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DREAMING AND PARASOMNIAS – A CASE WITH SEVERE PARASOMNIA OVERLAP DISORDER AND ITS TREATMENT

ABSTRACT

Dreams are experiences during sleep that are internally generated by the brain. Dreaming is a common phenomenon during normal sleep and may occur in all sleep stages. The brain is active during sleep, but perceptual connection to the environment is mostly turned off. However, the content of dreams can be affected by both external and internal stimuli. Dream recall is associated with higher frequency brain activity during sleep, typical of REM sleep and arousals.

During parasomnias, dream experiences may be disturbed, behaviourally manifested or mixed with waking reality. Parasomnias are sleep disorders characterized by incomplete transitions between sleep and wake. Abnormal motor, sensory or behavioural manifestations of parasomnias occur at sleep onset, within sleep or during arousal from sleep. Various sensory stimuli may be able to disturb sleep causing arousals or partial awakenings typical of parasomnias.

Differential diagnosis of parasomnias includes patient report of recalled and enacted dream content, timing and age at onset of parasomnia episodes, witnessed sleep behaviour, and polysomnographic findings about the sleep stage and the mechanism of episodes. In adults, parasomnias may have a significant negative effect on well-being and even violent consequences. A patient case with severe parasomnia overlap disorder and its treatment is presented.

KEY WORDS: DOA, DREAMING, PARASOMNIA, POD, POLYSOMNOGRAPHY, PTSD, RBD

INTRODUCTION

Dreaming, as an altered state of consciousness, has interested and inspired creative and scientific approaches to understanding the human mind and existence since time immemorial. Dreaming is mostly beyond our control, though we spend a third of our life asleep, in the realm of dreams.

Historically, psychoanalytic approaches in psychiatry have focused on dreams as the Freudian "Royal road to unconscious", updating to working with dreams to explore dissociative disorders (1). Despite technological advances of neuroscience in modern psychiatry and established knowledge of sleep functions in general, scientific understanding of dreams is still rudimentary.

Disturbing dreams are of clinical interest as they can be manifestations of mental distress, symptoms of psychiatric disorders, symptoms of sleep disorders, adverse effects of medications, outcomes of unhealthy behavioural and environmental factors or somatic illness. Parasomnias are common sleep disorders that can manifest with disturbing dreams, dream enactment and dream sensations during partial wakefulness.

Parasomnias are characterized by abnormal motor, sensory or behavioural manifestations at sleep onset, within sleep or during arousal from sleep. They can disturb sleep quality and decrease daytime alertness. Parasomnias can cause secondary insomnia, marked psychological distress and harmful social consequences. Violent and disoriented behaviour may cause accidents.

Parasomnias can be elicited by various sensory inner (e.g. pain) or outside stimuli (e.g. noise), physiological, chemical, psychological and behavioural factors. Some known risk factors for parasomnias are sleep-disordered breathing, fever, heavy exercise, alcohol, anxiety and irregular sleeping times. Parasomnias are classified by the sleep stages into REM parasomnias (e.g. nightmares), and NREM parasomnias (e.g. sleep walking), with characteristic differences in timing, degree of recall, type of dream content, behavioural features and psychological stressors.

Here, we review the phenomenology of dreaming and clinical features of the most important parasomnias, then present a special patient case presenting with severe overlapping parasomnia symptoms. The overlapping symptoms were challenging for differential diagnosis and treatment approaches for the lack of established guidelines. The relevance of psychiatric comorbidity and stressors were obvious in this case, but in particular, we hope that the case elicits interest in diagnosing and treating sleep disorders of psychiatric patients.

The presented case is also an encouraging example of early treatment response to severe, injurious and debilitating parasomnia followed with a return to work despite a concomitant, trauma-related psychiatric disorder requiring further treatment.

DREAMING

Sleep is a resting state of the brain and body that typically consists of behavioural quiescence and unresponsiveness to sensory stimuli. However, unresponsiveness does not equal unconsciousness. Consciousness is commonly defined as the ability to have experiences, while unconsciousness is a state without any experiences whatsoever (2,3).

During sleep, it is common for a sleeper to have subjective internally generated experiences which are disconnected from the environment. Static imagery and thoughts during sleep are called sleep mentation, and experiences involving sense of space and temporal progression are called dreams (4). However, during sleep-wake transitions and parasomnias this distinction between waking and dream consciousness can become blurred.

Dreaming is a common phenomenon during normal sleep. Although most of the dreams are not recalled, sleep laboratory studies suggest that people generally experience several dreams every night (5,6). There is no scientific consensus on why people dream. Nevertheless, several theories about dream function have been put forward.

Emotional regulation theories propose that dreaming has a psychological function as emotionally loaded memories are processed during dreams, which is considered necessary for maintaining mental health (7). Though refined over the years, this line of thinking can be traced all the way to the work of Freud (8).

Random activation theories such as continuity hypothesis of dreaming claim that dreaming has no function of its own and is just a by-product of brain activation during sleep (9,10). Neurophysiological-focused variants of these theories started with identity theory that REM sleep is dreaming, when REM sleep stage was discovered (11), and modern variants propose that dreaming reflects memory consolidation and related neurological processes that happen during sleep, but has no function of its own (12,13).

