PSA. Log-transformed of absolute γ activity was also found to be higher in awakenings with discrepancy than those without discrepancies at O1,O2, P7, and Oz (O1: $t = -2.29$,

Table 1. Means (*SD*) of sociodemographic data of participants

	Mean ± *SD*
Age (yr)	24.5 ± 4.0
Gender (male: female)	15: 21
Education (yr)	16.3 ± 1.7
Questionnaire	
ISI (mean ± *SE*)	4.6 ± 0.5
BDI (mean ± *SE*)	6.0 ± 0.9
BAI (mean ± *SE*)	3.7 ± 0.5

SE = standard error.

Table 2. Frequencies and percentages of subjective sleep perception for different stages of objective sleep

		Subjective sleep perception		
		Yes	No	sum
	Wake	7	13	20
Objective sleep stage	N1 sleep	**7 (58%)**	**5 (42%)**	12
	N2 sleep	**20 (69%)**	**9 (31%)**	29
Sum		34	27	**61**

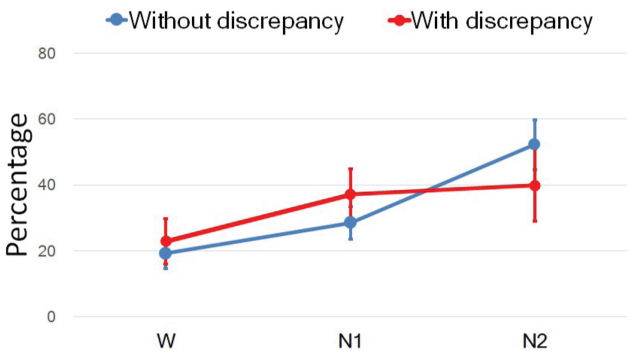

Figure 2. Percentage of different sleep stages (awake, N1 sleep, and N2 sleep) in the last 5 min before awakening for awakenings with and without subjective-objective discrepancy.

p = .029; O2: t = −2.14, p = .042; P7: t = −2.83, p = .008; Oz: t = −2.38, p = .025) (Figure 3).

Relative EEG PSA. Log-transformed of relative γ activity in awakenings with discrepancy was higher than those without discrepancies at O1, O2, F8, Fz, P7, and Oz (O1: t = −2.15, p = .039; O2: t = −2.29, p = .030; F8: t = −2.06, p = .048; Fz: t = −2.22, p = .036; P7: t = −2.35, p = .026; Oz: t = −2.29, p = .030) (Figure 3).

Log-transformed of relative α, β, and γ activities was also found to be higher in awakenings with discrepancy than those without discrepancies at P7 (Figure 3).

Correlation between EEG activity and subjective sleep perception

Absolute EEG PSA

Absolute δ power spectral values showed different pattern, a positive correlation between absolute δ power spectral values and subjective sleep perception degree at T8 (ρ = .431, p = .025). Log-transformed absolute α activity was found to correlate significantly with subjective sleep perception degree at FC1 (ρ = −.416, p = .034).

Relative EEG PSA

We also found that there was a significant negative correlation between log-transformed values of relative θ power spectral values and subjective sleep perception degree at FC2, O2, and P8 (FC2: ρ = −.404, p = .037; O2: ρ = −.392, p = .043; P8: ρ = −.402, p = .038), log-transformed relative α activity and subjective sleep perception at FC2 and T8 (FC2: ρ = −.406, p = .036; T8: ρ = −.412, p = .033), log-transformed relative γ activity and subjective sleep perception at F4, C4, P4, Pz (F4: ρ = −.552, p = .041; C4: ρ = −.596, p = .031; P4: ρ = −.610, p = .021; Pz: ρ = −.659, p = .020).

fMRI nALFF results

Group differences are shown in Figure 4 and Table 3. Relative to the group without discrepancy, awakenings of those with discrepancy exhibited higher nALFF values in the medial orbital frontal gyrus (MOF) [−6, 66, −10], the superior medial frontal gyrus (SMF) [−8, 58, 32], and the precuneus [−10, −40, 42], in voxel-wise analyses (Figure 4). Based on the results of the voxel-wise analyses, we extracted nALFF values of MOF, SMF, and the precuneus from the AAL template and compared across groups (Figure 4). ROI analyses indicated significant group differences between awakenings with and without discrepancy in MOF (p = .031) and SMF (p = .021) (Figure 4). To further illustrate the enhanced nALFF, the raw time courses of the three AAL brain regions are presented on the basis of single awakening case of each group with and without discrepancy in Figure 5.

