

Nightmares in obstructive sleep apnoea

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Submitted: 2021-01-07 *Accepted:* 2021-03-02 *Published online:* 2021-03-02

Key words: **Obstructive sleep apnoea; Sleep quality; Dream; Nightmares; CPAP; PTSD**

Neuroendocrinol Lett 2021; **42**(4):245–256 PMID: 34436845 NEL420421A08 © 2021 Neuroendocrinology Letters • www.nel.edu

Abstract

OBJECTIVE: Obstructive events in patients with obstructive sleep apnoea (OSA) cause recurrent sleep fragmentation and occasional desaturation, which can cause various parasomnias, including nightmares. Several lines of evidence suggest that OSA may be potentially associated with a higher frequency of nightmares.

METHOD: We searched for studies published from January 2000 until November 2020 in PubMed, the Cochrane Library, Web of Science and Google Scholar. The keywords Obstructive Sleep Apnoea / OSA / Nightmares / CPAP / PTSD / Sleep Quality / Dream / were used in various combinations. The literature search identified 1361 articles which were eligible to more careful examination. Secondary texts were also examined, evaluated for suitability, and added to the primary document list. Finally, a total of 168 articles were included in the review.

RESULTS: According to current findings, OSA could affect emotional regulation via activation of limbic system during sympathetic activation and suppression of REM sleep essential to emotional regulation. The reviews also found an increased prevalence of nightmares in OSA patients. OSA is significantly associated with psychiatric morbidity, as was proved in several studies. There seems to be a strong link between nightmares, OSA, PTSD symptoms and other disorder such as unipolar depression.

CONCLUSIONS: It is clear that therapy of OSA patients, especially those with psychiatric comorbidity, must be complex. In the case of nightmares, we should not forget to use psychotherapy as a first choice, particularly in patients with poor compliance to continuous positive airway pressure (CPAP) and poor sleep and overall life quality. In the same time, we should emphasise the healthy lifestyle and sleep hygiene.

INTRODUCTION

The basic characteristic of obstructive sleep disorder (OSA) is recurrent obstruction of the upper airways during sleep of varying severity, ranging from partial obstruction (hypopnea) to complete obstruction of the upper airways (apnoea) (AASM 2020). The main pathophysiological consequences of OSA are insufficient arterial oxygen saturation and sleep fragmentation (Eckert & Malhotra 2008). In the middle-aged population, the prevalence of OSA in men ranges from 3 to 18 percent, in women 2-17 percent, the prevalence is increasing over the lifetime and estimated to be 28-67 percent in older men and 20-54 percent in older women (Bixler *et al.* 1979, Klink & Quan 1987, Janson *et al.* 1995, Schredl 2010, Li *et al.* 2010, Franklin & Lindberg 2015, Arnold *et al.* 2017, Rostanski *et al.* 2017, Caldwell *et al.* 2017).

As early as the 19th century, doctors believed that recurrent insufficient oxygen saturation during sleep could lead to nightmares (Schredl 2009). Boerner (1855) specifically hypothesized that nightmares are caused by blocking the nose and mouth (Boerner 1855). Nightmares are defined as disturbing dreams, characterized by awakening from REM sleep and differ from other intense dreams by very vivid threatening images (Kuiken & Sikora 1993, Levin & Fireman 2002, Pagel & Kwiatkowski 2010, Creamer *et al.* 2018), typically fear-related but also with other emotions like anger, embarrassment, disgust, grief, frustration, or guilt (Spormaker *et al.* 2006, Nielsen & Levin 2007, Zadra *et al.* 2006). They present a coherent dream sequence that looks real and gradually evolves into more endangering scenes. Typical dream content is usually related to threats to safety, survival, or self-esteem (AASM 2020, APA 2013). The content of a nightmare most often focuses on the immediate physical danger to individuals (for example a threat of attack, fall, injury, death, or suffocation), but aggression towards others or grave personal failure may also occur (Schredl 2001, Schredl 2002, Pagel & Kwiatkowski 2010). A special type of nightmares – post-traumatic nightmares – arise in both REM and non-REM sleep and are usually associated with other sleep disturbances (Phelps *et al.* 2018).

In some clinical populations, including patients with insomnia, nightmares occur more frequently (Wood & Bootzin 1990, Schredl *et al.* 1998, Pagel & Shocknasse 2007). In sleep laboratory, nightmares constitute a significant complaint in 16 percent of patients and positively correlate with lower quality of sleep and worse medical results (Krakow 2006, Sopp *et al.* 2017). Individuals who experience nightmares, often report massively reduced quality of sleep, they are afraid to fall asleep, experience awakening from sleep, they may have difficulties with falling asleep again, subsequent sleep is more restless and less refreshing, and they also have impaired sleep patterns (Krakow *et al.* 1995, Köthe & Pietrowsky 2001, Paul *et al.* 2015). Nightmares

affect daily functioning, reduce overall well-being, lead to decreased mood and increased stress (Zadra & Donderi 2000, Köthe & Pietrowsky 2001, Blagrove *et al.* 2004, Miró & Martínez 2005, Antunes-Alves & De Koninck 2012, Gieselmann *et al.* 2019).