Simulation theories of dreaming posit that it is possible to learn from dream experiences and dreaming of themes

important for survival, including dangerous situations and important social interactions, and has been advantageous during evolution of the brain. Therefore, dreaming is an evolutionary adaptation and has a biological function (14,15). Variants of simulation theories include protoconsciousness theory, hypothesizing that simulating the world in dreams begins before birth and is necessary for brain development of a foetus (16).

Since dreaming consists of subjective experiences during sleep, studying it poses great challenges. There is no direct way of measuring or recoding experiences even though advances in brain imaging have identified several neural correlates of consciousness (17). Therefore, most information from dreams is based on retrospective dream reports given by the dreamer after waking up. This results in possible bias in related dream data due to unreliable recall and differences in reporting capability of individuals (18).

Regardless of these methodological challenges, scientific dream research has advanced in recent decades after a long hiatus, and it has been demonstrated that dreaming has a robust connection with well-being. Dreams that are of special interest regarding mental well-being are nightmares. In ICD-10, nightmares are defined as dream experiences loaded with anxiety and fear that are well remembered after awakening and some themes often reoccur from nightmare to nightmare (19). This sort of nightmare generally occurs during REM sleep stage though it is also possible to experience nightmarish imagery in NREM sleep.

Nightmares can be divided into idiopathic and post-traumatic varieties. Idiopathic nightmares have content that is not clearly linked to actual events experienced by the dreamer. They are relatively common, with around half of adults experiencing at least one nightmare per month and 3-5% suffering from frequent nightmares (20,21). While occasional nightmares are harmless, frequent nightmares can pose a significant clinical problem if they cause daytime distress and disturb sleep. Frequent nightmares are often associated with symptoms of depression and insomnia as well as stress and life dissatisfaction (22,23).

Most common themes in nightmares are those related to physical attack or a threat of such an attack, social conflicts, being chased and falling (24,25). However, more important than the actual content are emotions that are evoked by these dreams. Dreams can include violent or dangerous situations, but if the emotional tone is neutral or positive these dreams are not nightmares. On the other hand, there are nightmares in which nothing objectively threatening happens, but which evoke a strong negative reaction for the dreamer.

Post-traumatic nightmares contain clear references to, or even replications of, traumatic events that the dreamer has experienced in their life. These kinds of nightmares are a normal reaction to a traumatic event and most people experience some nightmares related to such an event in the following weeks after trauma. Typically dreams about trauma become less frequent with time and disappear on their own, but in some cases they may become a chronic problem.

In a study of veterans of the Second World War in Finland, increased frequency of nightmares among war veterans was observed over 30 years after the war had ended (21). Post-traumatic nightmares are also one of the key symptoms of full post-traumatic stress disorder that also includes heightened arousal, depressive symptoms and avoidance behaviour, and can be a long-term mental health problem (26).

NEUROPHYSIOLOGY OF DREAMING

Most of human adult sleep consists of NREM (non-REM, or basic sleep including doze, light sleep and deep sleep) and, to a lesser extent, REM (rapid eye movement or paradoxical) sleep (20-25%) (27). Normal adult sleep architecture consists of five sleep cycles, each of which starts in healthy people with NREM sleep, deepening gradually and ending with lightened sleep and transitioning into REM sleep. There may be awakenings at the end of the cycles. The first cycles of the night normally contain deep N3 sleep (slow wave sleep) that diminishes towards the end of the night, whereas the REM sleep increases towards the end of the night.

Dreaming may occur in all sleep stages, though the recall of dream content is more frequent and vivid for REM than NREM sleep. When awakening from REM sleep, the dream content is recalled 74-82% of the time (5,6,28). The REM dreams typically contain vivid sensory experiences and may have long and narrative content. Some of the rapid eye movement, characteristic of REM sleep stage, correspond to dream content related to gaze shifts within the dream, but some do not. Recall rate of NREM dreams is somewhat lower than for REM dreams, only 17-43%. NREM dream content is typically less narrative and consists of static scenes that the dreamer passively perceives. (5,6,28).

During REM sleep, there are shared neurophysiological phenomena with wakefulness. Some excitatory, glutamatergic brain stem neural circuits, dopaminergic limbic and motivational areas, and cholinergic projections from basal forebrain to cortex are active during REM sleep, but not during NREM sleep. The activation of wake system neurochemistry

contributes to active dream mentation, lower threshold of arousal and higher rate of dream recall (29,30).

Recall of sleep content is associated with local fast frequency, wake-like EEG activity. Gamma power (40Hz) increases the probability of dream recall at any sleep stage. Frontal activation is associated with more realistic dream content, as well as with conscious-like thinking in sleep, which relates to precise recall of dream content and misinterpretation of the stage as awake. Posterior activation is associated with more dreamlike, unrealistic content. The smaller size of delta waves during NREM sleep is associated with experience of dreaming and dream recall (5,6,31).

Special cases of dreaming with atypically active frontal activation are lucid dreams. They are typically REM dreams, but they may also occur at sleep onset when REM sleep is rare. In lucid dreams the sleeper becomes aware that he or she is dreaming and can sometimes control the dream scenery or guide the dream narrative (28). Recurrent, weekly lucid dreaming is quite rare (1%), but one half of the population has experience of lucid dreaming. Gamma power in prefrontal cortex is increased compared to non-lucid dreaming brain activity (32).

