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Extreme sleep state misperception: From psychopathology to objective-subjective sleep measures☆

Anna Castelnovo [a,b,c,*], Raffaele Ferri [d], Andrea Galbiati [e,f], Alessandro Rossi [g], Marco Zucconi [e], Vincenza Castronovo [e], Luigi-Ferini Strambi [e,f], Mauro Manconi [a,b]

[a] Sleep Medicine, Neurocenter of Southern Switzerland, Regional Hospital of Lugano, Lugano, Switzerland
[b] Faculty of Biomedical Sciences, Università della Svizzera Italiana, Lugano, Switzerland
[c] University Hospital of Psychiatry and Psychotherapy, University of Bern, Bern, Switzerland
[d] Oasi Research Institute, IRCCS, Troina, Italy
[e] Division of Neuroscience, Sleep Disorders Center-Neurology, IRCCS San Raffaele Scientific Institute, Milan, Italy
[f] School of Psychology, Vita-Salute San Raffaele University, Milan, Italy
[g] Department of Philosophy, Sociology, Education, and Applied Psychology, Section of Applied Psychology, University of Padova, Padova, Italy

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ABSTRACT

Study objectives: We tested the hypothesis that patients with extreme sleep state misperception display higher levels of psychopathology and reduced quantitative estimation abilities compared to other patients with insomnia. Secondary aims included the evaluation of group differences in subjective self-reported quality of life and sleep quality and objective sleep parameters.

Methods: In this cross-sectional, observational study, 249 patients with insomnia underwent a video-polysomnography with a subsequent morning interview to assess self-reported sleep estimates and filled in a large battery of questionnaires. Patients were classified into High Misperception (HM) and Moderate Misperception (MM) groups, according to the complement of the ratio between self-reported total sleep time and objective total sleep time (Misperception Index).

Results: No significant differences emerged in any of the psychopathological measures considered between the HM and the MM group. Similarly, no effect was observed in quantitative estimation abilities. HM patients displayed a significantly increased number of awakenings per hour of sleep and a reduced dream recall rate. Their overall sleep quality and quality of life was significantly impaired.

Conclusions: Future research on sleep misperception should focus on factors other than the level of psychopathology and estimation abilities, in particular sleep microstructure and quantitative EEG studies in both REM and NREM sleep.

1. Introduction

With a prevalence of about 7% in the general population, Insomnia Disorder (ID) is the most frequent sleep disorder encountered in clinical practice and one the most common mental disorders (Wittchen et al., 2011). ID is defined by difficulty in initiating and/or maintaining sleep or early morning awakening, often associated with a sensation of poor sleep quality and impaired daytime functioning (AASM, 2014).

Strikingly, the objective evaluation of sleep by video-polysomnography (v-PSG), the gold standard for the investigation of sleep disorders, is not recommended for the diagnosis of ID (AASM, 2014). This places the self-reported estimation of patients' sleep in a pivotal role for both the assessment and treatment of this disorder. However, the ability and accuracy of patients' sleep estimation might be

Abbreviations: AHI, apnea/hypopnea index; EEG, electroencephalogram; HM, high-misperception; ID, insomnia disorder; MI, misperception index; MM, moderate misperception; MMPI, Minnesota multiphasic personality inventory; NREM, non-rapid eye movement sleep; SCL, symptom checklist; PI, paradoxical insomnia; PLM, periodic limb movements; PLMSI, periodic limb movement in sleep index; PSG, polysomnography; PSQI, Pittsburgh sleep quality index; REM, rapid-eye movement sleep; SE, sleep efficiency; SF, Short form questionnaire; TST, total sleep time.

☆ Institution where work was performed: San Raffaele Hospital.All authors have seen and approved the manuscript.

* Corresponding author at: Via Tesserete 46, 6900 Lugano, Switzerland.
E-mail address: anna.castelnovo@eoc.ch (A. Castelnovo).

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impaired, as suggested by a tendency towards an might be impaired, as suggested by the tendency towards an underestimation of sleep duration and an overestimation of sleep latency and wake after sleep onset (Castelnovo et al., 2019). This error in sleep estimation is common among all ID patients, but a specific subpopulation of these patients systematically displays a marked discrepancy between objective and self-reported sleep. The magnitude of this error is so extreme that the existence of a separate pathological entity, namely paradoxical insomnia (PI), has long been postulated and discussed (Castelnovo et al., 2019; Manconi et al., 2010).

In a previous study by our group (Manconi et al., 2010), we tested the so called "misperception index" (MI) in a large sample of patients with ID to reliably measure sleep state misperception. MI is an index that takes into account both self-reported and objective (PSG-based) sleep parameters in the following formula: the difference between objective Total Sleep Time (o-TST) minus self-reported Total Sleep Time (s-TST), divided by the o-TST(Castelnovo et al., 2019). It allows to distinguish between a "high misperception" group (HM) versus a "moderate misperception" group (MM) (Manconi et al., 2010), classified according to a MI cut-off of 0.9, which essentially falls between the two peaks of the MI binomial distribution. We decided to set up the present study as a logical following step to explore whether specific clinical variables could be associated with the degree of sleep state misperception.

