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The autoimmune hypothesis of narcolepsy and its unexplored clinical features

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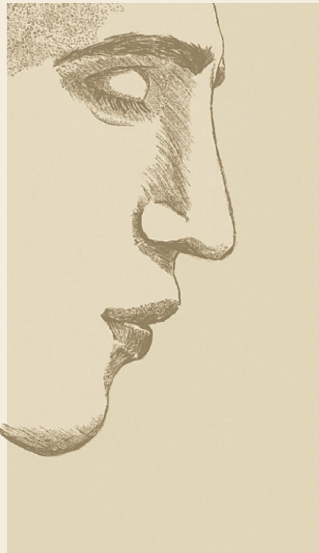
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Chapter 6

Daytime sleep state misperception in a tertiary sleep centre population

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Abstract

Study objectives: Sleep state misperception is common in various sleep disorders, especially in chronic insomnia with a prevalence ranging between 9-50%. Most prior studies used nocturnal polysomnography for the identification of sleep state misperception during nighttime. Our objective was to assess sleep state misperception during daytime in people with sleep disorders with excessive daytime sleepiness.

Methods: In this prospective observational study, we assessed the occurrence of, and factors influencing sleep state misperception in consecutive patients undergoing a routine multiple sleep latency test in a tertiary sleep-wake centre included between 2014 and 2017. Mixed models were applied to assess the influence of patients' clinical data on sleep state perception.

Results: People with narcolepsy type 1 (n=33) and type 2 (n=14), idiopathic hypersomnia (n=56), obstructive sleep apnea (n=31) and insufficient sleep syndrome (n=31) were included. The prevalence of both classical and reverse sleep state misperception did not differ between the sleep disorders (mean 25%, range 8-37%) after correction for sleep stage, sleep onset latency and age. Longer sleep onset latency and reaching only non-REM sleep stage 1 were significant predictors for classical sleep state misperception.

Conclusions: Sleep state misperception is common in people with narcolepsy type 1 and 2, idiopathic hypersomnia, obstructive sleep apnea and insufficient sleep syndrome. Classical sleep state misperception is more frequent in patients with longer sleep onset latencies who only reach non-REM sleep stage 1 during a nap.

Introduction

Sleep state misperception (or paradoxical insomnia) is common in chronic insomnia with a prevalence ranging between 9 and 50% (Bastien et al., 2014, Moon et al., 2015). The International Classification of Sleep Disorders, Second Edition (ICSD-2) defined sleep state misperception as a ‘consistent marked mismatch between objective findings from polysomnography (PSG) or actigraphy and subjective self-report or sleep diary’, but this concrete phrasing as a mismatch between objective and subjective measures has not returned in the ICSD-3 (ICSD, 2005, ICSD, 2014). Sleep state misperception has also been reported in other sleep disorders, such as obstructive sleep apnea (OSA), and in the general population (Castillo et al., 2014, Choi et al., 2016, Trajanovic et al., 2007). Most performed studies depend on nocturnal polysomnography for identifying sleep state misperception and finding patient-related predictors. Additionally, the focus is mainly on the situation in which subjective sleep time is lower than objective sleep time (classical sleep state misperception), while reverse sleep state misperception is not reported. Interestingly, sleep state misperception during daytime naps has not been well-studied.

Except for one study in OSA (Bishop et al., 1998), studies on sleep state misperception in sleep disorders with excessive daytime sleepiness (EDS) are absent, even though knowledge about sleep state perception seems highly relevant in the assessment of daily functioning for both the patient and the physician. Information about daytime sleep state perception could be an important addition to parameters such as subjective and objective sleepiness for the evaluation of disease severity, treatment decisions and fitness to drive (Liu et al., 2018).

Dreaming is another phenomenon which has not been extensively assessed during daytime naps. Emotions associated with dream perception are thought to be more intense in people with narcolepsy compared to healthy controls. This effect is even more pronounced during daytime naps and is associated with sleep-onset REM periods (SOREMPs (Fosse et al., 2002)).

We hypothesize that sleep state misperception is common in sleep disorders with EDS. Since we consider sleep state misperception in these disorders to be clinically most important during the day, we assessed sleep state perception and factors influencing it, including the occurrence of REM sleep, during the

20-minute nap opportunities of a multiple sleep latency test (MSLT). We also assessed the association between SOREMPs and dream perception.

