Sleep Medicine 15 (2014) 967–972

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Nightmares in narcolepsy: underinvestigated symptom?

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ARTICLE INFO

Article history:
Received 9 December 2013
Received in revised form 26 February 2014
Accepted 3 March 2014
Available online 13 April 2014

Keywords:
Nightmares
Narcolepsy
Cataplexy
Gender and age differences
Polysomnographic findings
Neurobiological basis

ABSTRACT

Objective: Besides main disease symptoms, disturbing dreams are often found in narcoleptics and may contribute to disturbed sleep. Our main goal was to study different types of oneiric activity in narcolepsy with cataplexy (NC) and narcolepsy without cataplexy (N).
Methods: We have analyzed the medical history of 118 narcoleptics (64 men, 86 with NC, 32 with N, mean age 41.6 ± 15 years). Their most frequent dreams were divided into four groups: (A) low recall/mundane dreams, (B) vivid dreams without disturbing negative emotion, (C) nightmares, (D) reduction of nightmares, possibly by medication. Associations with other features of the disease were statistically analyzed.
Results: Nightmares were found in one-third of the patients, proportionally distributed in N and NC groups; not negatively charged vivid dreams appeared more frequently in NC patients ($P < 0.005$). No/mundane dreams occurred with higher prevalence in men (48%) than in women (20%), ($P < 0.005$), without any significant influence of age. Occurrence of nightmares was significantly higher in patients with REM sleep behavior ($P < 0.05$), but lower in patients with obstructive sleep apnea ($P < 0.005$). Polysomnographic correlation of N and NC nightmare groups showed more wakefulness ($P < 0.05$) and higher percentage of NREM1 stage ($P < 0.05$) in NC patients with nightmares.
Conclusion: Compared with the general population, nightmares seem to be significantly more prevalent in both NC and N, and they are not sufficiently investigated and treated. The neurobiological basis of narcolepsy and patients' dreaming activities appear to be closely related.

1. Introduction

Narcolepsy, a rare severe disorder of the sleep–wake cycle, is known mainly for two symptoms: excessive sleepiness and cataplexy. According to the presence of cataplexy, narcolepsy is further divided into narcolepsy with cataplexy (NC) and narcolepsy without cataplexy (N). However, this disease may present with other and rather bizarre symptoms such as hypnagogic hallucinations, sleep paralysis, and automatic behavior [1]. The presentation of the disease is associated with abnormal characteristics of REM sleep, such as sleep onset REM periods and even greater REM sleep density [2,3], attributable to primary NREM–REM sleep dysregulation or possibly to other mechanisms [4]. Since REM sleep is associated with the most vivid dreams or at least the best dream recall, oneiric activity has been explored in several studies. Abnormal oneiric activity in narcoleptics has been found in multiple studies but with different results. Bourguignon [5] found a high prevalence of aggressive dreams in narcoleptic patients, including dreams with aggressive sexual themes, such as incest and raping. Schredl [6,7] found a negative tone of narcoleptic dreams more often than in healthy controls, whereas Vogel [8] detected high emotiveness, including positive emotions. Lee et al. [9] compared oneiric activity in patients with narcolepsy and insomnia, and found significantly more terrifying and repetitive dreams in patients with narcolepsy. Among other variables, higher recall, higher number of characteristics, and different types of bizarreness were found in narcoleptic patients [10]. Krishnan et al. [11] described interesting cases of narcoleptic patients with positive dreams of flying experience.

Most of these studies, though considerably detailed, included quite limited numbers of patients. Furthermore, since their designs vary a lot, their results are inconclusive. To our knowledge, no simple epidemiology of nightmares in narcolepsy – defined as negatively charged sleep-disturbing dreams – has yet been established. No clear comparison of oneiric activity between patients with and without cataplexy has yet been made. Although perhaps every textbook of sleep medicine mentions frequent vivid

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http://dx.doi.org/10.1016/j.sleep.2014.03.006
1389-9457/

and disturbing dreams in these patients, there is no exact knowledge of their impact on patients' life or of the therapeutic algorithm for this symptom. For example, quite a few studies have found disturbed night sleep in narcoleptic patients – and nightmares could contribute to this phenomenon [12–14]. Hence, our objectives were to assess oneiric activity in both NC and N, to determine and compare the occurrence of nightmares in both types of the disease, and to search for factors that might be related to vivid dreams and nightmares in particular. As already proposed, sleep fragmentation can enhance occurrence/recall of vivid dreams and vice versa. Other factors, such as age, gender, or personality may contribute to increased nightmare prevalence, but due to limitations of current knowledge, we treat other findings as rather exploratory. Furthermore, psychiatric comorbidities, such as depression, may lead to residual sleep disturbances, including nightmares, as suggested in a prospective study by Li et al. [15]. Understandably, there may be higher prevalence of major depressive disorder in narcolepsy [16]. As for pharmacological treatment, since we know that medication may improve but may also deteriorate the character of dreaming activity, we highlight that current treatment does not significantly reduce occurrence of nightmares, and that other approaches, such as imagery rehearsal therapy (IRT), should be systematically investigated in these patients.