Several possible factors have been implied behind the concept of misperception (Harvey and Tang, 2012) ranging from psychological distress causing magnification of symptoms to electrophysiological abnormalities causing a deterioration of sleep quality. Among these latter factors, an increased number of awakenings is an intuitive but surprisingly uninvestigated macrostructural parameter that could be linked to a deterioration of sleep continuity and perception. Indeed, there is some evidence that awakenings (and/or sleep instability) at the beginning of the night (Hauri and Olmstead, 1983; Hermans et al., 2020b), together with errors in time estimation (Hermans et al., 2020a), influence the perception of the sleep onset. We herein investigate some of the constructs that might interact in the genesis and maintenance of extreme sleep state misperception in a cohort of patients with insomnia, subclassified using the MI (Manconi et al., 2010). First, we investigated personality traits/psychopathological dimensions with the Minnesota Multiphasic Inventory (MMPI-2) (Butcher et al., 2001) and the Symptom Checklist (SCL-90) (Derogatis et al., 1973), under the main hypothesis that PI patients pay particular attention on their somatic complaints, managing psychological difficulties trough physical symptoms (van de Laar et al., 2010). Moreover, we explored a selective impairment in quantitative estimation abilities by means of the Cognitive Estimation Task (CET) (Della Sala et al., 2004; Shallice and Evans, 1978). Secondary aims were to compare between-group differences in several self-reported and macrostructural PSG parameters (like the awakening index), subjective sleep quality as measured by the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989) and the quality of life via the Short-Form Questionnaire 36 health survey questionnaire (SF-36) (Jenkinson et al., 1993a).

2. Methods

Two-hundred-and-forty-nine consecutive patients with ID were recruited at the Sleep Medicine Centre of the San Raffaele Scientific Institute (Milan). A subset of this sample overlaps with the patient's population used for a previous study by our group (Manconi et al., 2010).

All patients underwent: 1) a screening interview conducted by a psychiatrist and two board-certified neurologists, expert in sleep medicine, comprehensive of a detailed clinical history, and a neurological examination; 2) one full-night v-PSG study preceded by an adaptation night, and 3) structured questionnaire for the self-reported evaluation of sleep parameters the morning following the recording night.

PSQI and SF-36 were available for all participants, while CET, MMPI-2 and SCL-90 were available for a subset of participants.

All study procedures were reviewed and approved by the local Health Sciences Institutional Review Board and each patient signed an informed consent before the beginning of the study.

2.1. Patient selection

Inclusion criteria were: 1) a diagnosis of primary chronic (≥3 months) ID according to DSM-IV-TR criteria (APA, 2000); 2) age 18 years or over. Exclusion criteria were: 1) known neurological and medical disorders as well as mayor psychiatric disorders (psychotic disorders, bipolar disorders, mayor recurrent depression, obsessive compulsive disorder, post-traumatic and acute stress disorders, while personality traits or full-blown disorders were not a criterion of exclusion); 2) abuse of drugs or other substances; 3) an AHI (apnea/hypopnea index = number of apnea/hypopnea events per hour of sleep) >5, while no cut-off was considered for the number of leg movements per hour of sleep (PLMSI); 4) other significant sleep disorders, including a diagnosis of REM or NREM sleep parasomnia, circadian rhythm sleep-wake disorders, movement disorders, such as restless leg syndrome and periodic leg movement disorder. This dataset largely overlaps with the one presented in a recently published review by our group.(Castelnovo et al., 2019).

2.2. Insomnia subtypes

Following our previous conclusions (Castelnovo et al., 2019), we will use for the current study the so-called Mispeception Index (MI) (Manconi et al., 2010). Given that the estimation error is usually large (±120 min), an o-TST shorter than 120 min was also considered as a criterion in order to take into account the "resolution power" of the normal self-reported evaluation of o-TST. The statistical analysis of the distribution of MI disclosed the presence of two subgroups of Patients with ID: a High Misperception group (HM) and a Moderate Misperception group (MM), discriminated by an MI cut-off of 0.9 (Manconi et al., 2010). Based on this, we defined HM as patients who presented the following values: $MI = \frac{oTST - sTST}{oTST} > 0.9 \& oTST \geq 120$.

2.3. Video-polysomnographic recording and objective parameters

v-PSG recordings were performed in a sleep laboratory setting according to standard guidelines (Berry et al., 2012). Briefly, the nocturnal v-PSG retained for analysis was carried out after one adaptation night (not considered in the current analysis) in a sound-attenuated sleep laboratory room. Participants were not permitted to drink caffeinated and alcoholic beverages during the afternoon preceding the recordings. Lights-out time was based on individual habitual bedtime. Participants were allowed to sleep until their spontaneous awakening in the morning. The following signals were recorded: electroencephalogram (EEG) (at least 6 channels, including C3 or C4 and O1 or O2, referred to the contralateral mastoid); electro-oculogram (electrodes placed 1 cm above the right outer cantus and 1 cm below the left outer cantus and referred to the left mastoid), electromyogram of the submentalis muscle and of the right and left tibialis anterior muscles (bipolar derivations with two electrodes placed 3 cm apart on the belly of the tibialis anterior muscle of each leg), and electrocardiogram (CM4 derivation: anode in position V4 and cathode attached to the manubrium of the sternum). The sleep respiratory pattern of each patient was monitored using oral and nasal airflow thermistors and/or nasal pressure cannula, and wearable piezoelectric bands to detect thoracic and abdominal movements.

Sleep stages were scored visually by a single neurologist blind to the patients' identity, following standard criteria (Rechschaffen and Kales, 1968). The following traditional parameters were calculated: TST, number of awakenings, percentage of non-rapid eye movement (NREM) sleep stages 1–4 and rapid-eye movement (REM) sleep, sleep efficiency

(SE: total sleep time / time in bed × 100), sleep onset latency, and REM latency. Finally, apnea-hypopnea events and leg movements were also detected visually and related indexes calculated according to standard criteria (Iber et al., 2007).

2.4. Self-reported sleep parameters

Self-reported sleep parameters were collected in the morning within two hours after the end of the second PSG recording using a structured questionnaire. Standardized questions comprised: "At what time did you go to bed?" 2) "At what time did you wake up?" 3) "How long did you sleep last night? Please provide an estimate in hours and minutes" 4) "How many minutes did it take you to fall asleep at bedtime last night?" 5) "How many times did you wake up tonight?" 6) "Did you dream last night?" 7) "How did you sleep last night? Like at home, worse, or better than an average night at home?"