Discussion

The main finding of the study is that discrepancy between subjective perception of and objective measures of sleep is associated with lower θ EEG activity and higher α, β, and γ EEG activity. Moreover, fMRI-ALFF results evince elevated fluctuation levels in the prefrontal cortex when subjective report and objective measures do not align with one another. These results lend support to the conjecture that the discrepancy is associated with CNS hyperarousal particularly in the prefrontal cortex.

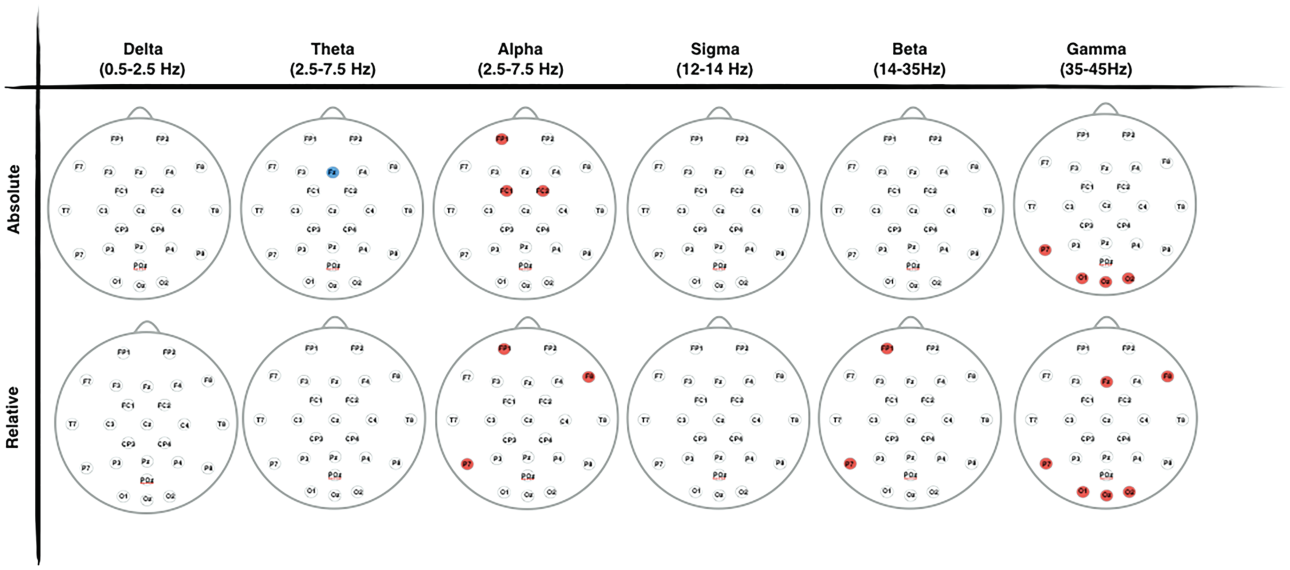

Figure 3. Comparisons of mean log-transformed values of absolute and relative EEG activity between awakenings with and without discrepancy.