Methods

Patients

In this prospective observational study, all consecutive patients undergoing a routine multiple sleep latency test between March 2014 and October 2017 in a tertiary sleep-wake centre were assessed for inclusion. All diagnosis were based on ICSD-3 criteria (ICSD, 2005). People with a diagnosis of narcolepsy type 1 (NT1) or 2 (NT2), idiopathic hypersomnia (IH), OSA or insufficient sleep syndrome were included.

Questionnaires

EDS was assessed using the Epworth Sleepiness Scale (ESS), which is validated in NT1 and NT2, IH and OSA (Johns, 1992). Sleep state and dream perception were assessed in the context of clinical care by asking patients after each nap whether they slept and dreamed during that specific nap. No feedback was given to the patient. Two types of sleep state misperception were defined: classical sleep state misperception was present when a patient did not report sleep when sleep was recorded, whereas reverse sleep state misperception was present when a patient did report sleep although sleep was not recorded. Dream perception was not defined as correct or incorrect.

Multiple sleep latency test (MSLT)

The MSLT was performed according to guidelines published before (Littner et al., 2005). It consisted of five sessions of 20 min in which patients had the opportunity to fall asleep. We did not extend these 20 minutes to allow for 15 min sleep after sleep onset. Nap opportunities were given with two hour intervals. The first session started at 09:00 hours. The night before the MSLT took place, a polysomnography was performed.

Statistical analysis

For assessing differences in ESS scores between sleep disorders with EDS, we used one-way ANOVA. Patients were stratified by diagnosis for these analyses.

Post-hoc analyses were performed to assess the differences between all separate groups. Differences in sleep stage sequences between sleep disorders with EDS were analyzed with *Pearson's* chi-squared tests with post-hoc testing to compare sleep disorders one by one. To assess whether other factors that were unevenly distributed amongst patient groups, such as age and sleep onset latency and sleep stages during the nap, might explain sleep state misperception, mixed models were applied to assess the influence of patients' clinical data on sleep state misperception. We included only the nap opportunities in which patients fell asleep and so focused on classical sleep state misperception only. Reverse sleep state misperception was insufficiently present in our dataset to be able to assess factors influencing this type of sleep state misperception. A linear mixed model with a random slope and a random intercept for each individual was fitted. The outcome was classical sleep state misperception. As main effects we added age, sleep disorder (NT1; NT2; IH;OSA; ISS), sleep onset latency, sleep stage reached and the presence of REM to the model. Differences in dream reporting between REM and NREM sleep were analyzed using *Pearson's* chi-squared tests. P-values below 0.05 were deemed significant. Bonferroni corrections were executed when needed. All analyses were conducted using the IBM SPSS Statistics 25 software package.

Results

Patient characteristics

A total of 165 people with 825 nap opportunities were included. People with NT1 and NT2 had a shorter mean sleep latency, had more SOREMPs and reported dreaming more frequently than people with IH, OSA and ISS (Table 6.1). People with NT1 had a shorter REM latency than others who had a SOREMP during the MSLT ($3.4 \text{ min} \pm 3.5$ vs. $5.7 \text{ min} \pm 3.7$; $p = 0.001$). Scores on the ESS differed significantly between sleep disorders, with people with NT1, NT2, IH and ISS scoring significantly higher than those with OSA (Table 6.2); median ESS of all sleep disorders were well above the cut-off value of 10. Information on polysomnography characteristics can be found in Supplementary table 6.1.

Table 6.1. Baseline and MSLT characteristics. In this table, baseline characteristics and information regarding the MSLT of all patients is summarized. Percentages of dream report are based on all naps, both with and without sleep.

