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Perception of sound stimuli during sleep in patients with paradoxical insomnia

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Paradoxical insomnia (Para-I) is characterized by complaints of severe insomnia that occurs without evidence of objective sleep disturbances or disruption of daytime activities [1], creating a paradox between objective findings (polysomnography) and subjective complaints. Marked differences between subjective and objective sleep, more than 6 h of sleep on polysomnography (PSG) and a sleep efficiency > 85% are often observed. Furthermore, "normal" nights are rare, while sleepless nights and no naps are usually reported on the sleep diary [2]. Diagnosis is based primarily on clinical and polysomnographic data. Although it seems to be a prevalent subtype of chronic insomnia, little is known about the etiology, course, or treatment responsiveness of Para-I. There is no standard or well-established treatment for these patients [3].

Insomnia classification is a field for many disagreements, especially with regard to "primary" vs "secondary" status. For some investigators, the over-estimation of sleep difficulty is a generic insomnia trait in which extreme cases might exist, whereas others suggest that a separate diagnostic category should be considered for a more severe small subgroup of chronic insomnia patients who consistently underestimate their sleep duration [4]. The ICSD-2 is based on the latter view, which allows the diagnosis of "Para-I" (so-called "sleep state misperception"), whereas the DSM-IV does not include this diagnosis under "primary insomnia" [5] because there is insufficient evidence to support its separate existence [6]. The ICSD-3 [7] unified the diagnosis of insomnia "primary" and "secondary" in the term chronic insomnia disorders. This decision did not mean to suggest that there are not important pathophysiological differences between chronic insomnia subtypes. Rather, it is the recognition that is still not able to reliably such distinction or translates them into more personalized therapeutic approaches [8].

The prevalence of isolated symptoms of insomnia is estimated between 30 and 48% of adults, [9] while approximately 10% suffer from an insomnia syndrome [10]. The prevalence of Para-I is unknown, but it is estimated to account for 5 to 9% of all cases of insomnia [1,11-13]. Many precipitating factors [14] and maintaining factors [15] have been suggested as being linked to the appearance or perpetuation of the disorder. Nonetheless, the underlying cortical mechanisms associated with chronic insomnia are just beginning to be better understood. [16-22]. Subjects with psychophysiological (Psy-I) and Para-I differ greatly regarding both objective and subjective sleep variables [23]. The main feature of Psy-I is that they display conditioned sleep difficulty and/or heightened arousal in bed. For example, an inability to initiate sleep when wanted, sleeping better away from home, intrusive thoughts at night (mind racing), somatic tension, and a difficulty to relax in bed are reported. On the other hand, Para-I severely overestimate their

sleep difficulties, presenting marked differences between subjective and objective sleep [2].

While polysomnographic analyses do not corroborate the severe sleep difficulty complaints of Para-I, power spectral analysis studies reveal that these individuals appear to display a perturbed microstructure of sleep compared to Psy-I [13,21,24,25]. Power spectral analysis differences in the EEG between normal subjects and individuals with insomnia are now well documented [16,19-21,24]. The Neurocognitive Model of Insomnia proposes that subjects with primary insomnia develop an increase in high-frequency EEG activity (i.e., beta/gamma activity) at or around sleep onset, besides the attenuation and/or suppression of the mesograde amnesia which is normally attendant upon sleep [26,27]. The increased beta/gamma EEG activity allows for increased sensory processing, information processing, and the formation of long-term memory [28]. The attenuation and/ or suppression of the mesograde amnesia would permit subjects with primary insomnia to recall and/or recognize information from sleep onset intervals rather than good sleeper controls [26,27]. Furthermore, other studies have identified that Para-I displayed greater beta and gamma activities (reflecting cortical arousal) and an absolute greater amplitude in alpha and beta activities in stages 2 and 4 of sleep compared to Psy-I [21,24]. These results indicate greater cortical activation in subjects with Para-I, therefore supporting the neurocognitive model of insomnia [26] that suggests that high frequency activity could interfere with sleep initiation as well as sleep maintenance. Furthermore, this increased cortical arousal would also lead to incompatible sleep activities such as enhanced sensory and information processing.