This review aimed to explore the relationship between sleep apnoea and nightmares. Based on the background, the following research questions were formulated:

- (1) Is OSA related to emotional regulation?
- (2) Do nightmares occur more frequently in OSA patients? Do they have specific content?
- (3) Are OSA and nightmares associated with psychiatric comorbidity?
- (4) Do nightmares affect OSA treatment and vice versa?

METHOD

The studies used in this narrative review were found through the databases PubMed, the Cochrane Library, Google Scholar and Web of Science from January 2000 to November 2020. The keywords Obstructive Sleep Apnoea / OSA / Nightmares / CPAP / PTSD / Sleep Quality / Dream / were used in various combinations. In the basic selection, these filters were applied: Clinical Review, Review, People, Adults: 19+ years old. Other links were found using sources of primarily obtained texts. The list also includes information from the books listed in the articles. The texts were collected, systematized according to their importance, and examined. The selected texts had to meet the criteria for inclusion: (1) published in peer-reviewed journals; (2) human studies; or (3) reviews on a related topic; (4) book chapters related to the topic. The exclusion criteria were as follows: (1) conference abstracts; (2) comments. The primary keyword search nominated a total of 1361 articles. In the next step, the inclusion and exclusion criteria were applied, leaving 199 texts for detailed evaluation. After an examination of the complete texts, 59 articles were chosen. Secondary texts were also examined, evaluated for suitability, and added to the primary document list (n = 109). Finally, a total of 168 articles were included in the review (Figure 1), according to PRISMA guidelines (Page & Moher 2017).

RESULTS

OSA and sleep

Obstructive events in OSA patients cause recurrent sleep fragmentation and occasional desaturation, which can lead to various parasomnias, including nightmares (Arnold *et al.* 2017, BaHammam & Almeneessier 2019). Conflicting results have been reported in OSA patients; while some researchers reported fewer dreams in OSA patients (Schredl *et al.* 2012, Di Pauli *et al.* 2018), others found that patients with OSA have more dreams with emotional content, especially violent and hostile (Sopp

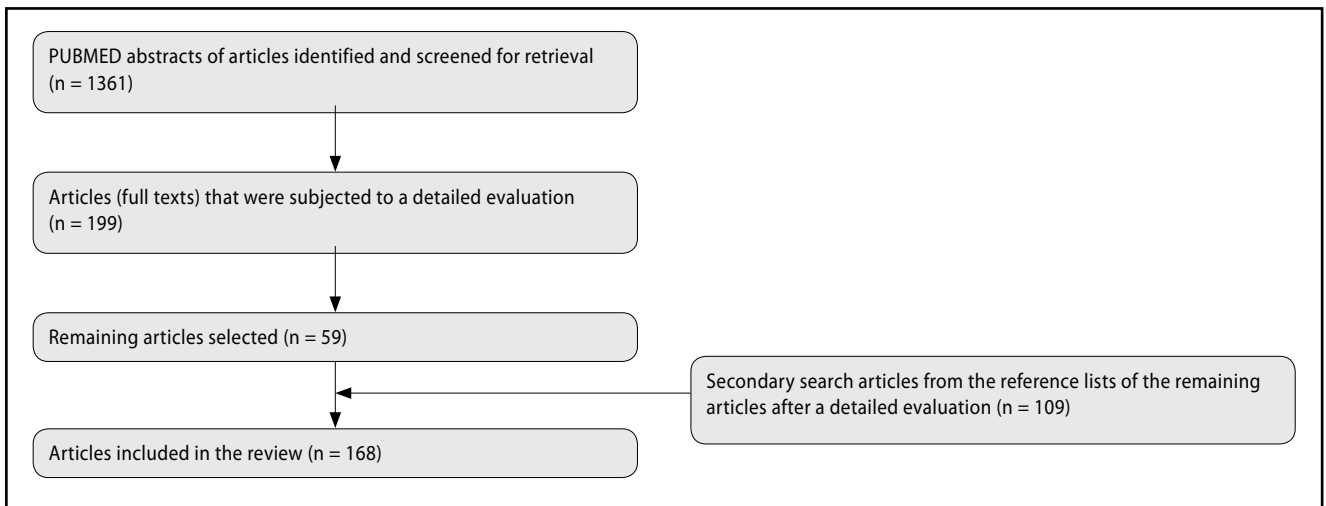


Fig. 1. Summary of the selection process

et al. 2017, Lundetræ *et al.* 2018). Although there are reports of breathing-related dream content in OSA patients, most studies evaluating the dreams in OSA patients have revealed that the dreams were not directly connected to OSA symptoms (Schredl *et al.* 1999, Macfarlane & Wilson 2006, Schredl *et al.* 2012).