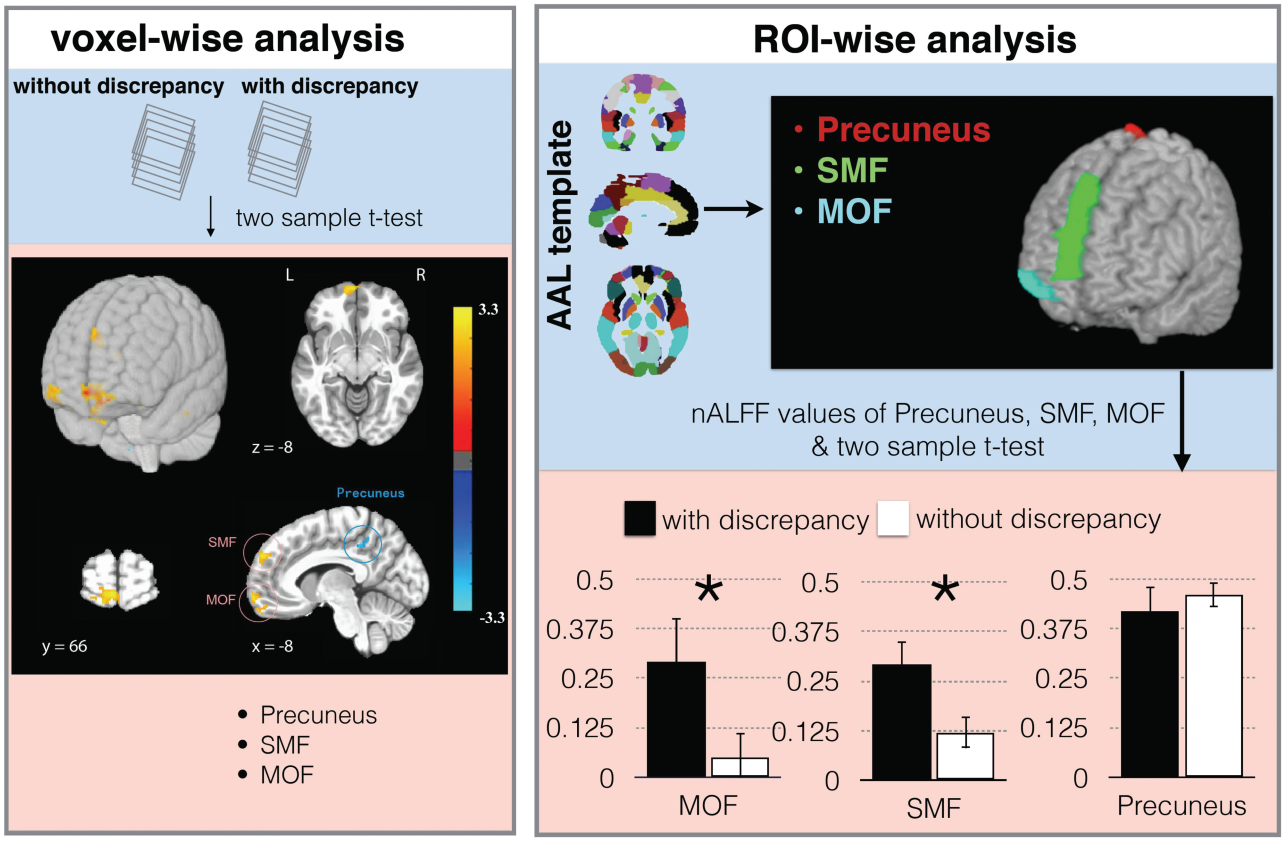

Figure 4. Comparisons of nALFF values between awakenings with and without subjective-objective discrepancy. MOF: medial orbital frontal gyrus [-6, 66, -10]; SMF : superior medial frontal gyrus [-8, 58, 32]; Precuneus [-10, -40, 42].

As mentioned previously, CNS hyperarousal has been found to be more commonplace among patients with insomnia than among healthy participants. The International Classification of Sleep Disorders, Second Version (ICSD-2), has described a subtype of insomnia—paradoxical insomnia—which is characterized by this very discrepancy between objective and subjective sleep [38]. "Paradoxical insomnia" is defined as a subjective complaint of sleep difficulties and related daytime impairment, even though objective polysomnographic recordings appear normal. Patients with paradoxical insomnia tend to underestimate their total sleep time and overestimate their sleep difficulties. One study reports that patients with paradoxical insomnia had elevated α, σ, and β activity (8.5–30 Hz) in NREM, relative to participants who exhibited healthy sleep patterns [39]. Correspondingly, our results indicate elevated α and γ activity when the discrepancy occurs, implying that sustained α rhythms might be a mediating factor in subjective awareness.

It is important to note that increased high-frequency EEG in the group with discrepancy is especially pronounced in regions that are engaged in attentional processing: prefrontal and parietal areas. Generally, frontal lobe activity involves executive functions, whereas the parietal lobe involves multisensory integration. The combined, fronto-parietal network (FPN), is thought to be involved in cognitive control [40]. Our findings suggest that there is increased cognitive control during states where EEG measures indicate sleep, but subjective reports indicate wakefulness. Since there was no significant difference in the distribution of sleep stages between the awakenings with discrepancy and those without, the increased EEG activity was not due to the difference in sleep stages. This increased cognitive control might involve higher levels of information processing and contribute to the subjective perception of wakefulness, thereby causing the inconsistency between the subjective perception and objective sleep.

Table 3. Group difference of nALFF values in awakenings with and without discrepancy between objective and subjective indices

Region	Voxels	BA	X	Y	Z	T value	Z value
With discrepancy > Without discrepancy							
MOF_L	225	11	-6	66	-10	5.4	4.63
SMF_L	115	9	-8	58	32	5.14	4.47
With discrepancy < Without discrepancy							
Precuneus_L	74	31	-10	-40	42	5.07	4.42

MOF = Medial orbital frontal gyrus; SMF = Superior medial frontal gyrus.