During REM sleep *muscle atonia*, mediated by medulla glycinergic and GABAergic regulation, paralyzes striated muscles in the body. This prevents movement corresponding to motor cortex activation in REM sleep and behavioural dream content. Failure in muscle atonia, in combination with aggressive dream content, may lead to violent dream enactment, behaviour that is typical to certain parasomnias. There is no muscle atonia during NREM sleep stage, and that is why sleepwalking is possible during NREM deep sleep with partial awakening. During sleepwalking, eyes opened, the sleeper perceives the environment enough to move somewhat purposefully, but without wakeful consciousness. The interpretation of the environment is dreamlike. (33,34).

CLASSIFICATION OF PARASOMNIAS

NREM PARASOMNIAS

NREM parasomnias (Disorders of Arousal, DOA) are motor behaviours that arise from slow wave sleep during the sleep stage N3. The mechanism is incomplete transition to wake from N3. NREM parasomnias comprise a variety of manifestations with an increasing complexity from confusional arousal to sleep terror to sleepwalking. Between them, on the continuum of motor behaviour is sleep terror, also known as pavor nocturnus. Sleep terrors are characterized by extreme fear, motor agitation, intense vocalization and high autonomous activity (35).

NREM parasomnias manifesting as partial arousals are *sleepwalking* (2-4% of adults), *sleep terrors* (1-2% of adults) and *confusional arousals* (3-15% of adults) (34,36). Variants of sleep walking, such as *sleep-related eating disorder* and *sexsomnia*, are also classified as NREM parasomnias. Subjects with NREM parasomnias often have comorbid anxiety and mood disorders, but the prevalence of sleep apnoea is also elevated (34).

Unlike common expectation, most adults with sleep terror or sleepwalking occasionally remember the dream content. The dreams are typically short, visual and unpleasant with themes of danger, threat or catastrophe (37). Dreamlike mentation most often (95%) consists of a single visual scene. The patients with dream mentation reported more severe daytime sleepiness after NREM parasomnia episodes (38).

Onset age is typically in early childhood and they are common phenomena among children, often relieved by puberty. They may, however, persist or relapse in adulthood more often than reported in epidemiological studies (39). While major psychiatric problems are not common among these patients, elevated rates of parasomnias are reported among individuals with psychiatric disorders (40).

Further, NREM parasomnias are triggered by factors increasing sleep fragmentation, such as psychosocial stress and anxiety in vulnerable individuals (41). Also, factors leading to increase of N3 sleep, such as sleep deprivation, night shifts or fever, predispose to disease episodes (41). Benzodiazepine receptor agonists and modulators, antidepressants, antipsychotics and beta-blockers are possible triggers for sleepwalking. The strongest evidence for medication-induced sleepwalking is for zolpidem and sodium oxybate (42).

REM PARASOMNIAS

REM parasomnias arise from REM sleep.

Nightmare disorder includes recurrent, extended, extremely dysphoric, intensive and well-recalled dreams that lead to awakening, and becoming rapidly oriented and alert on awakening. They cause significant distress or impairment by the unpleasant dream, or by disruption of the sleep, and sometimes by secondary insomnia. Nightmare disorder is more common in children than adults (4%). It is often related to psychological stressors, and nightmares are common symptoms in PTSD, depression and alcohol withdrawal (33,37).

At population level, nightmares relate to symptoms of insomnia, alcohol use, a core symptom of depression and negative attitude towards self (Sandman 2015). Various substances affecting glutamatergic, noradrenergic, dopaminergic, GABAergic, histaminergic or cholinergic neurons may disturb dreaming by causing nightmares (43). Many antihypertensive, antidepressant and dopaminergic drugs can induce nightmares (37).

Sleep paralysis is an incomplete transitioning from REM sleep to wake, so that the muscle atonia typical of REM persists while there is an intrusion of alpha activity (8-12Hz EEG) and consciousness during an otherwise desynchronized EEG. Sleep paralysis may be accompanied by a sensation of pressure on the chest and sometimes frightening hypnopompic hallucinations. Typical onset is in adolescence or young adulthood. Sleep paralysis is common in patients with narcolepsy, but occurs quite frequently (6%) as an isolated phenomenon in an otherwise healthy population (44).

REM sleep behaviour disorder (RBD) is a potentially violent and harmful motor enactment of dreams that is characterized by loss of muscle atonia during REM sleep. The behaviour occurs more towards the morning hours when REM sleep is more frequent (45). Patients with RBD often have violent dream content (46). Onset is typically in older age, often related to degenerative neural processes or medication. Earlier onset, from childhood to young adult, is typical of narcolepsy (33).

RBD is often related to synucleinopathies, such as Parkinson's disease, Lewy body dementia and multiple system atrophy, and it is usually an early sign of these diseases. However, RBD is also encountered in other neurodegenerative diseases, including Alzheimer's disease, Huntington's disease and amyotrophic lateral sclerosis (45).

Other parasomnias like catathrenia (sleep-related expiratory groaning), exploding head syndrome (a sudden, non-painful sensation of explosion) and nocturnal enuresis (recurrent involuntary voiding during sleep) may occur at any sleep stage. Hypnagogic (at sleep onset) and hypnopompic (at waking) hallucinations occur during transitions between sleep and wake as isolated phenomena, or along with sleep paralysis, or as a part of narcoleptic tetrad.