2.5. Psychopathology questionnaires

SCL-90 is a self-report psychometric inventory composed of 90 items scored on a five-point Likert scale, designed to evaluate a broad range of psychological problems and symptoms of psychopathology during the time reference of one week, on nine different subscales. It has been used widely as a measure of mental status, as a screening instrument, and as a treatment outcome measure (Derogatis et al., 1973). Single items cover distress expressed both inwards (depression, somatization and anxiety) and outwards (aggression, impulsivity and psychoticism). The transformation of the raw data to T scores, with the sociodemographic factors taken into consideration, makes an oriented classification of the individual case possible. T scores starting at 60 are considered slightly elevated, at 65 obviously, at 70 strongly and at 75 very strongly elevated.

MMPI-2 is a standardized psychometric test widely used worldwide that assesses psychopathologic symptoms covering several psychological areas. Although MMPI was originally designed in 1939, many additions and changes have been made over time to improve interpretability of the original clinical sub-scales. All 10 clinical scales and all 15 content scales were administered following standardized rules and scored accordingly (Butcher et al., 2001). T scores with a mean of 50 and a standard deviation of 10 were generated for all scales with reference to standardized tables of the general population; scores $\geq$65 (1.5 SD above the mean) indicate a significant deviation from the original normal standardized values and suggest a clinically significant pattern.

2.6. Cognitive estimation evaluation

CET is a tool assumed to be reliable for the assessment of frontal lobe function. It measures the performance on estimation tasks. The test is composed of 21 questions that require participants to quantify items or phenomena met in the everyday life with numerical responses. If patients are unable to produce a prompt estimate, they are encouraged to guess. Total scores range from 0 to 42 (Della Sala et al., 2004; Shallice and Evans, 1978). Higher scores indicate poorer performance. Scores are assigned, for each question, on the basis of the accuracy of the provided estimate (0 if the estimate ranged from 0% to 30% above or below the correct answer, 1 if it ranged from 31% to 90% above or below the correct answer, and 2 if it is >90% above and below the correct answer). Some questions in the CET questionnaire are related to time estimation abilities, in its strict meaning of being able to estimate the passing of time in the first person, like for example "How long does it take for a young man to walk one kilometer?", "Approximately how many coffees a barman in a motorway restaurant can make in one hour during rush hour?". Other items concern more dimensional estimation abilities like "How high is a traffic light?", or "How heavy is a horse?".

2.7. Quality of life and quality of sleep questionnaires

SF-36 is one of the most used patient-reported surveys of patient health. It consists of 8 scaled scores: vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning and mental health. The PSQI is a self-report questionnaire that assesses sleep quality and a number of sleep symptoms over a 1-month time interval. It differentiates "poor" from "good" sleep quality by measuring a global score derived from questions in seven areas (components): self-reported sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications, and daytime dysfunction.

2.8. Statistics

Data analysis was performed by using the R software (v. 3.5.3) [R-core project (Team, 2014, 2017) and the following packages were used to perform statistical analysis: 'esvis' (v. 0.3.1) (Anderson, 2020), 'ggplot2' (v. 3.1.0) (Wickham, 2016), and 'psych' (v. 1.8.12) (Revelle, 2018).

Preliminary assumption testing was conducted to check for normality, linearity, univariate and multivariate outliers, homogeneity of variance-covariance matrices, and multicollinearity, with no serious violations noted. Level of significance was a priori set to 0.05.

Considering the strong unbalanced size of the two samples (MM: 213, 85.5% vs. HM: 36, 14.5.%), multivariate analysis of variance (MANOVA) could not be performed. Thus, several Welch's independent sample *t*-test were performed for successive comparison analysis.

In the first series of *t*-tests, 9 dependent variables were used, corresponding to the symptomatic dimensions of the SCL-90: somatization, obsessive compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism.

In the second series of *t*-tests, 10 dependent variables were used, corresponding to 10 selected clinical scales of the MMPI-2: hypochondriasis, depression, hysteria, psychopathic deviate, masculinity/femininity, paranoia, psychasthenia, schizophrenia, hypomania, social introversion.

In the third series of *t*-tests, 15 dependent variables were used, corresponding to 15 selected content scales of the MMPI-2: anxiety, fears, obsessiveness, depression, health concerns, bizarre mentation, anger, cynicism, antisocial practices, type A behavior, low self-esteem, social discomfort, family problems, work interference, negative treatment indicators.

In each Welch's independent sample *t*-test analysis, MI (HM vs. MM) was used as an independent variable. Considering the different sample size between the two groups, the Hedge's *g* (Hedges, 1981) was used to quantify the strength of mean differences (effect size). In addition, the 'overlapping index' (η) (Pastore, 2019) – and its complement (1-η) – were computes to quantify the kernel density distribution overlap – and separation – between the two groups.

Because it is known that there is a strong gender effect in CET scores, a linear regression-based interaction was conducted to explore the impact of both MI and gender on estimation errors as measured by CET scores.

The cut-off for significance was set to 0.05 and was adjusted for multiple comparisons using the Bonferroni correction. Effect size was interpreted using the following benchmarks: null (< 0.20), small (from 0.20 to 0.49), moderate (from 0.50 to 0.79), and large (equal or greater than 0.80).

Group comparisons between HM and MM on several demographic parameters, SF-36, PSQI and self-reported and objective sleep variables were conducted using parametric (independent unpaired *t*-tests) or non-parametric (Mann-Whitney *U* tests or Chi-square tests for independence) according to data distribution.

3. Results

3.1. Group demographics and group MMPI, SCL-90 and CET rates

The overall sample was composed of 249 patients with ID (mean age 49.8 years, SD 13.16, range 18–81 years): 60% females, 43% drug-free, 57% under pharmacological treatment (mainly benzodiazepines and/or antidepressants).