	NT1	NT2	IH	OSA	ISS
N (MSLT)	33	14	56	31	31
Age (years \pm SD)	29.9 \pm 16.9	35.5 \pm 15.3	37.8 \pm 15.6	51.0 \pm 16.7	35.2 \pm 12.0
Gender (% male)	48.5	28.6	45.5	64.3	46.7
BMI (kg/m ² \pm SD)	23.7 \pm 3.6	24.4 \pm 4.3	25.5 \pm 4.7	28.2 \pm 4.4	25.7 \pm 4.4
Treatment (%)	3 (9%)	2 (14%)	9 (16%)	6 (19%)	2 (7%)
Sedatives	3	0	4	1	2
Stimulants	0	0	0	0	0
Antidepressants	0	0	4	5	2
Melatonin	0	2	2	1	0
MAD	0	0	0	1	0
CPAP	0	0	0	5	0
Naps (% sleep)	93.3	100	86.2	76.6	82.4
Sleep (n)	154	70	244	118	126
No sleep (n)	11	0	39	36	27
Sleep reported (%)	90.3	88.7	64.3	50.0	62.8
SOREMP (%)	58.8	44.3	1.5	2.1	4.7
Dreaming reported (%)	61.0	58.3	20.0	10.0	28.0
MSL (min \pm SD)	6.0 \pm 5.6	5.7 \pm 4.3	9.6 \pm 5.9	12.3 \pm 5.9	10.9 \pm 6.0

BMI = body mass index; CPAP = continuous positive airway pressure; IH = idiopathic hypersomnia; ISS = insufficient sleep syndrome; MAD = mandibular advancement device; MSL = mean sleep latency; MSLT = multiple sleep latency test; NT1 = narcolepsy type 1; NT2 = narcolepsy type 2; OSA = obstructive sleep apnea; SD = standard deviation; SOREMP = sleep-onset REM period.

Table 6.2. ESS scores. Sleep questionnaire scores of the patients that filled in the Epworth Sleepiness Scale to assess excessive daytime sleepiness.

Diagnosis	ESS	
	Median (range)	Above clinical cut-off
NT1	16 (2-21)	21/23 (91%)
NT2	15 (7-21)	10/11 (91%)
IH	15 (0-24)	36/48 (75%)
OSA	15 (0-24)	9/25 (36%)
ISS	13.5 (5-20)	23/30 (77%)

EDS = excessive daytime sleepiness; ESS = Epworth Sleepiness Scale; IH = idiopathic hypersomnia; ISS = insufficient sleep syndrome; NT1 = narcolepsy type 1; NT2 = narcolepsy type 2; OSA = obstructive sleep apnea.

Sleep state misperception is common in sleep disorders

In total, 72 people with sleep disorders had no classic sleep state misperception, 39 people with sleep disorders had 1 nap with classic sleep state misperception, 22 people with sleep disorders had 2 naps with classic sleep state misperception and 28 people with sleep disorders had more than 2 naps with classic sleep

state misperception. 4 patients did not sleep. Classical sleep misperception is common in NT1 and NT2 and even more so in IH, ISS and OSA ($p < 0.001$, Figure 6.1) with 25% of all nap opportunities in which sleep was recorded ($n = 712$), ranging from 7% in NT1 to 39% in OSA. Also reverse sleep state misperception is relatively common in NT1, IH, ISS and OSA with 26% of all nap opportunities in which no sleep was recorded ($n = 113$), ranging from 12% in OSA to 48% in ISS.