TREATMENT OF NREM AND REM PARASOMNIAS

Treatment of parasomnias is indicated if the symptoms cause considerable distress, worry, social disturbance or severely disrupt sleep leading to daytime tiredness. Treatment is also needed if they threaten the safety of the sleeper or sleeping partner. There is, however, a lack of randomized controlled trials on the efficacy of pharmacological or non-pharmacological intervention in parasomnias, with the exception of nightmares (47) and REM Behaviour Disorder (RBD) (48).

For all parasomnias, treatment is based on identification and elimination of factors triggering the symptoms, such as irregular sleep-wake schedule, drugs or other sleep disorders, as well as maintaining a safe environment for prevention of sleep-related injury.

TREATMENT OF NREM PARASOMNIAS

Since NREM parasomnias share the same pathophysiological mechanism, the typical treatments overlap for certain priorities according to clinical picture. There are no established treatment guidelines for NREM parasomnias (49). Possible underlying predisposing factors, such as sleep apnoea and periodic limb movement disorder, should be excluded or treated. Predisposing medication should be discontinued (42).

NREM parasomnias are usually benign, and in most cases there is no need for pharmacological therapy. Non-pharmacological interventions include environmental safety, patient education and reassurance of benign prognosis, sleep hygiene, avoiding sleep deprivation, scheduled awakening, relaxation, stress management, hypnosis and psychotherapy. Pharmacological treatment is indicated if episodes of parasomnia are frequent and non-pharmacological methods are not sufficient.

In NREM parasomnias, traditional pharmacological interventions aim to reduce deep N3 sleep and increase frontal inhibition without affecting too much REM sleep, if possible. Presently, the most commonly used drugs are GABA agonists such as benzodiazepines (e.g. clonazepam) or gabapentin. The authors also have preliminary positive experience with another gabapentinoid drug, pregabalin. Anti-epileptic drugs (e.g. topiramate, carbamazepine and sodium valproate), as well as antidepressants, such as tricyclic antidepressants, paroxetine and trazodone have been tried (34,49,50). No randomized clinical trials exist for any drugs.

TREATMENT OF REM PARASOMNIAS

As REM parasomnias have distinct mechanisms, the treatments are also different for each disorder. Also, in cases of REM parasomnias, the predisposing organic sleep disorders, brain diseases or toxic and pharmacological agents

should first be excluded. As RBD often precedes or presents with synucleinopathies in older age, a thorough neurological examination is necessary.

Idiopathic nightmare disorder and nightmares induced by psychological trauma are most effectively treated by image rehearsal therapy (IRT) (37,51). Other non-pharmacological interventions, with lower evidence include systematic desensitization, progressive deep muscle relaxation training, lucid dreaming therapy and self-exposure therapy.

Among pharmacological treatments, best evidence is for prazosin, a centrally active alpha-1 adrenergic antagonist (47). Lower grade evidence for medications are, for example, alpha-2 adrenergic agonist clonidine, antidepressants (e.g. trazodone, mirtazapine, tricyclic antidepressants), atypical antipsychotics (risperidone, quetiapine), gabapentin and certain long-acting benzodiazepines (37).

Sleep paralysis does not generally need any treatment except explanation and reassurance, and there is no evidence-based treatment. Sometimes sleep paralysis is such a frightening experience for the patient that it leads to secondary insomnia and anxiety at bedtime. Antidepressants have sometimes been used with possible benefits by reducing the REM muscle atonia (44). Secondary insomnia and anxiety can often be managed with non-pharmacological methods. Resolving sleep paralysis may be hastened by consciously focusing on an outer stimulus, like watching a clock and hearing its sound.

Treatment of *RBD* is closely linked to treatment of underlying neurological pathology. The safety measures and securing the sleeping environment are essential in management of RBD. Abrupt cessation of SSRIs and other antidepressants must be avoided, however, as they may provoke RBD attacks by increasing REM sleep as a rebound phenomenon. Possible pharmacological treatments, such as long-acting melatonin and clonazepam, may relieve symptoms (49,50). Melatonin has fewer adverse effects and it is more effective for elderly patients (44).

A PATIENT CASE WITH PARASOMNIA OVERLAP DISORDER

Here we present a young NREM parasomnia patient, who presented with comorbid RBD symptoms. RBD is extremely rare in young people without predisposing neurological or pharmaceutical factors and in the absence of narcolepsy.

A healthcare employee started to re-experience frequent, disturbing somnambulism and sleep terrors after moving back temporarily to his parents three years ago, at age of 26 years. The episodes were more disturbing and frequent than in his childhood. New types of violent behaviour emerged. The sleep of the patient was severely fragmented by recurrent parasomnias as he had 2-10 attacks per night.

When the violent parasomnia episodes emerged 3 years ago, he attacked his father while having a nightmare about an imaginary enemy. He sometimes broke pieces of furniture and rushed outside of the house. He could, for example, lift his bed against the door to protect himself, and carry his girlfriend out of the room to save her. He was also verbally aggressive during parasomnia episodes. Once he grabbed his girlfriend saying in English, “I kill you”, speaking to an imaginary dream enemy. Sometimes he was roaring like a bear, trying to scare away dream creatures.

No serious accidents took place, but the patient was overwhelmed, frightened and worried about his parasomnia symptoms. Furthermore, he developed secondary insomnia because he was afraid of his potentially dangerous and socially undesirable sleep attacks. He was exhausted and sleepy, and had problems with memory and concentration. He had been on sick leave for 6 months before coming to psychiatric sleep disorder consultation.