Considering the overall sample, on average, men were significantly younger (mean age 46.5 years, SD 12.88) than women (mean age 52.0, SD 13.08): $t_{(247)} = -3.303$, $p = 0.001$, $g = -0.426$, $\eta = 0.732$). Although numerically more women (n = 149, 59%) than men (n = 100, 53%) were taking drugs at the moment of the recording, this difference did not reach statistical significance ($\chi^2 = 0.895$, $p = 0.344$; Cramér's V = 0.060). Patients taking drugs were slightly older (mean age 51.2 years, SD 13.38) than patients who were not taking drugs, with borderline levels of statistical significance (mean age 47.9 years, SD 12.92): $t_{(247)} = -1.934$, $p = 0.054$, $g = -0.247$, $\eta = 0.739$.

All but three participants underwent the second PSG night, therefore, it was possible to calculate different indexes of misperception for 246 out of 249 patients with ID. According to MI, 36 patients (15%) were classified as HM. 237 patients with ID out of 249 filled in the CET, 221 patients with ID out of 249 filled in the SCL-90, 177 patients with ID out of 249 filled in the MMPI-2. No relevant differences emerged comparing HM and MM for age, gender and drug-status (see Table S1).

3.2. Objective and self-reported sleep parameters

Table 1 summarizes average values for objective and self-reported sleep parameters for the whole ID sample and for ID subgroups and their comparative statistics. The HM group gave significantly worse self-reported sleep estimates in terms of self-reported sleep latency, self-reported total sleep time, and reduced dream recall (large/medium effect sizes), but a lower self-reported number of awakenings as a measure of sleep fragmentation (moderate effect size). Interestingly, 29 patients self-reported a null total sleep time, and a concurrent sleep latency of 0 (by convention). HM and MM also differed in terms of self-reported sleep quality (moderate effect size), meaning that most of the HM patients reported that their overall perception of sleep the day of the PSG recording was worse than an average night at home, while MM patients reported they slept similarly to an average night at home. Moreover, as a group, HM displayed slightly reduced objective TST, SE and increased light sleep compared to the MM group, although these differences did not survive multiple comparison correction: 0.05/19 = 0.0026, except for a higher number of awakenings per hour of sleep (small effect size).

3.3. SCL-90 scale scores

Participants reached, on average, borderline scores for all SCL-90 subitems except for phobic anxiety; however, average values were below the pathological threshold for all subitems. The percentage of participants that exceeded the pathological threshold ranged from 3 to 7%, values that are in line with the psychiatric screening conducted at the moment of the enrollment.

As reported in Table 2, there were no statistically significant differences between the MM and the HM groups concerning psychological symptoms – measured by the SCL-90. The effect size revealed null-to-small strength of mean differences. Similarly, the complementary overlapping index (η) suggested a large density distribution overlap between the two groups (see Fig. S1).

3.4. MMPI-2 scores

Note: Independent-samples T-test was used for between-group comparisons.

Table 1
Comparisons between moderate misperception and high misperception insomnia groups on subjective and objective sleep parameters.

	Moderate misperception		High misperception		Group comparison		
	M	SD	M	SD	Type of statistics	p-value	Effect size
sTST (min)	246.8	113.57	3.0	7.17	T	<0.001*	0.80
sSOL (min)	68.6	72.84	17.8	51.04	W	<0.001*	0.57[c]
sAW	3.4	4.33	0.3	1.06	W	<0.001*	0.44
DREAMs	0.6	0.68	0.2	0.54	C	<0.001*	0.46[b]
sQUAL	1.8	0.85	2.3	0.75	C	0.005	0.21
oTST (min)	388.8	92.44	350.1	90.60	T	0.028	0.02
REMcyc	3.8	1.32	4.1	1.43	T	0.191	
oAW	12.4	5.85	15.2	6.19	T	0.015	0.02
oAWI	0.0	0.01	0.1	0.03	W	0.001*	0.22
N1 (%)	4.4%	3.48%	4.4%	2.35%	W	0.048	0.13
N2 (%)	51.2%	10.87%	51.2%	11.97%	T	0.967	
N3 (%)	13.7%	10.13%	13.7%	7.05%	W	0.332	
N4 (%)	9.7%	9.77%	9.8%	8.71%	W	0.508	
REM (%)	21.4%	8.12%	21.4%	7.67%	W	0.871	
oSOL (min)	30.6	37.41	31.7	33.66	W	0.486	
N2L (min)	26.1	35.48	23.4	32.81	W	0.679	
REML (min)	100,0	59.06	97.7	62.74	W	0.767	
oSE (%)	78.3	16.18	71.5	16.68	T	0.029	0.02
PLMI	11.9	22.89	9.5	14.36	W	0.859	

Note: Type of statistics selected according to data distribution (T: Independent-samples T-test; W: Mann-Whitney U Test; C: Chi-square test for independence). sTST: subjective total sleep time; sSOL: subjective sleep onset latency; sAW: number of subjective awakenings; DREAMs: dreams remembered where 0 means "no dreams", 1 "at least one dream", and 2 "I don't know"; sQUAL: subjective sleep quality from 1 to 3 where 1 stands for 'equal to an average night at home', 2 for 'better than an average night at home', and 3 for 'worse than an average night at home'; oTST: objective total sleep time; REMcyc: number of REM episodes; oAW: number of objective awakenings; oAWI: objective awakening index, i.e. number of awakenings per minute of sleep; N1(%): percentage of total sleep time spent in N1; N2(%): percentage of total sleep time spent in N2; N3(%): percentage of total sleep time spent in N3; N4(%): percentage of total sleep time spent in N4; REM(%): percentage of total sleep time spent in REM; oSOL: objective sleep onset latency; N2L: latency to N2; REML: latency from sleep onset to the first REM episode; oSE: objective sleep efficiency; PLMI: number of periodic leg movements per hour of sleep.