It has been proposed that hypoxemia linked to the apnoea, can trigger arousals, including sexual behaviour (Bornemann *et al.* 2006, Schenck *et al.* 2007, Soca *et al.* 2016, Grøndahl *et al.* 2017, Kryger *et al.* 2017). In US epidemiological study based on 15,929 telephone interviews, individuals with suspected OSA had a higher risk of sleepwalking (Pressman 2013, Grøndahl *et al.* 2017). Additionally, a comparable investigation with individuals from six countries (Finland, Germany, Italy, Portugal, Spain, and the United Kingdom) also with a representative number of participants (n = 19,961), recognized a significant link between sleep-related violence and breathing pauses throughout sleep (Ohayon & Schenck 2010). Nevertheless, these epidemiological investigations have a substantial limitation in fact, that OSA diagnosis was based on subjective information.

The sleep-related eating disorder has received similar attention. OSA can be closely connected with a sleep-related eating disorder as is supported by several investigations (Eveloff & Millman 1993, Schenck & Mahowald 2008, Santin *et al.* 2014). However, a considerable number of doubts still exist about the association between OSA and a sleep-related eating disorder. In terms of REM-parasomnias, severe OSA positively correlated with nightmares (Carrasco *et al.* 2006). However, the evidence in the studies mentioned above is based mostly on case reports or limited clinical trials (Eveloff & Millman 1993, Carrasco *et al.* 2006, Schenck & Mahowald 2008, Santin *et al.* 2014). The extensive study of Lundetræ *et al.* (2018) with 4,372 patients referred to a Norwegian university hospital with suspicion of OSA states that only sleepwalking

had a significantly higher occurrence in severe OSA compared to mild OSA. Other parasomnias, including nightmares and sleep-related violence, were not associated with OSA presence or severity when adjusting for sex and age.

OSA and emotional regulation

Sleep, with the emphasis on rapid eye movement phase (REM), helps to maintain brain homeostasis, which helps optimal social and emotional functioning (Sopp *et al.* 2017). Sleep is essential for creating emotionally bound information and for emotional regulation (Goldstein & Walker 2014). Sleep disorders in OSA patients may lead to neurological and emotional disorders (Goldstein & Walker 2014).

Studies have described an increased number of dreams with emotional content in OSA patients, particularly violent and hostile (de Groen *et al.* 1993, Carrasco *et al.* 2006, Schredl *et al.* 2006, Fisher *et al.* 2011, BaHammam & Almeneessier 2019). Obstructive events during REM sleep appear to activate the limbic system, which may lead to more intense dreams with strong emotional content (Carrasco *et al.* 2006).

Dream context and content in OSA

Stimuli during REM sleep can affect dream content (Eiser 2005). The effect of external sensory, acoustic or olfactory stimuli during REM sleep on dream content has been repeatedly demonstrated (Wollman & Antrobus 1986, Trotter *et al.* 1988, Schredl *et al.* 2009). However, it has not been sufficiently explored how the body's pathological stimuli affect dream content (Schredl & Schmitt 2019). Regarding dreams in OSA patients, the published results were contradictory. Some studies have found fewer dreams in OSA patients, but others report an increase in dreams (BaHammam & Almeneessier 2019).

A study evaluating 33 OSA patients, who slept for two nights in a sleep lab before and after CPAP

Tab. 1. Sleep disturbances in OSA

- Insomnia
- Sleep Fragmentation
- Nightmares
- Daytime sleepiness
- Sleepwalking
- Sleep-related violence
- Sexual acts during sleep
- Sleep-related eating

therapy, showed that after waking up from REM sleep due to obstructive events, there was a trend toward increased recall of dream content in contrast with waking up from REM sleep without obstructive events (Gross & Lavie 1994). Apnoea as a stimulus was not recorded in the dream content. However, after apnoea, dreams were significantly more negative than dreams in healthy sleep and involved significantly more characters, activities, and social interactions (Gross & Lavie 1994). Several studies evaluating the dream content of the OSA patients also showed that the breathing-related dreams were unusual (Schredl *et al.* 1999, Macfarlane & Wilson 2006, Schredl *et al.* 2012, Di Pauli *et al.* 2018). On the other hand, a prospective case study of 99 patients with OSA and nightmares reported that the dream content of most participants was asphyxiation (BaHammam *et al.* 2013). This is in correlation with our own experience – we had at least two patients with OSA and nightmares in our sleep laboratory. First one was 55 years old man with the posttraumatic disorder, former Czech soldier in Afghanistan mission. He was diagnosed with severe sleep apnoea syndrome by polysomnography. He reported having nightmares with asphyxiation content – patient recalled repeatedly dreams about being trapped in the ruins of the house destroyed by a bomb. Another 60 years old male patient, similarly diagnosed by severe sleep apnoea syndrome, who was a professional diver, claimed he had recurrent dreams with the same content – he ran out of oxygen in his oxygen-bottle, and he was suffocating. Both had sufficient CPAP compliance, and they do not experience this type of nightmares anymore.