Before that, during the sick leave, a complete neurological examination, including brain magnetic resonance imaging, polysomnography and laboratory screen, was performed. There was no drug abuse and laboratory screenings were normal. During neurological examination, the patient had a 2-month treatment trial with clonazepam with no response, only sedative and cognitive adverse effects. Self-medication with melatonin yielded no response either.

In psychiatric examination and sleep consultation he was diagnosed with post-traumatic stress disorder. In a few of his nightmares he re-experienced traumatic events from his childhood. His father’s behaviour had been uncontrolled and aggressive while he was drunk, and he had attacked the patient several times when he was a pre-teenager. Once his life was in danger when his father strangled him. He had put aside those memories, but they re-emerged in his dreams and his arousal threshold was very low. Even minor outside stimuli could trigger incomplete awakenings and violent parasomnia attacks. He had been watchful and alert during day and night since his childhood, getting so used to it that he did not automatically consider it abnormal.

Typical of NREM parasomnia, he was confused if woken up, had sleep inertia and sometimes sleep drunkenness with difficulty in waking up. He did not remember all the episodes, and the degree of dream recall varied. The timing, however,

was atypical for NREM parasomnia, as the episodes were occurring several times throughout the night, clustering around the early morning hours. Simultaneous nightmares and aggressive behaviour, corresponding to threatening and violent dream content, were also features referring to REM parasomnia rather than NREM parasomnia. He dreamed of escaping, fighting and defending himself against unreal enemies.

Polysomnography (PSG) with video recording was performed in sleep lab. Sleep apnoea and periodic limb movement disorder, as possible additional triggers for parasomnias, were excluded. PSG findings, such as RSWA (REM sleep without atonia) and repeated transitions from N3 sleep to wake with simultaneous motor behaviour, correlated with physiological mechanisms of REM as well as NREM parasomnia. However, no characteristic diagnostic behavioural manifestations (somnambulism and sleep terrors) were seen in the video in the sleep lab. It is typical of laboratory recordings that the full symptomatology does not emerge as it does at home.

The PSG recording showed 6 direct, abrupt transitions from deep N3 sleep to motor behaviour followed by waking EEG activity, characteristic of NREM parasomnia (*Figure 1-2*). Behavioural manifestations of these confusional arousals were crying, climbing up to sit on the bed, turning on the lights and grabbing the PSG equipment. PSG also revealed an elevated chin muscle tone and some irregular limb movements during REM sleep (*Figure 3-4*), manifestations of RSWA (REM sleep without atonia), a feature of RBD (REM sleep behaviour disorder), but no destructive behaviour was demonstrated in the sleep lab.

A new treatment approach had to be considered since the traditional treatment options had been proven to have a poor response. Clonazepam, with efficacy for both NREM and REM parasomnias, had shown no response, only adverse cognitive effects, malaise and increasing tiredness. Melatonin, a typical treatment option for RBD and sometimes used in somnambulism, had yielded no response, nor adverse effects. Scheduled awakening was out of the question, because there was no fixed time for episodes and they repeated several times a night.

A low-dose doxepin trial (5mg) was started while the patient was in the queue for the sleep nurse. Doxepin was intended to treat secondary insomnia and to stabilize sleep by increasing the arousal threshold. With doxepin, there was a risk of NREM parasomnia escalation by increasing the amount of deep sleep, and a risk of RSWA progression by possible increase of muscle tone during REM, at least with higher doses. The initial response to doxepin during the first two weeks was good, and the sleep was further stabilized by increasing the dose up to 7.5mg. Parasomnia episodes became milder and less frequent.

Psychoeducation, reassurance, behavioural guidance (risk minimization, optimal sleep timing, relaxation) and cognitive methods (stress and anxiety management, image rehearsal) were offered by a sleep nurse. The risks to the patient and his bed partner were addressed by counselling and education, avoiding violent consequences by sleeping apart, removing potentially injurious objects, providing soft obstacles to stop rushing around, locking the doors, etc. Image rehearsal therapy is an evidence-based treatment for nightmare disorder (51) in which the patient modifies the recurrent nightmare narrative into a more tolerable form, as well as working with the related self-attributions and emotions.

Finally, the patient reported a remarkable relief of symptoms after 2 months of treatment. Parasomnia episodes did not recede, but instead of several times a night they occurred now every second night and they were milder. Severe, violent attacks were remarkably reduced (2 times in 2 months) compared to previously (several times a night). The daytime tiredness receded and both physical and cognitive performance was so improved that the patient returned to work and his sport hobbies, enjoying them again.