* These p-values are below the 0.002 threshold set according to Bonferroni's multiple comparison correction (0.05/19).

[b] As 24 subjects in the MM group vs 0 subjects in the HM group scored 2 ("I don't know") at the dream recall question, the between-group comparison was tested also after excluding those subjects who scored 2 and confirmed a significant difference between groups.

[c] This comparison remained non-significant after the removal of subjects with a null s-TST.

Table 2
Comparisons between moderate misperception and high misperception insomnia groups on SCL-90 scales scores.

	Moderate misperception		High misperception		Group comparison		
	$M_{T\text{-}scores}$	$SD_{T\text{-}scores}$	$M_{T\text{-}scores}$	$SD_{T\text{-}scores}$	t	p-value	Effect Size
Somatization	66.7	16.76	72.3	17.59	−1.717	0.093	0.33
Obsessive compulsive	66.1	15.60	71.50	21.80	−1.363	0.181	0.32
Interpersonal sensitivity	61.0	16.40	66.0	22.16	−1.232	0.225	0.29
Depression	68.0	16.23	71.4	19.40	−1.075	0.289	0.23
Anxiety	68.0	17.30	71.6	21.90	−0.923	0.361	0.21
Hostility	60.3	16.46	61.8	23.54	−0.366	0.717	0.09
Phobic anxiety	56.7	15.70	59.9	18.21	−0.943	0.351	0.20
Paranoid ideation	61.4	16.13	65.6	19.15	−1.174	0.247	0.25
Psychoticism	66.5	19.72	72.6	27.93	−1.218	0.231	0.29

Hypochondriasis and depression item average exceeded the 65-point cut-off considered indicative of pathology [66.26 ± 12.88 (57%) and 68.53 ± 12.32 (57.6%)], and Hysteria reached borderline levels [64.42 ± 12.98 (46.5%)].

As reported in Table 3, there were no statistically significant between-group differences regarding psychopathological symptoms measured by the MMPI-2 clinical scales. In addition, there were no statistically significant differences between groups (HM vs. HM) regarding almost all the content scales of the MMPI-2 (see Table 4). The only exception was the social discomfort scale that reached single-level significance ($t = 3.152$, $p = 0.003$) with an associated effect size of moderate strength (0.579) and a moderate separation of densities distributions. However, using the Bonferroni correction for multiple comparisons, this result was no longer significant ($0.05/25 = 0.002$). See Supplementary Figs. 2 and 3 for a graphical representation of the overlapping index and its complement.

3.5. Interaction between misperceives and gender on CET scores

A linear regression-based model suggested that the interaction between groups (HM vs. MM) and gender (male vs. female) on CET scores was not statistically significant: $\beta = 1.296$ (se = 1.196), $t = 1.084$, $p = 0.279$; $R_2ajd = 0.057$. Moreover, also the group main effect (HM vs. MM) was not statistically significant: $\beta = -0.725$ (se = 1.999), $t = -0.362$, $p = 0.717$. However, there was a statistically significant main effect of gender (male vs. female) on CET scores, in line with the literature: $\beta = 1.203$ (se = 0.455), $t = 2.644$, $p = 0.008$. A graphical representation of this analysis is reported in Fig. 1.

3.6. Quality of life and quality of sleep questionnaires

Average values of SF-36 were well below standard values (Jenkinson et al., 1993b): physical functioning scores 77% (normal 92.5%), social functioning 53% (normal 91.3%), role limitations - physical 38% (normal 91.4%), role limitations - emotional 42% (normal 85.6%), mental health 53% (normal: 75.4%), energy/vitality 44% (normal: 64.0%), pain 56% (normal: 86.3%), general health perception 51% (normal: 78.8%). No significant difference emerged between groups (HM vs. MM) for any SF-36 sub-scale. The only exception was role limitations-emotional, which was significantly higher in the HM group compared to the MM group (moderate effect size). However, this

Table 4
Comparisons between moderate misperception and high misperception insomnia groups on MMPI2 content scale scores.

	Moderate misperception		High misperception		Group comparison		
	$M_{T\text{-}scores}$	$SD_{T\text{-}scores}$	$M_{T\text{-}scores}$	$SD_{T\text{-}scores}$	t	p-value	Effect Size
Anxiety	63.9	11.71	63.1	10.76	0.302	0.764	0.06
Fears	57.2	12.08	60.1	12.17	−1.046	0.305	0.23
Obsessiveness	56.7	11.37	56.0	10.04	0.299	0.767	0.06
Depression	61.4	13.07	58.1	9.73	1.445	0.158	0.26
Health concerns	64.2	12.11	64.1	11.46	0.028	0.977	0.01
Bizarre mentation	55.4	11.16	54.4	14.29	0.339	0.737	0.09
Anger	53.9	10.69	51.2	9.52	1.242	0.224	0.26
Cynicism	53.7	10.54	53.9	10.58	−0.105	0.917	0.02
Antisocial practices	51.5	9.67	52.5	9.96	−0.445	0.660	0.10
Type a behavior	52.8	9.40	50.4	10.11	1.046	0.305	0.25
Low self-esteem	56.5	11.72	55.0	10.82	0.601	0.552	0.13
Social discomfort	56.2	11.55	49.7	8.72	3.152	0.003	0.58
Family problems	57.8	11.68	54.2	11.37	1.375	0.180	0.31
Work interference	60.9	12.66	57.4	9.18	1.595	0.120	0.29
Negative treatment indicators	58.7	11.41	57.7	15.10	0.279	0.782	0.08

Note: Independent-samples T-test was used for between-group comparisons.

Table 3
Comparisons between moderate misperception and high misperception insomnia groups on MMPI2 clinical scale scores.