McFarland & Wilson (2006) also reported that patients who wake up because of respiratory problems are more likely to dream of asphyxiation than other patients in the sleep lab; however, this finding was not present in patients with sleep apnoea. The differences between the studies can be attributed to differences in the characteristics of the group included in each study (Schredl & Schmitt 2019).

Studies report contradictory results regarding the recall of dreams in patients with OSA (Gross & Lavie 1994, Carrasco *et al.* 2006, Schredl 2009). Initial studies evaluating dream recollections at home using retrospective questionnaires showed fewer dream recollections in OSA patients than in healthy controls (Schredl *et al.* 2006, Schredl *et al.* 2009). However, another study of 1,243 patients with OSA showed more memories

of dreams in OSA patients than in a representative sample from the general population (Schredl *et al.* 2012). In a recent study of 1,467 OSA patients, who completed a dream-focused questionnaire, an increased frequency of dream recall was noted in patients compared to the control group (Schredl & Schmitt 2019).

Several investigations showed no correlation between OSA severity parameters (e.g., apnoea/hypopnoea index – AHI, and desaturation index) and dream recall (Hartmann & Pavia 2006, Schredl *et al.* 2006, Schredl & Schmitt 2009, Fisher *et al.* 2011, Di Pauli *et al.* 2018). Studies evaluating the effects of CPAP on dream recall reported conflicting results. Some researchers have found less recall in OSA patients and improved recall after CPAP, others found that OSA patients have an increased frequency of recall (de Groen *et al.* 1993, Carrasco *et al.* 2006, Schredl *et al.* 2006, Fisher *et al.* 2011). Gross & Lavie (1994) showed that discontinuation of CPAP treatment for one night caused an increase in AHI and an increase in dream recall and dream reports were significantly longer on untreated nights. However, researchers did not assess the recall of dreams before the CPAP treatment. Moreover, it could be discussed that sleep without the CPAP therapy after two months of treatment may have caused concerns in the patients, which led to the recall of negatively tuned dreams that were not related to obstructive events.

Another study in patients with severe OSA found that despite the increase in REM density after the CPAP therapy, dream memories diminished both straight away and after three months initiation of CPAP (Carrasco *et al.* 2006). This outcome was independent of REM density and REM sleep amount. The authors believed that reducing sleep fragmentation after CPAP therapy could explain this finding. Also, an increase in the proportion of slow-wave sleep induced by CPAP has been proposed as an explanation for reducing the recollection of dreams (Carrasco *et al.* 2006).

Subsequently, Carrasco *et al.* (2006) suggested two theories that may affect the recall of dreams in OSA patients. The first is the theory of cognitive impairment, where impairment of cognitive function in the OSA patients may impair dream recall (Fulda & Schulz 2001). A second contradictory theory is the theory of frequent arousal, where frequent arousal and light interrupted sleep can increase recall. Another explanation for the decreased recall of dreams in some OSA patients includes the possibility, that the time spent awake after waking up caused by respiratory events, was too short to permit remembering the dream (Schredl & Schmitt 2019). There is also a possibility that cognitive deficits in OSA patients may counterbalance the proposed effects of frequent arousal on dream recall (Fulda & Schulz 2001, Schredl & Schmitt 2019).

Schredl & Schmidt (2019) found gender differences in the recall of dreams in OSA patients. More recall of dreams has been observed in women, consistent with the findings of previous studies (Schredl & Reinhard

2011). Future studies should take into account the duration of waking and obstructive events, AHI during REM sleep, and cognitive function and their impact on dream recall.

Nightmares in OSA

According to the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5; APA 2013), nightmares are defined as extremely dysphoric dreams that usually involve endangering the survival of an individual and / or one's emotional or physical sense of security. Several lines of evidence suggest that OSA may be potentially associated with a higher frequency of nightmares (Collen *et al.* 2012, BaHammam & Almeneessier 2019). The inclusion of somatosensory stimuli in dreams has been replicated in several classical studies (Berger 1963, Rechtschaffen & Foulkes 1964, Koulack 1969). Patients, who have sleep paralysis, and those, who sweat excessively, experience these symptoms more often in their dreams (MacFarlane & Wilson 2006). Wood *et al.* (1993) reported a higher frequency of nightmares in patients diagnosed with asthma and chronic obstructive pulmonary disease. Patients with OSA reported dream events where they were buried under sand, were underwater and could not emerge, or they tried to scream, and no sound came out. However, according to clinical experience, these descriptions are somewhat rare (Hartmann 1984). It is known that the recall of a dream increases with its prominence - the newer, more bizarre, the more emotional or experience-intensive the dream is - and with the individual awakening from the dream (Kuiken & Sikora 1993, Zadra & Donderi 2000).