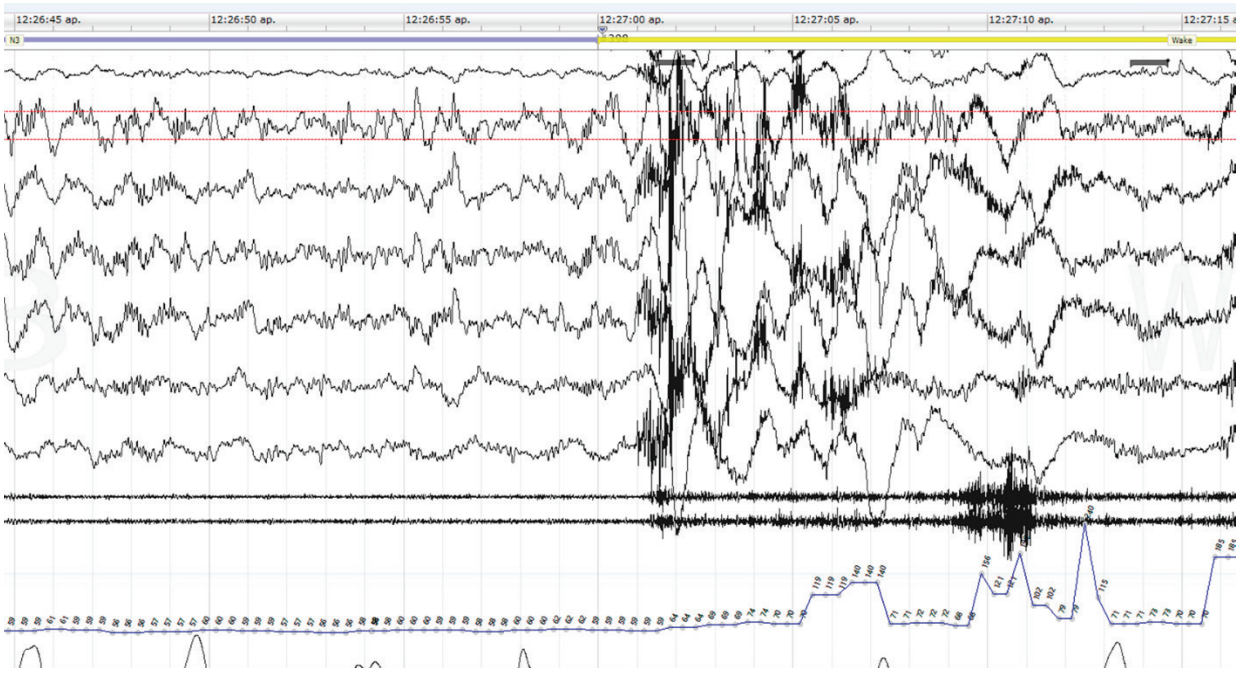

Figure 1. The first transition from N3 to wake, 17 minutes after falling asleep. Focus on 30 seconds between epochs. There is some fast alpha activity running on the delta waves just before waking. Movement artifact on EEG and an elevated chin muscle tone, and marked increase in pulse are shown upon waking.

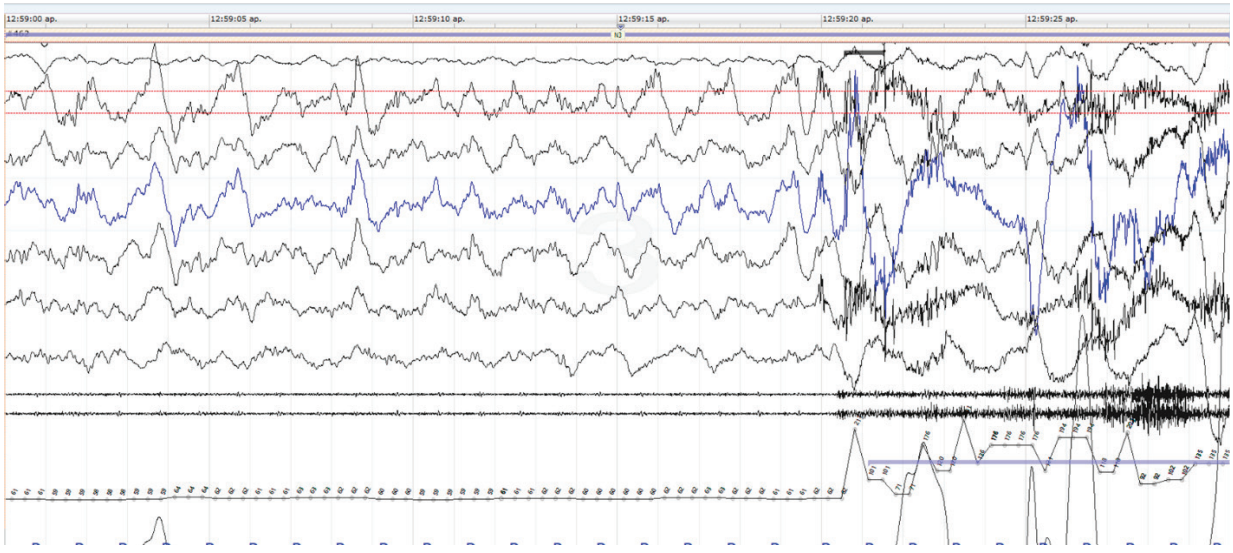

Figure 2. The second transition from N3 to wake, 50 minutes after falling asleep. A full 30-second epoch. There is some mild hypersynchronous delta waves before waking, and an autonomous arousal characterized by elevation of pulse.