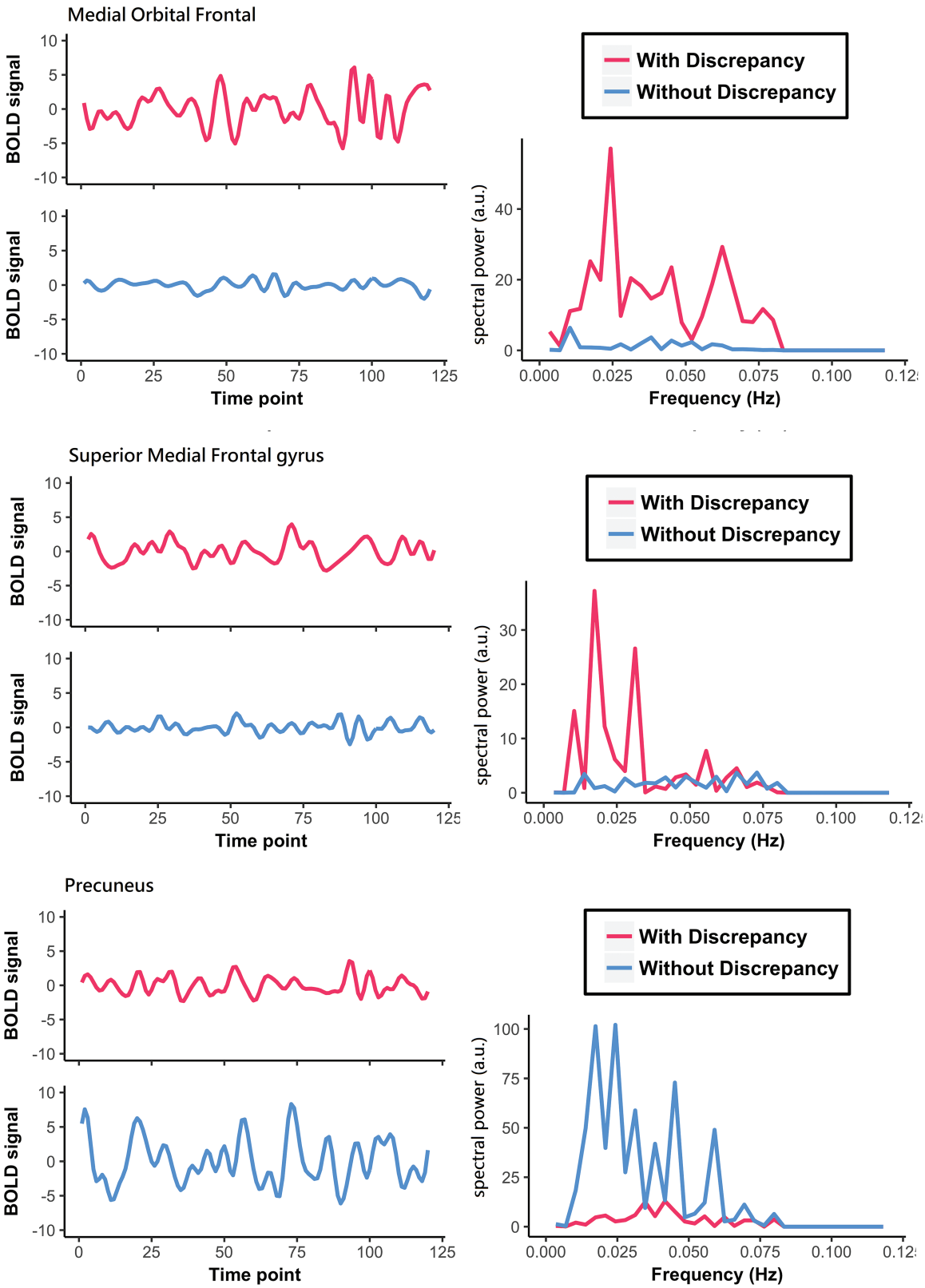

Figure 5. The raw time courses of the three AAL brain regions were presented on the basis of single awakening case of each group with and without discrepancy. (Top: MOF = Medial orbital frontal gyrus; SMF = Superior medial frontal gyrus; Precuneus); x axis: frequency (Hz); y axis: spectral power (a.u.).

Even without discrepancy, significant negative correlations were found between θ, α, and γ power and the subjective perception of sleep depth. Therefore, it seems that the level of cortical arousal plays an important role not only in determining the perception of wakefulness, but also in the perception of how deeply one sleeps. On the other hand, a positive correlation was found

between δ power and sleep perception. δ is the main indicator of deep sleep. Previous studies also found that δ activity increases within the duration of wakefulness that precedes sleep and suggested that δ activity might be related to sleep drive [41]. Our results further support the finding that δ activity is associated with the perception of deeper sleep.