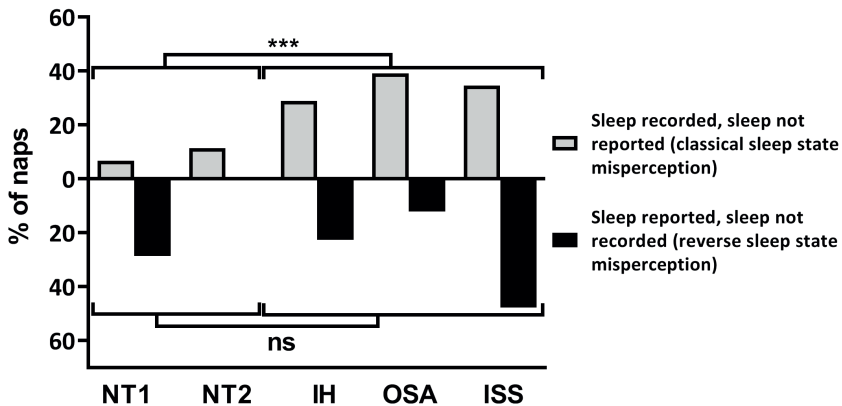


Figure 6.1. Sleep state misperception percentages in MSLT nap opportunities. This figure depicts the percentage of nap opportunities in which patients misperceived sleep per sleep disorder. Nap opportunities in which a patient did not report sleep when sleep was recorded (classical sleep state misperception) are shown in grey; nap opportunities in which a patient reported sleep when no sleep was recorded (reverse sleep state misperception) are shown in black. For classical sleep state misperception, percentages are based on nap opportunities in which sleep was recorded, whereas for reverse sleep state misperception, percentages are based on nap opportunities in which no sleep was recorded. Statistical significance of differences between NT1 and NT2 patients and IH, OSA and ISS patients is shown by the horizontal bars.

*** $p < 0.001$; IH = idiopathic hypersomnia; ISS = insufficient sleep syndrome; NT1 = narcolepsy type 1; NT2 = narcolepsy type 2; OSA = obstructive sleep apnea.

Long sleep onset latency and only N1 stage sleep predict sleep state misperception

Mixed model analysis took into account other parameters that might have influenced this seemingly strong effect of the sleep diagnosis on classical sleep state misperception during the MSLT. In the mixed model, only nap opportunities were used in which sleep was recorded. A long sleep-onset latency ($\beta = 0.114 \pm 0.033$; $p < 0.001$) and not reaching N2 stage sleep ($\beta = -0.708 \pm 0.329$; $p = 0.043$) were shown to be important predictors for sleep state

misperception during MSLT. Even though the diagnosis NT1 and age were predictors that were not statistically significant, the magnitude of their effect suggests there may be a clinically significant influence of these parameters on sleep state misperception (Table 6.3).

Table 6.3. Linear mixed model of sleep misperception. The linear mixed model of sleep misperception is fitted with a random slope and random intercept per individual for naps in which sleep was recorded. A positive value for B indicates a higher probability of sleep misperception. P-values are based on the parameters in the model. For specific categories within the parameters, such as sleep stage, the confidence interval for the coefficient of each category relative to the other categories is shown.

Parameter	B	95% confidence interval		p-value
		Lower boundary	Upper boundary	
Age (per year)	0.014	-0.005	0.032	0.143
Sleep onset latency (per min)	0.114	0.050	0.177	<0.001
Sleep stage reached				0.043
N1	0			
N2	-0.708	-1.352	-0.063	
N3	-0.204	-1.141	0.733	
SOREMP	-0.735	-1.784	0.313	0.169
Diagnosis category				0.273
NT1	0			
NT2	0.455	-0.734	1.643	
IH	1.043	-0.066	2.152	
OSA	1.112	-0.113	2.336	
ISS	1.289	0.097	2.480	
Nap (#)				0.302
1	0			
2	-0.354	-0.901	0.193	
3	-0.227	-0.828	0.374	
4	-0.141	-0.717	0.435	
5	-0.599	-1.217	0.019	

EDS = excessive daytime sleepiness; IH = idiopathic hypersomnia; ISS = insufficient sleep syndrome; NT1 = narcolepsy type 1; NT2 = narcolepsy type 2; OSA = obstructive sleep apnea; SOREMP = sleep-onset REM period.

Dream perception is partly dissociated from REM sleep

In 29.3% of naps in which patients had only NREM sleep, patients reported to have dreamed (Table 6.4). The distribution of these findings was different between sleep disorders: when a SOREMP was absent during the nap, people with NT1 and NT2 reported having dreamed more often than those with IH, OSA and ISS. Patient reported not to have dreamed in 25.8% of naps with a SOREMP. Interestingly, in 9 nap opportunities patients (1 NT1, 2 IH, 3 OSA, 3 ISS) reported having dreamed, even though no sleep was recorded.

Direct transition from wake to REM sleep or from wake via N1 to REM sleep is not a highly sensitive measure for NT1 and NT2

People with NT1 and NT2 transitioned from wake to REM sleep and from N1 to REM sleep significantly more often than those with IH, OSA or ISS when all naps were taken into account ($p < 0.001$ for both sleep stage sequences; Figure 6.2A). However, when only naps with a SOREMP were analysed, transitions from wake to REM sleep and from N1 to REM sleep were not found more often in NT1 and NT2 than in IH, OSA and ISS ($p > 0.05$ for both sleep stage sequences; Figure 6.2B).