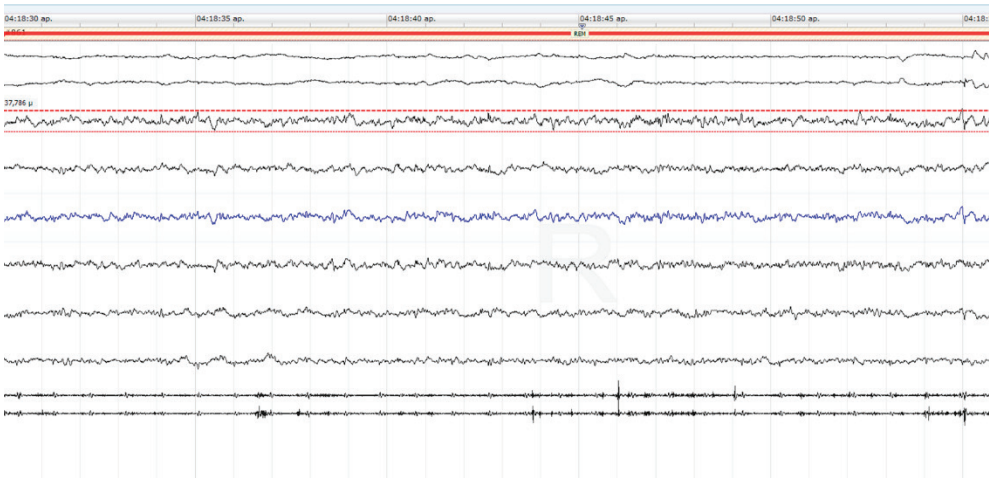

Figure 3. The second REM phase at midsleep. Mild RSWA is seen in the 30-second epoch. Chin muscle (EMG) tone is slightly elevated with frequent small twitches. There are simultaneous facial and limb movements detected on video, not presented here.

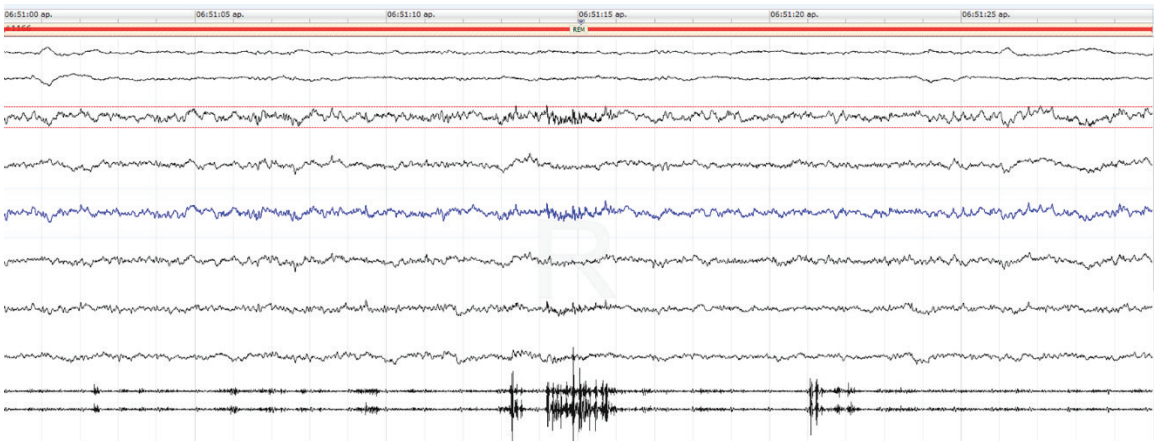

Figure 4. The third REM phase with a more pronounced RSWA seen in the 30-second epoch as an elevated chin EMG tone (two lowest derivations).

DISCUSSION

Here we present a parasomnia patient who suffered from violent enactment of nightmares clustering in the early morning hours, consistent with REM sleep behaviour disorder. However, his young age was atypical of RBD in the absence of predisposing neurological disease or drugs. He responded well to low-dose doxepin, which was somewhat unexpected for RBD, as in small doses it does not decrease REM sleep as much as other, more commonly used antidepressant medications.

However, in favour of a predominant NREM sleep disorder, our patient had a childhood history of NREM parasomnias (sleep terrors, somnambulism), and typical of NREM parasomnia he was often confused if woken up, with frequent amnesia of sleep attacks and often only vague dream recall. The video-PSG findings showed signs of both REM and NREM parasomnias: the partial lack of muscle atonia during REM, and transitions from deep sleep to wake, both with motor behaviour.

For the lack of a more accurate sleep disorder diagnosis, we diagnosed the patient with parasomnia overlap disorder, POD. In ICSD-3, POD is classified as a subtype of RBD occurring with NREM parasomnias. However, considering the predominant NREM parasomnia symptoms, younger age of onset and lack of underlying neurological disease, POD most likely is a distinct entity instead of an RBD subtype (52). An updated classification of POD also comprises RBD sleep-related eating disorder, RBD sexsomnia, RBD rhythmic movement disorder and POD with neurological disorders (53), further blurring the clear phenomenological distinction between NREM and REM parasomnias.

Two-thirds of PODs are idiopathic whereas a third are related to neurological morbidity, especially alpha-synucleinopathies (54). Though the pathophysiology of POD is unknown, it is possible that in some cases there is an evolution of sleep-related motor dyscontrol by ageing, with a more prominent DOA component earlier in life and RBD becoming more prominent during later years (52). RBD symptoms in patients under 50 years are often associated with narcolepsy (33). Other pathologies linked to POD are multiple sclerosis, brainstem structural anomalies or lesions, head trauma, ethanol abuse and post-traumatic stress disorder (PTSD) (54).

Despite the association between POD and PTSD, there is no such association between psychological trauma and RBD, which is linked to neurological disease, often a neurodegenerative process. Instead, post-traumatic and current psychological stressors are typical of REM nightmare disorder and psychological stress is associated with NREM disorders (34,36,37). Emotionally loaded events, even positive ones, are commonly reported to precede NREM parasomnias, possibly explained by high arousal and sleep stage dissociation (39).