According to a simple behavioral definition, sleep is defined as a state of behavioral quiescence and perceptual disengagement [29]. A possible problem for individuals with insomnia may be an inability to inhibit processing during sleep onset and within sleep. However, since it is impossible for individuals to respond behaviorally or verbally while they are sleeping, the study of information processing during the process of falling asleep and during sleep itself is very limited. Cortical activity of Para-I and Psy-I was assessed by event-related potentials and was compared to good sleepers [2]. N1 and P2 were recorded in the evening, at sleep-onset and in early stage 2 sleep in all participants. Three different waves were also computed to evaluate the transition

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from wakefulness to sleep onset, from sleep onset to sleep and from wakefulness to sleep. This study concluded that Psy-I appears to present an inability to inhibit information processing during sleep onset, while Para-I seems to present overall enhanced attentional processing that results in a greater need for inhibition.

The poor sleep experienced by insomnia individuals may be the result of an inability to inhibit external information processing of irrelevant stimulus during sleep onset and sleep and this enhanced information processing may result in hyperarousal. The objective of this study is to evaluate whether patients with Para-I perceive sound stimuli presented during sleep, by comparing them to healthy subjects.

Methods

Patients

A total of 10 patients with Para-I (study group) who are followed at the Neuro-Sono Clinic of the Discipline of Neurology, Federal University of São Paulo – Paulista School of Medicine (UNIFESP / EPM) were selected for the study. In addition, seven healthy volunteers matched for age and body mass index (BMI) were selected to serve as a control group (CG).

The diagnosis of Para-I was based on American Academy of Sleep Medicine (AASM) criteria, as follows: [1] presence of a subjective complaint of insomnia, defined as difficulty initiating (i.e., sleep-onset latency > 30 min) and/or maintaining sleep (i.e., time awake after sleeponset > 30 min) present at least three nights per week; [2] insomnia duration of at least six months; [3] total sleep time of more than 6h 30min and a sleep efficiency greater than 85% on nocturnal PSG; [4] marked discrepancies between subjective and objective sleep measures (i.e. a difference of 60 min or more for total sleep time, or a difference of at least 15% between subjective and objective measures of sleep efficiency). The following observation was also common: complaint of severe sleep difficulties most of the time (sleepless nights on sleep diaries being an indicator of severe difficulties) [23]. Patients with an Epworth Sleepiness Scale (ESS) score scale equal to or greater than 5 and/or a complaint of hearing loss were excluded. The control group consisted of volunteers matched for age and BMI. Those with [1] complaints suggesting any form of insomnia, [2] daytime sleepiness, [3] an ESS score equal to or greater than 5, or [4] a complaint of hearing loss were excluded from serving as controls.

All study participants underwent overnight PSG at the Neuro-Sono Sleep Center laboratory.

This study was approved by the UNIFESP/Hospital Sao Paulo Research Ethics Committee (CAAE: 27853514.8.0000.5505).

Evaluation

Participants were evaluated clinically and through anthropometric parameters such as age, height, weight, and BMI. Daytime sleepiness was assessed by the ESS. All participants were submitted to only one PSG evaluation according to experimental protocol described below.

Experimental Protocol

Polysomnography. Participants spent only one night in the sleep laboratory. They were instructed to arrive at around 7:00 pm for electrode montage and preparation. Participants were asked to refrain from alcohol, drugs, excessive caffeine and nicotine before coming to the laboratory. Bedtime and time in bed were determined according to reported time on sleep diary (SD). For all participants, lights-out was

initiated after a bio-calibration, with no less than a fixed 8 h of PSG recordings. Overnight PSG was performed using an Alice 5 diagnostic sleep system (Respironics Philips, Amsterdam, Netherlands). The parameters monitored were: electroencephalogram, electrooculogram, submental and tibial electromyogram, electrocardiography, chest and abdominal movements (plethysmography belt), airflow (thermistor and nasal cannula), and peripheral oxygen saturation, following the AASM manual criteria [30]. Interelectrode impedance was maintained below 5 k Ω . Respiration and tibialis EMG were monitored during the PSG recording in order to rule out sleep apnea and periodic limb movements. Participants diagnosed with another sleep disorder were excluded.

Auditory stimulation. During PSG, patients were exposed to sound stimuli specific to each sleep stage (N2, N3, and REM). Study participants were informed that sounds would be played overnight but were unaware of the nature of these sounds. It was chosen stimuli that would be easy to recognize, and it would sound unexpected in a large urban area such as the city where the study was conducted to facilitate reporting and to avoid bias in our results once the similarity between the standardized sounds with those which could come from outside the sleep laboratory was a possibility. Sound stimuli were consisted of a rooster crowing, a horse whinnying, and a cow mooing, applied during the N2, N3, and REM stages respectively.