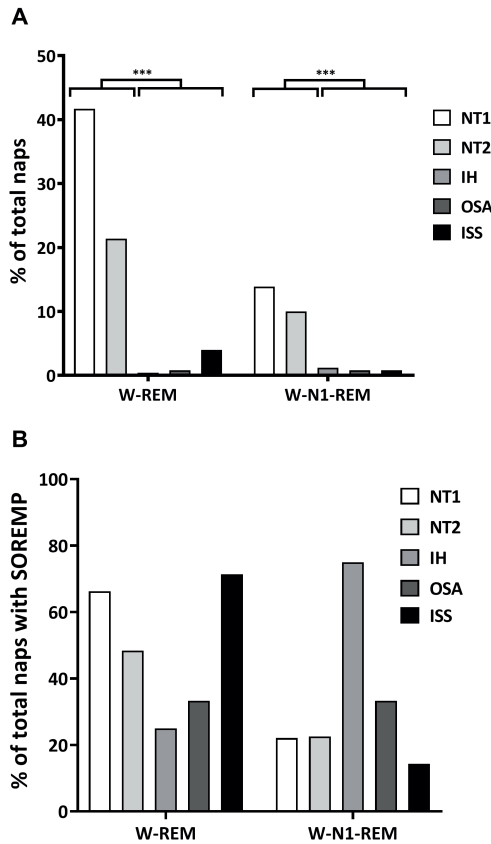


Figure 6.2. Sleep stage sequences in MSLT nap opportunities. A. Sleep stage sequences in all nap opportunities. Wake to REM and wake via N1 to REM sequences are represented for NT1, NT2, IH, OSA and ISS patients as a percentage of the total nap opportunities for that diagnosis. Statistical significance of differences between NT1, NT2 and IH, OSA and ISS patients is shown by the horizontal bars. B. Sleep stage sequences in nap opportunities with a SOREMP. Wake to REM and wake via N1 to REM sequences are represented for NT1, NT2, IH, OSA and ISS patients as a percentage of the nap opportunities with a SOREMP for that diagnosis.

*** $p < 0.001$; ns $p > 0.05$; IH = idiopathic hypersomnia; ISS = insufficient sleep syndrome; NT1 = narcolepsy type 1; NT2 = narcolepsy type 2; OSA = obstructive sleep apnea; W = wake.

Discussion

Sleep state misperception during the short nap opportunities of an MSLT was frequently seen in people with NT1, NT2, IH, OSA and ISS. Classical sleep state misperception was more common than reverse sleep state misperception, mostly due to the fact that in most nap opportunities sleep was recorded.

People with NT1 and NT2 patients misperceived their sleep less than those with IH, OSA and ISS. Multifactorial modelling on nap opportunities in which sleep was recorded, showed that this decreased prevalence of classical sleep state misperception in people with NT1 and NT2 is at least partly due to the fact that they were, on average, younger, had a shorter sleep latency and reached deeper sleep during a nap than those with IH, OSA and ISS. Despite this, a slightly lower percentage of classical sleep state misperception in people with NT1 and NT2 persists, albeit not significant after correction for other factors of influence in a linear mixed model, that could not be explained by the other factors in the model. The fact that sleep state misperception was almost absent in naps with dream reporting (data not shown) and the higher percentage of dream reporting in NT1 and NT2 supports the hypothesis that more intense emotions upon dream perception (Fosse et al., 2002) in people with NT1 and NT2 might explain part of the difference.

The increasing percentage of classical sleep state misperception with age, is in contrast with a study in people with chronic insomnia, where those with sleep state misperception were significantly younger than those without sleep state misperception (Moon et al., 2015). Other studies on sleep state misperception in chronic insomnia find no factors influencing sleep state perception, apart from those dictated by the sleep disorder itself (e.g. total sleep time (Dittoni et al., 2013, Moon et al., 2015)).