Surprisingly, PSG and neurologically examined NREM parasomnia patients later reported frequent violent and injurious behaviour with simple dream enactment (55). Possible mechanisms presented were sleep stage dissociation and impaired inhibitory control of motor systems (39), further supporting the theory of symptoms evolving from NREM parasomnias towards POD with behavioural and PSG features of RBD, and POD being distinct from RBD (52).

In PTSD, nightmare disorder is frequently reported (up to 80% of patients), but this diagnosis does not acknowledge the presence of disruptive nocturnal dream enactment behaviour. However, disruptive nocturnal motor behaviour accompanied by autonomic hyperarousal, abnormal vocalizations and replay of traumatic experiences in nightmares are frequently reported in trauma survivors with and without PTSD. Even if secondary REM sleep behaviour disorder is reported in PTSD patients, with the lack of REM atonia in PSG accompanied with dream enactment behaviour, no accurate diagnosis to encompass the complex and disruptive motor behaviour in PTSD is available. For these patients, a new diagnostic entity is suggested as "Trauma associated sleep disorder", TSD (55).

Typical TSD dream content is different from RBD and POD. The nightmares of RBD tend to have quite similar themes of animals and self-defence against enemies, whereas the nightmares of TSD are unique to each patient with replay of traumatic experiences (55). The preliminary TSD treatment approache (IRT, prazosin) focuses on nightmares (55). Our patient, despite having PTSD, reported no recurrent, identified nightmare narrative to offer focus for IRT and the replay of traumatic experiences was infrequent. Rather, the dream content showed features of vague NREM dreams and violent fighting themes typical of RBD.

Traumatic nightmare enactment may share the same mechanism (sleep stage dissociation and impaired inhibitory control of motor systems) that is suggested to lie behind disruptive enactment of NREM dreams (39). However, there is no clear explanation for the dysregulation of REM sleep muscle tone in PTSD patients with nightmares. Simultaneous hyperarousal with deficient filtering of stimuli, continuous alertness and hyper-reactivity to potentially "threatening" external cues, and consequent disruption of sleep with incomplete transitions between sleep and wake typical of

parasomnia, may contribute to increased sympathetic and muscle tone with consequent enactment of nightmares. Other possible explanations include incomplete transitions between NREM and REM sleep, as the disruption of REM sleep may lead to increased homeostatic sleep pressure for intrusions of REM sleep into NREM sleep.

The patient himself was described to be continuously at "hyperarousal state" day and night. According to his girlfriend, he reacted to even the smallest outside stimuli with violent attacks during sleep. He recognized motor hyper-reactivity, tension and restlessness both day and night. The "hyperarousal state" could be related to central sensitization, low parasympathetic tone and high sympathetic tone (56). In PTSD, sensitizing of the central nervous system's arousal centres can lead to pronounced central and physiological hyperarousal (57).

After treatment for POD, his sleep quality and daytime well-being were better, probably with bidirectional causality. He returned to his work after a long sick leave, showing the clinical importance of treating comorbid sleep disorders of patients with psychiatric disability.

There is no established treatment for POD. Sustained release melatonin and benzodiazepines have been commonly used medications for patients with POD, and usually the response has been good. In some cases, the symptoms have resolved after discontinuation of provoking medications, such as antidepressants, antipsychotics or zolpidem (50,58). Behavioural and psychotherapeutic techniques aimed at lowering arousal, stabilizing sleep and coping with stress may be useful for POD. In this case, the treatment of secondary insomnia may have reinforced the initial positive response to doxepin by further stabilizing sleep and offering coping strategies for anxiety. Because of PTSD, the patient was also referred to psychotherapy, which probably advances the recovery from parasomnias by relieving anxiety and hyperarousal.

As far as we know, this is the first report of doxepin used successfully used in the treatment of parasomnia overlap disorder. In small doses, doxepin acts primarily as a histamine H1 receptor inverse agonist. With doses above 10mg it has an antimuscarinic action that reduces REM sleep, thus potentially lowering the occurrence of REM parasomnias. Low-dose doxepin is recommended by the AASM (59) and the Finnish Sleep Research Society (60) for treatment of insomnia disorder, and our patient was suffering from secondary insomnia. Based on this case, we are cautious in making conclusions about the mechanism of response. At least part of the positive response can be linked to the normalizing action of doxepin on both NREM sleep and REM sleep without affecting brain processing or emotional pathways to the same degree as, for example, benzodiazepines.

Further trials are needed to establish effective and safe pharmacological treatment options and to standardize non-pharmacological methods for complex parasomnias with overlapping clinical pictures. In psychiatric patients, the predisposing antidepressant and antipsychotic medications should be considered as a possible secondary aetiology for RBD symptoms. Antidepressants indicated for concomitant anxiety disorder, common in NREM parasomnias, can increase the muscle tonus during REM sleep, thus predisposing to POD (61).

The quality of sleep and sleep-related symptoms are of clinical importance for psychiatric assessment, addressed by differential diagnosis as focus of treatment, and noted as possible factors behind relapses, residual symptoms and treatment-resistant psychiatric disorders. As an example of diagnostically challenging, debilitating and injurious parasomnia symptoms with psychiatric comorbidity, we present a patient case. The clinical picture could not be classified clearly to either main parasomnia category (REM nor NREM parasomnia), but something between them, better described as a parasomnia overlap disorder.

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Figure 5. “With wings of dream” Ulla Santanen.

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