In BOLD fMRI studies, a significant increase in the fluctuation level of the BOLD signal was observed in the visual cortex, and several cortical areas during light sleep. To the best of our knowledge, our study is the first attempt to use fMRI index (nALFF) to probe the association between local, spontaneous patterns of intrinsic brain activity and sleep-related states of consciousness. We found that the discrepancy between objective and subjective sleep evinced higher nALFF values in left medial superior frontal gyrus (SFG). The SFG, located at the superior part of the prefrontal cortex, has been reported to be involved in higher levels of executive functioning, such as working memory [42–44], attention [45, 46], monitoring, and manipulation of information processing [47]. Recent studies have identified three SFG subregions—anteromedial (SFGam), dorsolateral (SFGdl), and posterior (SFGp) subregions—and each connects to a distinct network. SFGam has been reported to correlate mainly with the cognitive control network [48]. What is more, the nALFF result is consistent with our findings on EEG spectral analyses, lending support to the conjecture that greater cognitive control might be a key factor that contributes to the perception of waking, even though the PSG evinces a sleep EEG pattern. In addition to hyperarousal in awakenings with discrepancy, we observed one region—left precuneus—with weakened nALFF values in discrepancy. This weakened nALFF value during a high arousal state seems consistent with the idea that the neocortical synchronization which occurs during sleep causes increases in amplitude of the fluctuation. This in turn is consistent with previous findings of increased amplitude of ALFF during sleep onset [23, 24]. Besides, both prefrontal gyrus and precuneus play pivotal roles in the DMN [25, 49]. Previous neuroimaging studies showed that DMN connections between the precuneus and prefrontal regions decrease as sleep deepens, but the nALFF changes in DMN were not revealed. Our findings imply that during the dynamic functional plasticity in sleep, participants with discrepancy might experience an abnormal reorganization process in the DMN.

Although this study enhances our understanding of the neurocognitive mechanisms associated with the sleep perception, in view of the study's limitations, the findings should be interpreted with caution. First, due to the noisy and uncomfortable environment of the scanner, it was difficult for the participants to remain in stable sleep for a lengthy period of time. Therefore, we could only obtain a limited number of sleep samples for analysis. Second, a limitation of this study is that we did not employ a power analysis to estimate the optimal sample size; we could not do this because falling asleep inside the MRI scanner is difficult for many participants. But we did calculate the effect size for the MOF, SMF, and precuneus of the differences between awakenings with and without discrepancy (MOF: 0.71; SMF: 0.76; precuneus: 0.18). Although we were able to obtain significant findings with current sample size, the procedure should be conducted in the future studies. Third, the data analyses of power spectral data were conducted without correction for multiple comparisons. Due to the exploratory nature of this study, we conducted comprehensive comparisons. Thus, our finding would need to be replicated in a future study. Fourth, we know little about the potential changes in ALFF during the sleep onset period. Therefore, ALFF results should be interpreted with caution. Further study of brain alteration during the period of sleep onset is necessary. Fifth, another reason for caution is that we woke the participants up from stages N1 or early N2 sleep to assess their subjective experiences. We did not obtain data from more stable N2 sleep, N3 sleep, or REM sleep (Table S1). Future studies are needed in order to generalize our results to other sleep stages. Sixth, the nALFF values reflect local, spontaneous activity of the brain areas, not patterns of connectivity among different brain areas. To better understand distributed patterns of connectivity, further investigation will also be required. Finally, the focus of our study is investigation of the state differences between the sleep with and without subjective–objective mismatch. Therefore, we divided the awakenings into those with and without discrepancy for comparison. In a future study, it would be important to try to correlate the actual value of discrepancy of a sleep parameter with ALFF to further investigate the underlying mechanisms of individual differences.

Supplementary Material

Supplementary material is available at *SLEEP* online.

Funding

Financial support for this research has been provided by Taiwan's Ministry of Science and Technology. For T.J.L.: 104-2420-H-038-001-MY3, 105-2410-H-038-004-MY, 105-2632-H-038-001-MY3, 106-2410-H-038-003, and 106-2632-H-038-001-MY3. For C.W.W.: 105-2628-B-038-013-MY3. For C.-M.Y.: 103-2420-H-004-004-MY2.

Note

Conflict of interest statement. This was not an industry-supported study. Financial support for this research has been provided by Taiwan's Ministry of Science and Technology. The authors have indicated no financial conflicts of interest.

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