The laboratory room was equipped with two speakers, positioned side by side at the headboard, 15 cm from the patient's head (Figure 1). The stimuli were triggered by the investigator according to a preestablished protocol. Stimuli were administered after the standard pattern corresponding to each sleep stage had been present for at least 2 minutes. Each stimulus (lasting three seconds) was presented in ascending intensities of 10 dB (from 40 to 100 dB) until resulted in arousal or awakening, following the criteria established in the AASM manual [30]. If the stimulus did not result in arousal or awakening, the minimum interval for the next stimulus was 1 minute. For each patient, it was administered as many stimuli as needed, until it was obtained at least two (maximum of five), which were associated with arousal or awakening for each sleep stage. The amount of stimuli associated with arousal or awakening was used to evaluate the performance index for both groups in order to increase the probability of their auditory processing. Stimuli associated with arousal or awakening were logged in a spreadsheet containing the hour, stage of sleep, and stimulus intensity performed, for further confrontation with the information obtained through patients' answers.

The next morning, after PSG, patients were interviewed about their night to ascertain whether they had perceived the standardized sound stimuli and, if so, which and how many stimuli they had heard.



Figure 1. Sketch of the laboratory room

Subjective and objective sleep parameters

The sleep diary (SD) [31] is a daily journal used to assess subjective sleep quality. The various sleep—wake parameters derived for this study were sleep-onset latency (SOL); wake after sleep-onset (WASO); total sleep time (TST); time in bed (TIB); and finally, sleep efficiency (SE), defined as the ratio of TST divided by TIB, expressed as a percentage. The SD was completed by the participants upon arising in morning after the PSG. Objective measures of sleep included SOL, WASO, TST, SE, and proportion (%) as well as time spent (min) in stages 2, 3 and rapid eye movement (REM).

Outcome variables

The variables used to compare the behavior of the two groups in relation to the N2, N3, and REM stages were: [1] total of stimuli reported; [2] the performance index, which represents a ratio between stimuli with arousal or awakening reported by patients in the interview conducted after the PSG exam and all stimuli with arousal and awakening performed during the entire night; [3] number of correctly reported stimuli associated with awakening, [4] arousal, or [5] both; [6] average intensity of the stimuli necessary to trigger a valid stimulus; [7] average number of stimuli presented; [8] percentage of patients who correctly reported the stimulus; [9] percentage of patients who experienced arousal or [10] awakening; [11] percentage of patients who correctly reported the stimulus and experienced arousal or [12] awakening; and percentage of patients who experienced [13] arousal or [14] awakening and correctly reported stimuli.

Statistical analysis

The Student's *t*-test was used to analyze differences between the study and control groups regarding age, height, weight, BMI, ESS score, number of reported stimuli, performance index, successfully reported stimuli associated with arousal and/or awakening, stimulus intensity, and average number of stimuli presented. The chi-square test was used to establish a relationship between the percentage of patients who correctly reported the stimuli in the presence of arousal or awakening, and to compare the incidence of arousals or awakenings between groups. P-values <0.05 were considered significant.

Results

Characteristics of participants

The study included a total of seven patients with Para-I (five women and two men, mean age 58.1 ± 15.7 years). Among the three other patients selected for the study, one had no consistent history of Para-I, another was unable to sleep in the laboratory, and the last was unwilling to participate. The CG consisted of six healthy volunteers (five women and one man, mean age 50.0 ± 21.2). One patient of this group was excluded due to inability to sleep in the lab. Patients in both groups were matched for age, sex, height, weight, and BMI (Table 1). No differences in ESS score were observed between the study and control groups $(2.3 \pm 1.7 \text{ vs. } 3.0 \pm 1.1, \text{ p} = .38)$.

Subjective and objective sleep parameters

Between group differences: Table 2 shows mean subjective and objective sleep laboratory parameters for the two groups of participants. Analyses revealed significant differences among groups on all subjective measures (SOL, WASO, SE and TST). Para-I reported spending the longest time awake after sleep onset (181.8 \pm 61.3), sleeping the less time (171.4 \pm 74.9), taking more time to fall asleep (110.7 \pm 59.3) and having the lowest sleep efficiency (36.9 \pm 16.2), while CG reported spending

the less time awake (25.8 ± 9.2), sleeping the longest time (408.6 ± 9.5), taking less time to fall asleep (20 ± 8.4) and having the highest sleep efficiency (89.9 ± 2.7). With regard to the objective sleep variables, there were no significant differences among groups (Table 2). There were also no differences among groups observed for percentage and time spent in all sleep stages (N2, N3 and REM).