Hicks *et al.* (2002) found no correlation between reported snoring and nightmare frequency. MacFarlane & Wilson (2006) did not find an increased incidence of suffocation and strangulation dreams in sleep apnoea patients. Schredl *et al.* (2006) in a study of patients with severe apnoea, found that the average respiratory index (RDI) correlated negatively with the reported frequency of dreaming and nightmares recall. Pagel & Vann (1995) noted both a decrease in the frequency of dream recall and waking up in OSA patients. Authors from the same sleep laboratory reported that individuals who report an absolute lack of dream recall are more likely to have OSA (Pagel 2003).

In a study by Pagel & Kwiatkowski (2010, n=393), individuals with higher AHI reported nightmares less frequently, demonstrating that severe OSA can suppress the recall of nightmares. Both the AHI and the apnoea index (AI) were significantly higher in a group that reported only occasional recall of nightmares. With increased AHI scores, the percentage of participants with frequent recurring nightmares declined linearly. In a study using night-time polysomnography in the sleep lab, dreaming and nightmares were significantly lower in subjects with AHI > 15 (Pagel & Shocknasse 2007). On the other hand, in the study of Fisher *et al.* (2011),

patients with AHI > 15 reported more nightmares than healthy controls. The decline in nightmare recurrence can occur secondary due to REM sleep suppression, which presents in severe OSA. Findings above suggest that OSA suppresses the cognitive experience of evoking a nightmare. This effect occurs independently of the effects of OSA on the reported recall frequency. This is an essential and quite surprising finding since many studies have supported the opposite hypothesis. Work of Pagel & Kwiatkowski (2010) shows that more severe OSA has a higher negative impact on the frequency of recall of nightmares than on the recall of dreams.

The findings that worse OSA results in a significant decrease in the frequency of recalling nightmares could potentially be a secondary effect of drowsiness induced by OSA. Patients who struggle more with maintaining alertness report a lower frequency of nightmares (Hicks *et al.* 2002). Furthermore, individuals with shorter sleep latencies exhibit a lower frequency of dream recall in the multiple sleep latency test, supporting the hypothesis that that OSA-associated sleepiness contributes to a lower frequency of nightmare induction (Myers & Pagel 2001). However, daytime sleepiness is not present in all OSA patients, with studies reporting excessive sleepiness in 15.5 to 22.5 percent of middle-aged patients (Young *et al.* 1993).

In addition to daily drowsiness, OSA is known to cause cognitive impairments, which include a decrease in working memory and deficiencies in executive frontal cortex functions (Lis *et al.* 2008, Felver-Gant *et al.* 2007). The cognitive process that allows recalling a dream after awakening is probably a manifestation of the executive functions of the frontal cortex. However, cognitive deficits are not present in all OSA patients, and it has been challenging to describe their changes in the disease process (Morrell & Twigg 2006). Thus, the potential impact of OSA-induced cognitive deficit does not again explain why worsening OSA could significantly affect nightmare recall, as opposed to dreams recall.

While dreaming occurs at any time during sleep, nightmares are generally described as parasomnia associated with REM sleep (Nielsen & Zadra 2000). REM sleep is the sleep phase most sensitive to abnormal respiratory events, with OSA selectively suppressing REM sleep (Sanders & Givelber 2006). It is suspected that suppressed REM sleep in OSA patients is the basis for reducing the frequency of nightmares recall compared to other dreams. The OSA patients, who have an increase in REM sleep and restore normal sleep during the CPAP treatment, are also expected to increase nightmare recall. Tamanna *et al.* (2014), however, found no significant correlation between REM AHI and the number of nightmares, signifying that obstructive events during REM sleep may not be the only trigger for nightmares.

Studies that showed an association between nightmares of individuals with posttraumatic stress disorder

(PTSD) and OSA might reflect a presence of a dysfunction of the emotional processing system, including both nightmares and REM sleep (De Groen *et al.* 1993, Krakow *et al.* 2001, Krakow *et al.* 2002, Levin & Nielsen 2007). The potential finding that a decrease in REM sleep in OSA patients leads to less recall of nightmares supports the potential functional role of REM sleep and nightmares in emotional neuroregulation (Levin & Nielsen 2007).

Nightmares, OSA and psychiatric disorders

The relationship between OSA and mental disorders is two-way (Kendzierska *et al.* 2017, Vanek *et al.* 2020). The presence of one disorder worsens the other (Gupta & Simpson 2015). OSA has been described mainly in patients with depression (BaHammam *et al.* 2016, Kendzierska *et al.* 2017), anxiety disorders (Rezaeitalab *et al.* 2014) and PTSD (Youakim *et al.* 1998, Gupta & Simpson 2015, Zhang *et al.* 2017). On the other hand, patients with OSA are also more likely to develop a mood disorder, anxiety disorder, PTSD, and psychotic disorder compared to patients without OSA (Sharafkhaneh *et al.* 2005, BaHammam *et al.* 2016, Kendzierska *et al.* 2017, Lu *et al.* 2017). The coexistence of co-morbid psychiatric disorders and OSA may interfere with the content of dreams or nightmares (Agargun *et al.* 2004, Michels *et al.* 2014). A recent study in psychiatric patients stated that the prevalence of sleep breathing disorders is 14.5 percent (Hombali *et al.* 2019). Fehr *et al.* (2018) examined the associations between OSA and major depressive disorder, PTSD, or bipolar disorder. The study presented a high prevalence of OSA, particularly with major depressive disorder (37.8%) and PTSD (35.5%) and less so with bipolar disorder (16.7%).