The significant percentage of nap opportunities in which people with different sleep disorders misperceived their sleep is in line with previous studies that describe significant poor sleep state perception in a variety of patient groups, such as chronic insomnia (up to 73% sleep state misperception), epilepsy, OSA and even healthy controls (Nam et al., 2016, Goulart et al., 2014, Ng and Bianchi, 2014, Mercer et al., 2002). All studies focused on classical sleep state misperception.

A SOREMP in a nap was not a significant predictor of sleep state misperception in our model. A reason could be the low number of SOREMPs in people with

other sleep disorders than narcolepsy. This may have led to a larger effect of narcolepsy in our model, that would otherwise be assigned to the presence of a SOREMP. A negative effect of selective REM-sleep deprivation on sleep state perception was shown in a study in healthy volunteers (Goulart et al., 2014), indicating a role of REM-sleep in sleep state misperception. Paradoxically, a strong positive correlation between amount of REM-sleep and perceived wakefulness in people with chronic insomnia has been described (Feige et al., 2008).

The fact that longer sleep onset latencies in nap opportunities were associated with more daytime classical sleep state misperception has been reported before in OSA patients (Bishop et al., 1998) and could also have another explanation. Due to the fact that a longer sleep onset latency unequivocally means that sleep duration during that nap was shorter, the increased sleep state misperception could therefore also be due to this shorter sleep duration. Another factor to consider is the limited duration of the nap, which restricts generalization of the relation between sleep onset latency and sleep misperception to these 20 minutes only.

A contribution of circadian factors to sleep state misperception was hypothesized in a PSG study in insomnia (Bianchi et al., 2012). In our study, we did not find a significant effect of nap timing, which argues against a role for circadian factors. Our study design did not allow for assessing the specific influence of psychiatric comorbidity, personality traits and coping mechanisms on sleep and dream perception, which were earlier described as potential determinants of sleep misperception (Fernandez-Mendoza et al., 2011). Based on the data that we had on psychiatric comorbidity, we did not see any effect on either sleep or dream perception (data not shown).

Medication and device use in our cohort was low, since most MSLTs were performed as part of the diagnostic process before medication was first prescribed. When patients using sedatives, CPAP, MAD and antidepressants were excluded from the analysis, significance of factors influencing sleep state misperception did not change (data not shown). Moreover, stimulants and sedatives were never used on the day of the MSLT. Additionally, we are not aware of any studies showing an effect of medication on sleep state misperception.

Most theories on sleep state misperception focus on the role of increased cognitive arousal and overgeneralization in people suffering from this condition (Takano et al., 2016, Maes et al., 2014, Bonnet and Arand, 1997). However, many

more mechanisms are described, that include a role for selective attention and the influence of transient awakenings (Harvey and Tang, 2012). Unfortunately, we were not able to include the effect of transient awakenings in our model.

Comparison of our findings on reverse sleep state misperception with other studies is challenging, since only few studies mention this type of sleep state misperception, almost exclusively during night time sleep in chronic insomnia (Attarian et al., 2004, Schneider-Helmert and Kumar, 1995, Trajanovic et al., 2007). It was proposed that increased alpha activity during sleep might play a role in reverse sleep misperception (Schneider-Helmert and Kumar, 1995, Schneider-Helmert, 2005).

Notably, dreaming was reported in a considerable amount of naps with only NREM sleep, consistent with extensive (nocturnal PSG) evidence on dreaming in NREM sleep with several studies disputing the paradigm of dreaming being confined to REM sleep (Aserinsky and Kleitman, 1953). Dream recall from NREM sleep stages is reported in 17.9% of NREM naps (both during night and day) in healthy males, while in only 51.2% of REM naps dream experiences were reported (Suzuki et al., 2004, Cavallero et al., 1992), broadly comparable with the percentages we found in this study. When dream perception was assessed only during daylight, it was also shown to be partly dissociated from REM sleep (Chellappa et al., 2009). Our results contribute to the notion that focusing on differences in dream content rather than crude dream perception between NREM and REM dreams might be more worthwhile in understanding the association between dreams and sleep physiology (Solms, 2000).