Perception and recall of sound stimuli

Stage N2

During the stage N2, Para-I perceived more stimuli [2.0 \pm 1.15 (CI = 1.72 to 2.94)] and had a greater performance index [81 \pm 38 (CI = 0.81 to 0.81)] as compared with controls [0.67 \pm 0.82 (CI = 0.02 to 1.32) and 28 ± 39 (CI = -0.03 to 0.59), respectively] (Table 3). The percentage of patients experiencing arousals who successfully reported the corresponding stimulus was higher in the Para-I group (100% vs 40%, p = 0.02). Eighty six percent of patients from study group correctly reported the stimulus, against fifty percent from the CG (p = .16). For the correctly reported stimuli with arousal and/or awakening no significant difference among groups was observed (Table 3). Despite no significant difference among groups, the percentage of patients who correctly reported perception of the emitted stimuli associated with arousal was higher in the study group; however when associated with awakening, CG had higher perception (Table 4). It was observed a trend toward occurrence of a greater number of arousals among Para-I as compared to controls and the opposite relationship for awakenings. There were no statistically significant differences between groups when considered the mean intensity of valid stimuli and the average number of stimuli presented (Table 3).

Stage N3

At the stage N3, all patients in the Para-I group who correctly reported perception of the stimulus experienced arousals (100% vs 0%, p = 0.01); however, in the control group, all experienced awakening (0% vs 100%, p = 0.01). Nevertheless, the number of reported stimuli and the performance index did not differ between the two groups [1.43 \pm 1.51 (CI = 0.31 to 2.55) vs 0.5 \pm 0.84 (CI = -0.17 to 1.17) and 50 \pm 50 $(CI = 0.13 \text{ to } 0.87) \text{ vs } 22 \pm 40 \text{ } (CI = -0.10 \text{ to } 0.54), \text{ respectively}]$ (Table 5). The percentage of patients who correctly reported the stimulus was higher in Para-I, however, no significant difference among groups was observed (Table 6). Once again, for the correctly reported stimuli with arousal and/or awakening no significant difference among groups was observed (Table 5). As observed in stage N2, Para-I experienced more arousals and CG more awakenings. Furthermore, the percentage of patients experiencing arousals who successfully reported the corresponding stimulus was higher in Para-I. Nonetheless, no significant difference among groups was observed (Table 6). Similarly to stage N2, there were no statistically significant differences between groups when considered the mean intensity of valid stimuli and the average number of stimuli presented (Table 4).

REM

Regarding REM sleep, few patients in both groups experienced arousals or awakenings; however none of them reported perception of the sound stimulus corresponding to that stage.

Discussion

Summary

The data acquired in this study suggests that subjects with Para-I can perceive a greater amount of stimuli and recognize more of

Table 1. Profile of participants in the study and control groups.

	Paradoxical insomnia group (n=7)	Control group (n=6)	p-value (< 0.05)
Age (years)	58.1 ± 15.7	50.0 ± 21.2	0.46
Sex	5♀/2♂	5♀/1♂	_
Weight (kg)	66.71 ± 11.76	61.83 ± 6.24	0.36
Height (m)	1.65 ± 0.07	1.60 ± 0.02	0.16
BMI (m/kg²)	24.57 ± 3,69	24.07 ± 2.65	0.78
Epworth Sleepiness Scale	2.3 ± 1.7	3.0 ± 1.1	0.38

Table 2. Means and standard deviations of laboratory sleep parameters for paradoxical insomnia and control groups.

	Paradoxical insomnia group (n=7)	Control group (n=6)	p-value (< 0.05)
Subj. measures			
SOL	110.7 ± 59.3	20 ± 8.4	< 0.01
WASO	181.8 ± 61.3	25.8 ± 9.2	< 0.01
TST	171.4 ± 74.9	408.6 ± 9.5	< 0.01
SE	36.9 ± 16.2	89.9 ± 2.7	< 0.01
Obj. measures			
SOL	19.3 ± 8.1	15.5 ± 6.9	0.38
WASO	24.3 ± 4.0	21.4 ± 2.4	0.14
TST	420.3 ± 11.5	417.5 ± 9.5	0.63
SE	90.6 ± 2.1	91.9 ± 1.7	0.24
Stage 1 time (min)	47.6 ± 17.0	45.1 ± 15.9	0.79
Proportion (%)	11.3 ± 4.0	10.8 ± 3.6	0.80
Stage 2 time (min)	242.7 ± 45.2	216.0 ± 34.0	0.25
Proportion (%)	57.7 ± 10.4	51.7 ± 8.0	.26
Stage 3 time (min)	70.0±32.5	84.2±26.0	.40
Proportion (%)	16.7±7.7	20.1±6.1	.39
REM time (min)	60.0±24.5	72.2±19.8	.34
Proportion (%)	14.2±5.7	17.4±4.9	.31

Note: SOL = Sleep-onset latency, WASO = Wake after sleep onset, TST = Total sleep time, SE = Sleep efficiency.