2. Methods

2.1. Subjects and their categorization

The medical history of 118 narcoleptics (64 men, 54 women, 86 with NC, 32 with N, mean age 41.6 ± 15 years) was retrospectively analyzed. This cross-sectional study involved patients followed at our Sleep Center in the past 13 years. Only those who underwent a face-to-face interview focused on their oneiric activity were enrolled in this study. The patients answered the following questions: 'Do you have vivid–sensually vivid, emotionally charged, bizarre or complicated story-like dreams? Do you frequently have dreams that awake you during the night? Do you often have frightening, humiliating or otherwise emotionally negatively charged dreams? Do your dreams comprise only mundane contents, such as non-emotional themes from your daily life?' All patients had signed informed consent and our research complied with the stipulations of the Helsinki Human Rights Committee. Furthermore, most of our patients regularly attend our center, so we can monitor the development of this symptom over time and observe the effect of medication. The data from polysomnography and multiple sleep latency test (MSLT) were gathered only from drug-naive patients and/or after withdrawal of their treatment.

For statistical analysis, we were able to identify the following groups of patients: (A) low/no recall of dreams or banal mundane dreams; (B) reports of vivid dreams without disturbing negative emotional charge; (C) complaints about nightmares, i.e. dreams with negative emotion, mostly fear, that disturb nocturnal sleep and often interfere with daily activities; (D) nightmares possibly reduced by medication. Only those who explicitly and repeatedly complained of disturbing, unpleasant, and terrifying dreams in their medical history were designated as 'nightmare patients'. If experienced as extremely bizarre, fantastic, sensual, simply 'emotional', but not negatively toned, although disturbing, we classified them as just having vivid dreams rather than as nightmare sufferers. Potentially successful medication – without proof of causal association – included selective serotonin reuptake inhibitors, modafinil, and sodium oxybate. Although this group was too small to be included in the statistical testing, we included it for comparative purposes.

2.2. Data analysis

The dream categories were statistically compared with other clinical aspects, such as age, gender, body mass index, age at the onset of first symptoms and cataplexy, medication, and presence of other symptoms – sleepiness, cataplexy, hypnagogic hallucinations, sleep paralysis, REM sleep behavior disorder (RBD), obstructive sleep apnea (OSA), restless leg syndrome (RLS), and periodic limb movements in sleep (PLMS). Excessive daytime sleepiness was evaluated using the Epworth Sleepiness Scale (ESS); other symptoms were detected by detailed medical history and polysomnographic records (OSA, RBD, and PLMS). Possible associations between dream categories and polysomnographic data (PSG) were also analyzed; and the multiple sleep latency test (MSLT) was employed as a measure of daily sleepiness [17]. The PSG data included sleep latency, REM latency in nocturnal sleep, proportions of each of the sleep stages, number of awakenings, and total sleep time. The MSLT data included mean sleep latency and number of sleep onset REM stages (SOREMs). The analyzed sample consisted of 118 patients, but because of the long-term nature of the study, the data were partially incomplete in some cases. However, the overall sample size for each parameter was always more than adequate for general statistical evaluation.

We used the Pearson χ^2-test for contingency tables to define the statistical significance of possible associations between dream types, comorbidities and other study features with no statistically significant results. Whenever necessary, we merged categories to meet test assumptions (adequate expected cell counts $\geqslant 5$). Parametric one-way analysis of variance was used to determine average inter-group differences. The equality of average values between two groups was tested by Student's t-test. Binomial proportion was calculated for testing the equality of relative frequencies in the categories concerned. Statistical analyses were performed using Microsoft Excel 2010 SP1 MSO and SPSS Release 10.1.0.

3. Results

Fig. 1 illustrates the prevalence of dreams in the whole group, low-recall/mundane dreams (group A) were reported in 42 patients (36%); vivid, but not unpleasant dreams (group B) in 31 patients (26%); nightmares in 39 patients (33%); and reduction of nightmares (group D) in five patients (5%). A comparison of oneiric activity between N and NC is shown in Fig. 2. Whereas nightmares were reported with the same frequency in N and NC, the vivid but not nightmarish dreams appeared more frequently in NC patients ($P < 0.005$); on the other hand, low-recall/mundane dreams predominated in N cases ($P < 0.05$). As for the gender influence, there were significantly more no/mundane dreams in men (48%) than in women (20%), $P < 0.005$ (Fig. 3). Surprisingly, there was no age-related difference in the character of our patients' dream activities.

To sum up the influence of the most frequent sleep comorbidities (OSA, PLMS, RLS, RBD) on the character of dreams, the patients with nightmares seemed to have a lower prevalence of OSA (37% vs 26%; $P < 0.005$), whereas no changes in oneiric activity were found in patients with PLMS. Patients with RLS had increased occurrence of vivid dreams (32% vs 23%; $P < 0.05$), but other dream categories seemed to be diminished in this category. The most significant changes were found, as suspected, in patients with narcolepsy and RBD (both NC and N). Low-recall dreams were suppressed (5% vs 42%; $P < 0.001$), whereas vivid dreams (33% vs 26%; $P < 0.01$) and nightmares (52% vs 20%; $P < 0.05$) increased. No significant correlation was found between dream type and hypnagogic hallucinations and/or sleep paralysis.

Table 1 compares our aforementioned dream categories with the patients' clinical and PSG parameters. Assessment of paramet-