Nightmares are a common co-morbidity of most psychiatric disorders. For example, up to 50 percent of patients, who have a borderline personality disorder (BPD), reported frequent nightmares (Hartmann *et al.* 1981, Hafizi 2013, Semiz *et al.* 2008, Schredl *et al.* 2008, Paul *et al.* 2015, Holley *et al.* 2020). Frequent nightmares are a hallmark of PTSD (Yehuda and McFarlane 1995, Grillon 1996, Fawzi *et al.* 1997) occurring in 42 to 56 percent of affected patients (De Groen *et al.* 1993, Swart *et al.* 2012, Mayer *et al.* 2016, Baird *et al.* 2018, Senaratna *et al.* 2016, Lundetræ *et al.* 2018), with some studies reporting up to 77.2 percent of veteran subpopulation being at risk (Collen *et al.* 2012, Forbus *et al.* 2015). The OSA prevalence is about 2 to 3 times higher (50 to 67 percent) among active-duty soldiers, who also have deployment-related PTSD (Mysliwiec *et al.* 2013, Williams *et al.* 2015), and among refugees (Arnetz *et al.* 2012). Moreover, OSA severity is directly associated with suicidal ideation in PTSD (Gupta & Jarosz 2018). Krakow *et al.* (2002) report that as many as 90 percent of individuals, who have experienced sexual assaults and had PTSD, were also symptomatically affected by impaired breathing. A smaller study by the same

authors using polysomnography found significant OSA in 40 of the 44 victims of crimes (Krakow *et al.* 2001).

Nightmares are a symptom of impaired emotional processing in patients with PTSD (Levin & Nielsen 2007). To study nightmares, it is necessary to distinguish idiopathic nightmares from post-traumatic nightmares that are part of the PTSD as a result of a traumatic event (Spoomaker *et al.* 2006). Both types of nightmares have been associated with increased levels of periodic limb movements, although only post-traumatic nightmares appear to be associated with a prolonged night waking (Levin & Nielsen 2007). Nightmares have also been repeatedly associated with so-called neuroticism, independent of the type of mental disorder (Köthe & Pietrowsky 2001, Li *et al.* 2010). Individuals with PTSD often report sleep disorders, including difficulty falling asleep and maintaining sleep, recurrent trauma-related nightmares, and other distressing night-time behaviours such as anxiety and nightmarish attacks during sleep (Rothbaum *et al.* 1992, Neylan *et al.* 1998, Ohayon & Shapiro 2000, Farrahi *et al.* 2009, Kobayashi & Delahanty 2013, El-Solh 2018). The nightmares usually occur early in the morning when REM sleep covers more extended periods, and the density of REM is increased. Increasing evidence suggests that sleep disturbance is a core feature of PTSD rather than just a secondary symptom (Ohayon & Shapiro 2000, Kobayashi *et al.* 2007, Spoomaker & Montgomery 2008). Hypoxia, sympathetic activity from respiratory problems, dysfunctional REM sleep, and abnormal REM mechanism are areas of interest in finding a connection between sleep apnoea and PTSD symptoms (Pillar *et al.* 2000, Schredl *et al.* 2006, Kobayashi *et al.* 2012). The nightmare-related stress and its impact on day-to-day functioning, including daytime sleepiness, can function as an intermediate variable (Spoomaker *et al.* 2006).

Several studies have found a clear association between post-traumatic stress disorder, co-morbid OSA, and nightmares (Holley *et al.* 2020). OSA in PTSD veterans shows atypical manifestation, the main symptom being insomnia instead of daytime sleepiness, and patients do not have to possess common risk factors such as obesity (Colvonen *et al.* 2015, Rezaeitalab *et al.* 2018). One study showed that nearly 50 percent of women in active military service had clinically significant OSA without the presence of typical risk factors (Capener *et al.* 2018). Untreated OSA highlights the symptoms of PTSD in sleep, especially the number and intensity of nightmares, repeated waking, difficulty returning to sleep, and increasing daytime sleepiness and fatigue (Gross & Lavie 1994, Schredl 2009, Pagel & Kwiatkowski 2010, Fisher *et al.* 2011).