Table 3. Between-group comparison of variables of interest during the N2 stage.

N2 stage	Paradoxical insomnia group (n = 7)	Control group (n = 6)	p-value (< 0.05)
Average number of stimuli presented	2.57 ± 0.78	2.66 ± 0.5	0.80
Stimuli reported	2.0 ± 1.15 (CI = 1.72 to 2.94)	0.67 ± 0.82 (CI = 0.02 to 1.32)	0.03
Performance index (%)	81 ± 38 (CI = 0.81 to 0.81)	28 ± 39 (CI = -0.03 to 0.59)	0.03
Correctly reported stimuli with arousal	2.3 ± 0.5 (CI = 2.26 to 2.34)	2.0 ± 1.1 (CI = 1.12 to 2.88)	0.57
Correctly reported stimuli with awakening	0.3 ± 0.5 (CI = 0.26 to 0.34)	0.7 ± 0.8 (CI = 0.06 to 1.34)	0.35
Correctly reported stimuli with arousal and awakening	2.6 ± 0.8 (CI = 2.00 to 3.19)	2.7 ± 0.5 (CI = 2.3 to 3.1)	0.80
Mean intensity of valid stimuli (dB)	47.37 ± 10.71 (CI = 39.42 to 55.32)	54.72 ± 6.88 (CI = 40.22 to 60.22)	0.17

Table 4. Comparison of variables rated among the groups during the N2 stage

N2 stage	Paradoxical insomnia group (n=7)	Control group (n=6)	p-value (< 0.05)
Patients who correctly reported the stimulus	86%	50%	0.16
Patients who experienced arousal	100%	83%	0.26
Patients who experienced awakening	29%	50%	0.43
Patients who correctly reported the stimulus and experienced arousal	100%	67%	0.13
Patients who correctly reported the stimulus and experienced awakening	33%	100%	0.06
Patients who experienced arousal and correctly reported stimuli	100%	40%	0.02
Patients who experienced awakening and correctly reported stimuli	100%	100%	_

these stimuli compared to healthy controls during the N2 and N3 stages of sleep. There were no differences in the rate of correct answers associated with arousal and awakening in the two groups. The percentage of patients experiencing arousal and successfully reporting perception of the correct stimulus was higher in the

study group, but for awakenings, the success rate was higher in the control group. CG reported perception of stimuli more often when the sound was able to elicit an awakening. Those stimuli which generated arousals were not as well perceived by controls as they were by Para-I.

Table 5. Between-group comparison of variables of interest during the N3 stage.

N3 stage	Paradoxical insomnia group (n = 7)	Control group (n = 6)	p-value (< 0.05)
Average number of stimuli presented	3.0 ± 1.0	2.7 ± 0.5	0.46
Stimuli reported	1.43 ± 1.51 (CI = 0.31 to 2.55)	0.5 ± 0.84 (CI = -0.17 to 1.17)	0.19
Performance index (%)	$50 \pm 50 \text{ (CI} = 0.13 \text{ to } 0.87)$	22 ± 40 (CI = -0.10 to 0.54)	0.29
Correctly reported stimuli with arousal	2.9 ± 1.2 (CI = 2.01 to 3.79)	1.8 ± 1.5 (CI = -5.94 to 9.54)	0.21
Correctly reported stimuli with awakening	0.1 ± 0.4 (CI = -0.20 to 0.40)	0.5 ± 0.8 (CI = -0.14 to 1.14)	0.37
Correctly reported stimuli with arousal and awakening	$3.0 \pm 1.0 \text{ (CI} = 2.26 \text{ to } 3.74)$	2.3 ± 0.8 (CI = 1.66 to 2.94)	0.21
Mean intensity of valid stimuli (dB)	62.13 ± 11.96 (CI = 53.3 to 71.0)	69.17 ± 2.04 (CI = 67.54 to 70.80)	0.17

Table 6. Comparison of variables rated among the groups during the N3 stage.