	Moderate misperception		High misperception		Group comparison		
	$M_{T\text{-}scores}$	$SD_{T\text{-}scores}$	$M_{T\text{-}scores}$	$SD_{T\text{-}scores}$	t	p-value	Effect Size
Hypochondriasis	66.5	12.82	67.6	13.87	−0.364	0.719	0.09
Depression	69.7	12.20	63.7	13.27	2.001	0.055	0.49
Hysteria	64.3	12.28	66.5	17.96	−0.568	0.575	0.17
Psychopathic deviate	59.5	13.39	57.6	11.88	0.696	0.492	0.14
Masculinity/femininity	55.3	11.01	53.9	10.07	0.585	0.563	0.12
Paranoia	61.1	12.74	58.2	9.83	1.215	0.233	0.23
Psychasthenia	60.4	13.43	60.5	9.69	−0.045	0.964	0.01
Schizophrenia	60.0	10.87	57.5	11.22	0.985	0.334	0.23
Hypomania	51.8	10.46	50.3	12.86	0.525	0.604	0.14
Social Introversion	58.8	11.73	54.3	9.97	1.942	0.062	0.39

Note: Independent-samples T-test was used for between-group comparisons.

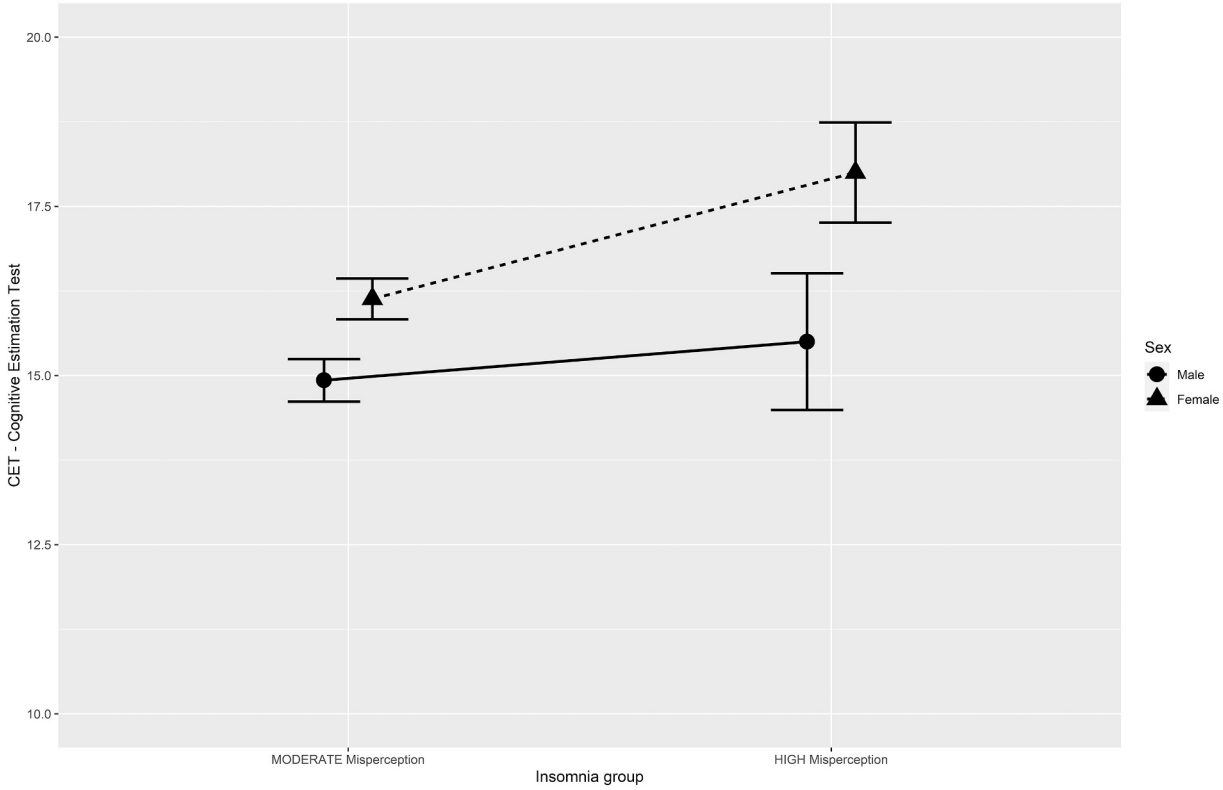

Fig. 1. Interaction between Insomnia Misperceiver Groups and sex on CET scores.

difference was no longer significant after multiple comparison correction.

All participants scored 5 or more at the PSQI (mean 14.5, SD 2.94) and no differences could be observed between the two groups: $t_{(235)} = -0.998$, $p = 0.325$.

4. Discussion

In this cross-sectional, observational study, we compared two standard psychopathology scales (SCL-90 and MMPI-2) in a large sample of patients with ID, divided in HM and MM, according to their MI. While as a group, patients with ID displayed high level of psychopathology and psychological distress, HM and MM did not differ for any psychopathologic dimension except for social discomfort. Our negative findings do not support the view that HM (as a surrogate of PI) is an expression of psychological distress or latent psychopathological traits.