Grønli *et al.* (2017) studied sleep disturbances in 42 survivors of the mass terror attack at a summer camp on the Norwegian island (Utøya). In comparison with the matched controls, there was a significantly higher prevalence of insomnia, frequent nightmares (27.5% versus 2.3%), symptoms of obstructive sleep apnoea

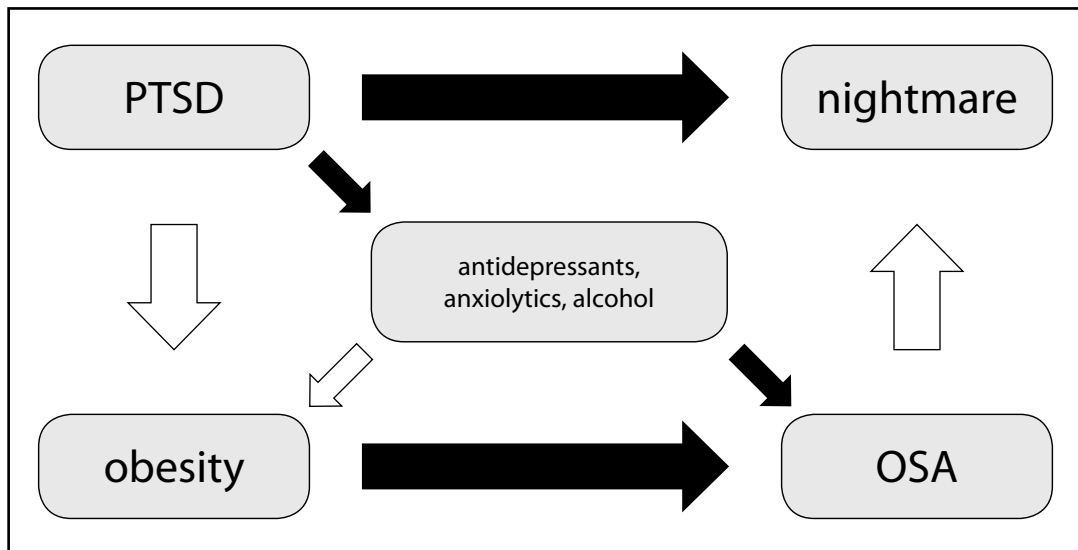


Fig. 2. Possible relationships between OSA, obesity, nightmares and PTSD, white arrows indicate weaker relations, and black arrows indicate stronger relations

(18.8% versus 0%), and excessive daytime sleepiness in the survivors. People exposed to World Trade Center (WTC) catastrophe display multiple disorders that disturb sleep, including OSA (Ayappa *et al.* 2019).

Chronic sleep disturbances associated with nightmares reduce the effectiveness of first-line PTSD medications; therefore, targeted sleep examination has been recommended to accelerate improvement in sleep quality, nightmares, and general symptoms of PTSD via the usage of continuous positive airway pressure (CPAP) (Spoomaker & Montgomery 2008, Krakow *et al.* 2000, BaHammam *et al.* 2013, Youakim *et al.* 1998). However, low compliance with CPAP has been reported in PTSD patients (El-Solh *et al.* 2010).

Treatment of nightmares in OSA

Several studies in recent decades have shown that nightmares can be treated in several cognitive-behavioural ways (Spoomaker *et al.* 2006). The treatment of choice in nightmares is imagery rehearsal therapy. Regarding OSA nightmares, a reduction in the frequency of nightmares during treatment (CPAP) has been shown (Holley *et al.* 2020). Individuals reporting recurring nightmares, who were diagnosed with mild OSA based on apnoea screening, were found to experience a significant improvement in sleep quality and daily functioning with the CPAP treatment. However, the study was conducted on a limited sample (N=14) (Krakow *et al.* 2000). Carrasco *et al.* (2006) in another small study of 20 patients versus 17 healthy controls showed that recall of dreams in severe OSAS patients in REM sleep was as frequent as in healthy controls, but patients' dreams had a higher emotional quality and were longer. Authors also showed that highly anxious dreams diminished with the CPAP treatment. In a larger sample of patients (N = 69), who were diagnosed with OSA and PTSD, the treatment of OSA

with CPAP was associated with a reduction in nightmares and daytime sleepiness (Tamanna *et al.* 2014). Several other studies showed a decrease of nightmares and PTSD symptoms with CPAP therapy (Orr *et al.* 2017, El Solh *et al.* 2017, Ullah *et al.* 2017). The CPAP therapy significantly reduced both the average sleepiness and the average number of nightmares per week. It was also found that CPAP compliance was the most important predictor of this change (Ullah *et al.* 2017).

BaHammam *et al.* (2013) reported that CPAP therapy leads to a significant decrease in nightmares. There was no significant difference in CPAP compliance between REM and non-REM OSA groups, consistent with the finding by Conwell *et al.* (2012).

El-Solh *et al.* (2017) studied 47 combat veterans with PTSD and OSA in prospective cohort design. There was a dose-dependent response of PTSD to the duration of CPAP usage. The use of CPAP was recognized as the only significant predictor of the subjective reducing of symptoms of PTSD and changes in Nightmare Distress Questionnaire and Nightmare Frequency Questionnaire scores. In another randomized crossover study, El-Solh *et al.* (2018) compared the efficacy of the CPAP treatment to Mandibular Advancement Device in 42 subjects, stating CPAP to be more efficacious in improving sleep apnoea. Both treatment modalities led to increased quality of life and alleviating of PTSD symptoms.

