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Editorial

REM parasomnias: Straddling the sleep-wake line

Sleep is a dynamic process marked by the cyclical transition between non-rapid eye movement (NREM) and rapid eye movement (REM) phases, each lasting 90–100 min. Approximately 75–80 % of total sleep time is devoted to NREM, particularly stage N3, with REM constituting the remaining 20–25 %. The dominance of NREM in the early part of sleep gives way to progressively increasing and more pronounced REM cycles towards the end. Clinically, REM sleep is identifiable by closed eyelids, rapid eye movements, relative immobility, atonia, and complex, bizarre and emotionally charged dreams. These are reflected in neurophysiological studies in the form of markedly reduced or absent EMG activity (atonia) and rapid eye movements on the electrooculogram (EOG). EEG typically shows fast rhythms and theta activity, sometimes with a sawtooth morphology.

Parasomnias, which are undesirable physical events or experiences that occur at entry into sleep, during sleep or during arousal from sleep, encompass both NREM and REM sleep and signify dissociations between wakefulness and sleep states. They often involve complex, seemingly purposeful actions but the patient usually remains unaware of the behavior. REM sleep parasomnias include abnormally emerging or persisting REM phenomena during wakefulness, such as atonia in sleep paralysis and intense dreaming in nightmare disorder. Conversely, REM sleep behavior disorder (RBD) is characterized by the absence of one of the normal features seen during REM sleep, resulting in the loss of atonia.

This issue of *Clinical Neurophysiology Practice* features a comprehensive review of the clinical neurophysiology of 3 REM parasomnias: RBD, recurrent isolated sleep paralysis and nightmare disorder (Bergmann et al., 2024). Although RBD can be secondary to a number of conditions, including narcolepsy, established neurodegenerative disease, autoimmune disease, and stroke, the authors focus on isolated RBD. This well-organized article delves into the clinical neurophysiology of isolated RBD, providing detailed insights, while summarizing the limited data regarding the other two conditions. REM sleep dissociative phenomena (hypnagogic hallucinations, cataplexy and sleep paralysis) also occur in patients with narcolepsy, but this is not considered to be a parasomnia and is not discussed in this review. The article also does not address rare forms of RBD such as parasomnia overlap disorder or status dissociatus.

RBD is the best characterized type of REM parasomnia because of the widespread availability of polysomnography (PSG) and the need for this study to establish the diagnosis. It also has considerable clinical importance due to the medical and sometimes legal consequences of dream enactment behavior including sleep disruption, injuries and violence to a bed partner. In patients with RBD, dreams are usually unpleasant, often involving chasing or attacking themes, that may result in aggressive behavior. Interestingly, this often contrasts with the placid and mild-mannered daytime temperament of these individuals. In addition, isolated RBD can be a marker of alpha-synucleinopathies such as Lewy body disease, multiple system atrophy and Parkinson's disease, as well as tauopathies, which can develop several years later.

In this review, the authors compare diagnostic criteria for RBD from the American Academy of Sleep Medicine (AASM) and the International REM Sleep Behavior Disorder Study Group (IRBDSG). They describe a number of features including technical details, but the major difference between the two criteria is the need to demonstrate an actual episode of RBD on video-PSG in the latter. The AASM criteria allow a presumption of occurrence of vocalizations or complex motor behaviors during REM sleep based on clinical history of dream enactment. Both criteria require PSG demonstration of REM sleep without atonia (RWA). The authors appropriately highlight this and also provide a helpful table illustrating all the differences between these 2 diagnostic approaches. They also emphasize the importance of recording muscle activity not only from the chin but also the upper extremities. It is worth noting that although RWA is generally associated with RBD, use of antidepressants such as selective serotonin uptake inhibitors (SSRI) and selective norepinephrine uptake inhibitors (SNRI) may result in RWA without the motor activity of RBD (Szucs et al., 2022).

Apart from the defining feature of RWA, a number of other neurophysiological abnormalities can occur even during wakefulness and NREM sleep, as described in detail by the authors. Given the high rate of conversion to an alpha-synucleinopathy, there has been considerable interest in identifying neurophysiological biomarkers that could predict the development of these disorders. This review suggests that EEG changes such as slowing during wakefulness and sleep, lack of suppression of beta rhythms and alterations in sleep spindles and K-complexes during NREM sleep could reflect this risk. In addition, the cyclic alternating pattern (CAP), which occurs during NREM and indicates micro-instability, has been studied in RBD. Some groups have found a low rate of CAP (i.e. greater stability) both in patients with isolated RBD and in those progressing to a synucleinopathy, where the reduction is greater (Melpignano et al., 2019, Szucs et al., 2022). However, contrasting results have also been reported and additional work needs

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to be done in this area. Similarly, changes in autonomic functions, evoked potentials, transcranial magnetic stimulation and corticomuscular coherence and their predictive value deserve further investigation.

Although not discussed in this review, video-PSG with an extended EEG montage is also helpful to distinguish RBD and other parasomnias from nocturnal seizures. Sleep related hypermotor epilepsy (SHE) is a specific entity characterized by seizures with prominent motor activity (Tinuper et al., 2016). Although SHE can be clinically mistaken for RBD, the seizures occur predominantly during NREM sleep and only rarely during REM. Unlike the motor activity seen with RBD, the seizures are brief (<2 min) and have a stereotyped pattern within individuals. Moreover, seizures are very frequent and clustering is characteristic. There is no report of dreams associated with seizures. A diagnosis of SHE can be confirmed with video-EEG documentation of hypermotor seizures during sleep, associated with a clear-cut epileptic ictal pattern or with interictal epileptiform abnormalities. However, epileptiform activity may not be observed in interictal and ictal scalp EEGs either because of a deep-seated focus or prominent artifact from the motor activity during seizures.

As the authors acknowledge, there are very few neurophysiological studies in patients with isolated recurrent sleep paralysis. The findings confirm that there is a REM-wake dissociated stage with simultaneous alpha activity on EEG with muscle atonia, but the reports do not provide any additional insights into why this phenomenon recurs in such patients. Neurophysiological studies could also attempt to elucidate differences, if any, between the sleep paralysis in patients with this disorder and that seen in narcolepsy or normal individuals.

There are limited data regarding the neurophysiology of nightmare disorder. The authors cite small studies indicating that features of wakefulness are present during REM sleep. They also comment on links between nightmare disorder and post-traumatic stress disorder (PTSD) as well as sleep apnea, but emphasize the need for additional research in this area. Interestingly, other authors have also noted an association between RBD and PTSD (Elliott et al., 2020). In fact, due to the frequent co-occurrence of these conditions, a new term-trauma associated sleep disorder, which includes features of both these conditions, has been proposed (Mysliwiec et al., 2014).

This review provides a wealth of neurophysiological details in REM parasomnias, but could have been enhanced further by a deeper exploration of the clinical significance of the various findings and their impact on clinical practice. The authors could also have enriched this article by discussing some of their own work in this area and providing their own perspective. Additional figures and tables would have been helpful. Nonetheless, this review serves as a valuable resource, paving the way for further investigation into these fascinating and intriguing group of disorders. Future studies could not only provide more information regarding these entities but also shed light on the connections between REM parasomnias and narcolepsy, autoimmunity and PTSD. Neurophysiological changes predictive of progression from RBD to neurodegenerative disorders need to be better characterized. REM parasomnias may also provide a better understanding of the influence of psychopathology and antidepressants on sleep regulation.

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