Psychopathological abnormalities in ID, compared to healthy participants, have been previously assessed using the MMPI by several authors with controversial results (Harvey and Tang, 2012). Relevant studies found higher levels of psychopathology in patients with ID compared to normative values, especially in the depression and hypochondriasis sub-scales (Kales et al., 1976; Tsushima and Ingolfsdottir, 2004), in line with our results. These results have also been substantially corroborated by a comparison between patients with ID and healthy control participants in large-scale studies (Fernandez-Mendoza et al., 2011; Kales et al., 1983; Levin et al., 1984). However, these findings pertain to ID in general, without focusing on the PI subtype. Few small-sized studies (sample size <10) compared PI patients to healthy participants (Bonnet and Arand, 1997; Dorsey and Bootzin, 1997; Salin-Pascual et al., 1992) using the MMPI (Bonnet and Arand, 1997; Salin-Pascual et al., 1992) or the Eysenck Personality Inventory (Dorsey and Bootzin, 1997) that overall suggested increased hysteria or neuroticism levels. Vanable et al. (2000) found pathological scores of MMPI in the areas of hypochondriasis, hysteria and psychasthenia, as well as trends for depression and psychopathic deviate sub-scores in patients who underestimated their sleep, in comparison to those who overestimated or correctly estimated their sleep. The population studied (n = 74) consisted of a heterogeneous group of patients affected by various sleep disorders (psychophysiological insomnia and PI, according to the International Classification of Sleep Disorders, 2nd Ed [52], clinical criteria, obstructive sleep apnea, periodic limb movement disorder) classified in sleep under-estimators and normal or over-estimators, according to criteria largely overlapping with the MI. More recently, Dittoni et al. (2013) studied several psychological measures using a large battery of tests (Self-Administered Anxiety Scale, Beck's Depression Inventory, Maudsley's Obsessive Compulsive Inventory, Snaith–Hamilton Pleasure Scale, Eating Attitude Test) in sleep state misperception compared to other insomnia subtypes. The study did not find any predictor of sleep misperception. Interestingly, they used the MI, but they did not consider the suggested cut-off of 0.9, and instead divided "misperceptors" and "non-misperceptors" on the basis of the median value of the MI score. Indeed, the MI distribution was mono-modal and not bi-modal as the one observed by our groups, perhaps due to the smaller sample size considered (n = 74).

PI patients might also be characterized by a tendency to over-report their symptoms (Harvey and Tang, 2012). However, it should be noted that PI patients do not overemphasize every symptom since they do not usually report excessive daytime sleepiness (Galbiati et al., 2018) and they may even underestimate the number of their awakenings during sleep (Carskadon et al., 1976; Coates et al., 1982). Our study confirms this latter data, showing a reduced number of remembered awakenings (despite an increase in objectively recorded awakenings during sleep). This is probably related to the fact that patients selected in the HM group represent the "extreme" tail of sleep misperception, including patients who reported no sleep or a very limited amount of sleep.

We also compared the MM versus the HM group on quantitative estimation abilities as assessed by CET scores, obtaining negative results. These data are in line with the available literature (Rioux et al., 2006;

Tang and Harvey, 2005) that do not support the presence of a generic time estimation impairment in ID. No study ever attempted to specifically characterize PI. A previous PSG study did not find any correlation between MI and CET scores in patients with ID; a distinction between HM and MM was not provided (Galbiati et al., 2018). However, based on a previous experiment (Tang and Harvey, 2004), it is plausible to predict that the estimation error is specific for sleep in these patients, and modulated by their negative subjective expectations about sleep.

Contrary to our expectations, the most thought-provoking findings emerged from the analysis of self-reported and objective sleep variables. Given the definition itself of MM and HM, HM participants gave significantly poorer rates of self-reported sleep estimates (except for the number of awakenings, as mentioned above) and had only slightly decreased objective total sleep time and increased stage 1. Despite claiming a limited amount of sleep or no sleep at all, subjective sleep onset latency was relatively short in the HM group. This was related to the fact that they mainly complained of waking up soon after falling asleep. Very intriguingly, our HM group had a largely reduced dream recall rate compared to MM. This observation supports a relevant line of research linking REM sleep to sleep misperception (Feige et al., 2008; Feige et al., 2018; Riemann et al., 2012). In this view, patients with insomnia tend to misperceive dreaming with wakefulness. Therefore, it is plausible that HM might report a decreased frequency of dream recall in comparison to MM in spite of a comparable amount or REM sleep. Even more notably, the number of awakenings per hour of sleep was significantly higher. An increased number of awakenings can potentially influence subjective sleep duration by directly decreasing sleep efficiency and/or by altering sleep quality and perception (without affecting other macrostructural indices). Under this perspective, separate but closely distributed objective awakenings are merged together in a single sustained event, possibly due to the enhanced amount of activation and unstable sleep between two consecutive awakenings (Parrino et al., 2009). Indeed, the falling asleep process is highly asynchronous at the cortical level (Magnin et al., 2010). In the framework of the "local sleep" view, local isles of the brain may maintain a wake-like pattern for a protracted period of time, despite the global manifestation of sleep at the scalp level. This phenomenon might be more evident in patients with insomnia, who are known to show a state of "hyperarousal" (Riemann et al., 2010). Moreover, an increased awakening rate might be associated with a more generic increase in phasic EEG activations (including arousals, phases A of the so called cyclic alternating pattern or CAP (Parrino et al., 2012; Terzano and Parrino, 2000)). According to this second hypothesis (which does not exclude the first), the increased awakening rate is the manifestation of a broader sleep instability. Finer microstructural analyses, such as CAP analysis or quantitative EEG measures, might help to further elucidate more clearly these alternative (or complementary) hypotheses.