Veterans with newly diagnosed OSA were enrolled in Ullah *et al.* (2017) study and followed for six months of CPAP use. The treatment led to reducing PTSD symptoms and nightmare frequency. Unfortunately, CPAP adherence was lower in PTSD veterans with OSA than in those without PTSD (El-Solh *et al.* 2010), and one study showed ethnic differences in adherence (Means *et al.* 2010). Excessive sleepiness positively predicted CPAP adherence, whereas frequent

nightmares and worse quality of life-related to poor adherence to therapy with CPAP (Lettieri *et al.* 2016). One study showed that PTSD veterans with OSA with CPAP treatment profited more from evidence-based psychotherapy than PTSD veterans with OSA without the CPAP treatment, discussing that untreated OSA could be a major factor in the failure of PTSD targeted treatment (Mesa *et al.* 2017).

Pharmacotherapy and psychotherapy of nightmares in OSA

According to a meta-analysis, PTSD-related nightmares, sleep disorders, and the overall severity of the disease showed a significant response to prazosin treatment (George *et al.* 2016). However, the study of Raskind *et al.* (2018) found no significant effect of prazosin in PTSD veterans. Nothing is known about prazosin influence on OSA nightmares in particular. Another medication used for the treatment of nightmares has only sparse and low-grade data (level of evidence C) – trazodone, atypical antipsychotic medications, topiramate, low dose cortisol, fluvoxamine, triazolam and nitrazepam, phenelzine, gabapentin, cyproheptadine, and tricyclic antidepressants (Aurora *et al.* 2010). Most of the antidepressants have (as a side effect) weight gain (at least in some patients), and anxiolytics cause more frequent obstructive sleep apnoea by muscle relaxation. Patients with PTSD are more frequently alcohol abusers (Gilpin *et al.* 2017), which is also connected to both obesity and OSA severity. In the same time, PTSD patients are more frequently overweight (Smith *et al.* 2015). Figure 2 shows schematic relationships between OSA, nightmares, obesity and PTSD.

On the other hand, there is a strong recommendation to start treatment of nightmares with psychotherapeutic modes – e.g., Image Rehearsal Therapy (level A), or Systematic Desensitization and Progressive Deep Muscle Relaxation training (level B) (Aurora *et al.* 2010). Even though almost nothing is known about psychotherapy in OSA nightmares, it should be recommended in those patients, where CPAP therapy alone does not eliminate nightmares or nightmares causes lower CPAP compliance as a current best praxis.

CONCLUSION

Nightmares are likely to be independent of objective sleep disorders, but cause waking stress, reduced feeling of refreshment after sleep, daytime fatigue and affect mood. Patients in the sleep laboratory with severe OSA, assessed by higher AHI, show a significantly lower frequency of nightmares. OSA suppresses the cognitive nightmare experience, an effect that occurs independently of the effects of OSA on the frequency of dream recall. This effect on nightmares recalls is believed to occur secondary to REM sleep suppression, which occurs in patients with significant OSA.

The effort to answer the original basic question is as follows:

(1) Is OSA related to emotional regulation?

According to current findings, OSA could affect emotional regulation via activation of limbic system during sympathetic activation and suppression of REM sleep essential to emotional regulation.

(2) Do nightmares occur more frequently in OSA patients? Do they have specific content?

There is an increased prevalence of nightmares in OSA patients. Contemporary literature is not consensual on a specific dream content of nightmares with some studies reporting more breathing-related topics. However, the significant body of the studies does not find the increased frequency of a specific nightmare content.

(3) Are OSA and nightmares associated with psychiatric comorbidity?

OSA is significantly associated with psychiatric morbidity, as was proved by several studies. Most explored is the link between OSA nightmares and PTSD, especially in the subpopulation of veterans. There seems to be a strong link between nightmares, OSA, and PTSD symptoms. Nightmares and comorbid OSA has been described in other disorder such as unipolar depression.

(4) Do nightmares affect OSA treatment and vice versa?

Current knowledge on the topic suggests that higher frequency and severity of nightmares leads to lower adherence to the CPAP treatment. Several studies, on the other hand, showed that the CPAP treatment leads to a decrease of nightmares frequency and to increase in quality of life. It is recommended that all patients with PTSD should be clinically assessed for OSA, and those who meet the criteria should undergo polysomnography. If OSA is diagnosed, the CPAP treatment should be used, and every effort should be made to improve CPAP compliance to maximize the benefits of nightmare control.

Future clinical studies on changes in REM sleep mechanism after exposure to psychological trauma can help explain the underlying mechanism and links between OSA and nightmares.

It is clear that therapy of OSA patients, especially those with psychiatric comorbidity, must be complex. In the case of nightmares, we should not forget to use psychotherapy as a first choice, particularly in patients with poor compliance to CPAP and poor sleep and overall life quality. At the same time, we should emphasise the healthy lifestyle and sleep hygiene.

DISCLOSURE

The authors report no conflicts of interest in this work.

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