Our study design did not allow for a distinction between hypnagogic hallucinations, which people with narcolepsy may describe as a dream-like sensation in this context, and ‘normal’ dreams, since we only asked patients whether they dreamed or not. Theoretically, this might have led to an overestimation of the percentage of naps, both with and without SOREMP, in which patients reported to have dreamed.

Additionally, as reported before (Zhang et al., 2018), people with NT1 in this study have a shorter REM latency than other patients who have a SOREMP during MSLT. Also, the sleep stage sequences wake-REM and wake-N1-REM in the naps of the MSLT were found frequently in people with narcolepsy, in line with earlier findings (Marti et al., 2009, Ferri et al., 2016, Murer et al.,

2017). However, several earlier studies reported these sleep stage sequences in the naps of the MSLT to be highly narcolepsy-specific (Drakatos et al., 2016, Drakatos et al., 2013), while we also observed these transitions in the scarce naps with SOREMPs of people with IH, OSA and ISS.

As the study was performed in a tertiary sleep-wake centre, the makeup of the population is different than would be expected in a secondary sleep-wake centre. The relatively small amount of people with narcolepsy in this study, for example compared with people with idiopathic hypersomnia, is explained by the fact that many people with narcolepsy that are admitted to our tertiary centre have already undergone an MSLT in the referring sleep-wake centre and/or already on medication that cannot be interrupted. Repeating our approach in a secondary sleep-wake centre is therefore warranted to assess the generalizability of our findings.

The fact that research on daytime sleep state misperception is scarce (Bishop et al., 1998) led to a limitation in comparing our results with those of others. Most studies focus specifically on nocturnal sleep state misperception in which different definitions are used to describe the condition. Data is generated using nighttime PSG, while we use daytime data to describe and assess sleep state misperception. To be able to validate our findings, comparisons with other, more extensive, patient groups measured during daytime nap opportunities is needed. These cohort studies could also focus on reverse sleep state misperception. This type of sleep state misperception was scarce in this study and could therefore not be further analyzed using mixed models.

Conclusion

Both classical and reverse sleep state misperception during the short naps of an MSLT is common in NT1, NT2, IH, OSA and ISS. Classical sleep state misperception is more frequent in patients with longer sleep onset latencies who only reach non-REM sleep stage 1 during a nap. The fact that classical sleep state misperception is common in NT1, NT2, IH, OSA and ISS is relevant for patients and sleep physicians when assessing disease severity and fitness to drive and making treatment decisions in sleep disorders with EDS. Notably, dreaming was frequently reported even when REM sleep did not occur.

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Supplementary material

Supplementary table 6.1. Polysomnography characteristics. In this table, polysomnography characteristics of the night before the MSLT was performed are summarized. All values are presented as median (interquartile range).

	NT1	NT2	IH	OSA	ISS
N	33	14	56	31	31
Total sleep time (h)	7.2 (6.0-8.2)	7.0 (6.2-7.8)	7.0 (6.4-7.7)	6.8 (6.0-7.7)	7.0 (5.3-7.6)
Sleep efficiency (%)	89.8 (82.8-93.9)	88.7 (75.1-96.2)	91.8 (85.0-94.3)	82.5 (74.7-90.8)	93.2 (85.7-95.9)
Sleep latency (min)	5.2 (2.3-9.1)	4.8 (2.9-8.5)	10.7 (5.5-25.4)	15.1 (12.1-26.5)	8.8 (4.3-14.3)
REM sleep latency (min)	10.5 (2.0-125.0)	13.5 (4.5-90)	75.8 (57.5-117.4)	95.5 (64.0-168.0)	88.5 (51.1-110.4)
Wake-index (n/min)	3.4 (2.3-4.5)	2.3 (0.8-3.6)	2.3 (1.6-3.0)	3.0 (2.2-5.2)	2.1 (1.5-2.8)
AHI (n/min)	0.6 (0.1-2.4)	1.0 (0.2-3.5)	1.1 (0.1-3.0)	6.1 (2.2-17.1)	0.5 (0.0-4.0)

AHI = apnea/hypopnea-index; IH = idiopathic hypersomnia; ISS = insufficient sleep syndrome; MSL = mean sleep latency; NT1 = narcolepsy type 1; NT2 = narcolepsy type 2; OSA = obstructive sleep apnea.