Feige et al. (2008) found an increased arousal index in both REM and NREM sleep (the REM sleep effect being more pronounced) in a group of 100 patients with a clinical diagnosis of physiological insomnia and that REM sleep time contributed significantly to the longer perception of wake time during sleep in patients with physiological insomnia. It's possible that this effect is accentuated in patients with higher sleep state misperception, increasing the mismatch between perceived and observed total sleep time. Parrino et al. [43] found a higher sleep instability (CAP rate, awakening rate and objective/subjective awakening ratio) in 20 patients with PI versus 20 healthy control participants. However, they did not compare patients with PI versus other ID subtypes and the level of misperception in patients classified as PI – calculated according to a complex combination of self-reported and objective total sleep time and sleep latency parameters - was relatively low. St-Jean et al. (2013) found increased delta activity in the left hemisphere in NREM sleep of 20 patients with PI compared to 26 patients with psychophysiological insomnia (as classified by a very complex index based on both self-reported and objective total sleep time, sleep onset latency and sleep efficiency), suggesting a deactivation of the left or a hyperactivation of the right hemisphere in these participants. The comparison with 21 good sleepers failed to show significant differences; hover, the low number of electrodes, and issues related to the multiplicity of statistical comparisons hamper the interpretation of the results. Highly interesting results emerged from quantitative high-density EEG analysis. A small pilot study on 8 subjects with ID revealed a local alpha increase during slow wave sleep over the sensory-motor areas (Riedner et al., 2016). A different larger high-density EEG study recently revealed that, in the general population, sleep state misperception (measured as mismatch between objective and self-reported TST) is associated with increased high frequencies relative to lower frequencies (beta/delta ratio) in both REM and NREM sleep (Lecci et al., 2020). The same study showed similar results, mainly limited to NREM sleep and central-posterior brain regions, and concluded that ID patients ($n = 10$) may correctly perceive subtle shifts towards wake-like brain activity. Although these results are limited to ID in general and do not specifically refer to PI, they support the idea that future research on PI should point towards the direction of objective and quantitative EEG analyses and that this analysis should not be restricted to NREM sleep. Under this view, PI might be particularly associated with more pronounced microstructural sleep abnormalities, especially in REM sleep, in this differing from other ID subtypes. Future polysomnographic studies with the aim to compare the severity of fragmentation during NREM vs. REM sleep in patients with high level of misperception vs. insomniacs with low level of misperception are warranted.

Last but not least, we found that, while patients with ID as a whole complained of a decreased quality of life, HM and MM shared similar complaints, except for higher emotional-related limitations in HM compared to MM. These results, on one hand suggest that, although PI patients tend to be unfairly labeled as complaining for a mere misattribution of wake while asleep, the degree of daytime impairment is relevant and comparable to other ID subtypes. On the other hand, the higher levels of daytime consequences in the emotional domain, goes along with the finding of impaired dreaming in PI and with the hypothesis of REM-sleep abnormalities, given the role of REM sleep in emotional regulation (Diekelmann and Born, 2010; Perogamvros and Schwartz, 2015).

4.1. Limitations

Despite the strength provided by the large sample size, some limitations should be highlighted. Our negative findings on MMPI-2 have been obtained in a large population of patients with ID, tested with a structured interview performed after a PSG evaluation and by using a validated method to measure sleep misperception and subdivide patients into HM and MM. While the reproducibility of the index used to classify HM versus MM needs further confirmation, especially with regard to its across-night stability, according to our recent review of the literature (Castelnovo et al., 2019), MI more closely resemble the clinical definition of PI (high discrepancy between self-reported perception and objective measures of sleep). However, it should be noted that no international agreement currently exists on which should be the best objective definition of PI, neither the existence of this ID subtype is recognized by all authors in the field. Indeed, a critical issue that makes very difficult any comparison between the studies in this field concerns the different and highly heterogeneous way to define "sleep state misperception insomnia", as recently reviewed by our group (Castelnovo et al., 2019).

Furthermore, although MMPI-2 and SCL-90 are two widely used and comprehensive questionnaires to assess psychopathologic levels, it cannot be excluded that they are not able to capture subtle differences that would have instead shown up from a thorough in person psychiatric interview. In particular, they might have missed to capture pathological personality traits according to the DSM-5 criteria as SCL-90 and MMPI-2 are not diagnostic instruments.

CET was used as a screening estimation questionnaire and finer

differences on temporal estimation abilities might have been overlooked. As mentioned in the methods, only few questions in the CET questionnaire are strictly related to time estimation abilities i.e., to estimate the passing of time in the first person. Therefore, finer cognitive questionnaires assessing frontal function and time estimation tasks might also be an area of further exploration, although no suggestive finding emerged from our data and the scarce literature on the topic.

Another potential flaw is the impact of medications, as half of the patients enrolled in the study were in mono- or polytherapy for ID. Indeed, another source of misperception concerns the pharmacological treatment for ID. Benzodiazepines reduce slow wave sleep (Borbely et al., 1985), reduce CAP rate and increase the power of higher frequency EEG band, when studied using spectral analysis (Manconi et al., 2017). BDZ might also affect cognitive function, such as memory, making more difficult the morning self-reported sleep estimation, and serotoninergic antidepressants suppress REM sleep (Gursky and Krahn, 2000). Benzodiazepines and antidepressants might affect sleep estimation and favor misperception. However, the percentage of treated participants were equivalent in both MM and HM groups.

Finally, our conclusion cannot be generalized to patients with major psychiatric diagnoses, who were excluded from this study. Studies specifically focused on these specific populations might yield new insights, given the heterogeneity of sample populations among ID subjects.

5. Conclusions and future directions

Many authors have doubted the existence of a group of patients with extreme sleep misperception as a distinctive entity, to the point that the current diagnostic criteria lump together all ID subtypes (AASM, 2005). Although the aforementioned negative results may support this point of view, the bimodal distribution of MI, together with the difficulties in the ID field related to the heterogeneity of ID itself, and the specific difficulties posed in clinical practice by these patients, support the idea that digging into the phenomenon of PI is warranted.

Overall, our results suggest that neither psychological distress nor quantitative estimation abilities are at the root of sleep state misperception and that future research should focus its efforts towards other directions. In particular, the analysis of sleep microstructure and quantitative EEG features, in both NREM and REM sleep, which have not been sufficiently covered by earlier research, deserve specific attention.

A meaningful change in perspective the field will probably emerge from a multimodal approach on large datasets combining different objective, self-reported, and clinical measures, as well as a combination between data-driven and definition-driven approaches.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijpsycho.2021.06.011.

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