N3 Stage	Paradoxical insomnia group (n=7)	Control group (n=6)	p-value (< 0.05)
Patients who correctly reported the stimulus	57%	33%	0.40
Patients who experienced arousal	100%	67%	0.10
Patients who experienced awakening	14%	33%	0.42
Patients who correctly reported the stimulus and experienced arousal	100%	0%	0.01
Patients who correctly reported the stimulus and experienced awakening	0%	100%	0.01
Patients who experienced arousal and correctly reported stimuli	57%	0%	0.06
Patients who experienced awakening and correctly reported stimuli	0%	100%	0.08

Implications

The findings of this study suggest that patients with Para-I have a higher ability to perceive and process information during the N2 and N3 stages of NREM sleep. These results come in accordance to some data present in literature. Subjects with Para-I exhibit decreased delta band relative power and increased alpha, sigma, and beta bands in EEG frequency spectra during NREM sleep, and these findings are associated with subjective sleep complaints [20,24,26, 32, 33]. During REM sleep, increased activity in the beta frequency has been reported in these patients [20,34]. They also present enhanced attentional processing and/or a greater need for inhibition during wakefulness, sleep onset, and sleep [2]. In addition, a study of transcranial magnetic stimulation showed that patients with chronic insomnia have increased absolute cortical excitability [35]. These findings support the hypothesis that Para-I may have greater cortical activation, potentially interfering with the initiation and maintenance of sleep, which is consistent with the findings of the present study.

This increase in cortical excitability would lead to activities incompatible with sleep, such as information processing [26]. The excess occurrence of high frequency EEG activity can hinder the inhibition of consciousness to perception of the sleep state, thus exposing the patient to stimuli from the external environment. We do not have enough data to assert whether this neurophysiological pattern results in impaired ability to suppress information processing during this period; however, in light of our findings in this study, we can suggest this as a possibility.

Considering previous data [2,20,24, 26, 32,33,35] and the findings of the present study, we may suggest that patients with Para-I may have a deficit in the ability to suppress information processing during NREM sleep, probably secondary to a larger contingent of high frequency EEG activity during sleep, as verified in the EEG frequency spectra. Although these patients also exhibit increased activity in the beta frequency during REM sleep, [20,34] the patients in our experiment were not influenced by sound stimuli at this stage. In addition, our findings also support the theory of the attenuation/suppression of

the mesograde amnesia [28] that would be the reason subjects with paradoxical insomnia are able to recall and/or recognize information from sleep onset intervals better than good sleepers.

Study Strengths

The present paper obtained relevant data regarding information processing during sleep in patients with Para-I. The experimental protocol presented in this study suggest the possibility of evaluating information processing during sleep, since this neurophysiological state imposes a major limitation to the verbal response and to other behavior. Our design could be used as a model to evaluate this process in patients with Para-I, through a highly strict protocol in which sound stimuli were standardized for each stage of sleep. Using this procedure, we were able to identify whether perception of the standard stimulus occurred and recognize the stage of sleep at which such perception occurred.

Study Limitations

Some limitations of this study must be mentioned. Although we found differences between the groups that support our hypothesis, the small number of participants prevented us from obtaining more robust statistical data. In addition, we did not perform spectral evaluation of EEG tracings, which would have enabled us to demonstrate whether variation in the number of high frequency EEG activity occurs during sleep and if such variation influences the performance index of patients with Para-I. The lack of an insomnia disorder comparator group without sleep state misperception was a limiting factor because we do not know if the findings of this study are a feature related to patients with Para-I or whether it is a characteristic of all with chronic insomnia. A small number of auditory stimuli used and the fact that they were repeated over the course of the night, and the use of air borne stimuli via speakers (vs. earbuds) may have resulted in the failure to detect some stimuli owing to body position. The study uses a single point measure of perception of sleep and that it would be more powerful to have repeated measures assessment in order to take into account night to night variability in sleep perception. The last point that should be mention

is the fact that not all of the stages of sleep were assessed including naturally occurring wake during the sleep interval and stage N1.

Future Directions

Future research should aim at expanding the experimental protocol presented in this study. The inclusion of an insomnia disorder comparator group with or without the state of misperception of sleep would be interesting to see if the trend observed in this study is (or not) a characteristic related to all subjects with chronic insomnia. In addition, some modifications to the protocol could be taken into consideration: increasing the number of stimuli and performing more than one evaluation with polysomnography.

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Potential Conflicts of Interest

Nothing to report

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