

Sleep and REM Behaviour Disorder: Much More than Sleep Walking

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Clinical Points

- REM sleep is characterised by saccadic eye movements, muscle atonia, and vivid dreams
- The key complaint in RBD is violent dream enacting behaviour during REM sleep which results in harm to the patient and their bed partner
- RBD is linked to neurodegenerative conditions especially Parkinson's disease and dementia, as well as narcolepsy
- RBD is a chronic disorder but highly treatable with clonazepam taken at night before sleeping
- RBD must be differentiated from nocturnal seizures, sleep walking, sleep terrors, obstructive sleep apnoea with agitated REM-related arousals, periodic limb movement disorders and malingering

ABSTRACT

Rapid eye movement (REM) sleep is characterised by the active neurological processes which underpin dreaming and result in the paralysis of all somatic musculature, except extra-ocular muscles and the diaphragm for continued respiration. Recently, a sleep parasomnia, termed REM Behaviour Disorder (RBD), has been described, in which patients physically act-out their dreams in an excited and sometimes violent manner. This paper presents two clinical vignettes describing patients with RBD and reviews the available literature on the subject.

CLINICAL VIGNETTES

Mr B, 67 year old male, presents electively to the neurology outpatient clinic following episodes of acting out during his dreams. These spells occur most nights around 3 a.m., when the patient is likely to be in REM sleep. He describes a typical dream where he is a child on a flight home from Alaska which stops over in Seattle. He misses his connection and a stranger offers to take him on a sightseeing tour of the city. When he gets into the stranger's car a gun is pointed at his head. In order to escape he jumps from the car, at which point, he physically jumps off his bed and dives to the floor, injuring his neck. On this particular occasion he also kicked his wife in the chest and, as a result, she now sleeps in a separate room.

Mr S, 23 year old male, reports having trouble with his sleep since childhood. His main complaint is that he sometimes has intense dreams which he re-enacts. Recently, he dreamt his wife was attempting to place a spider on his face, resulting in him assaulting her via a blow to the stomach. His wife is understandably distraught and feels he needs medical attention.

INTRODUCTION

Normal Sleep

Sleep is defined as a state of unconsciousness from which a person can be aroused with a stimulus and restored to a state of full responsiveness¹. This definition

serves to distinguish sleep from a coma where a person cannot be aroused to a state of full responsiveness, regardless of the intensity of the stimulus¹.

Sleep is an essential function of the brain and is organized to produce predictable electrophysiologic patterns that form the basis of behavioral sleep². The neural centers involved in the production and regulation of sleep patterns are located in the brainstem, diencephalon, thalamus and also involve the cortex secondarily². Sleep is also generated by the influence of hormones, neurotransmitters, and active peptides².

The sleep-wake cycle is coupled with the external alteration of light and dark. It follows a 24 hour pattern, or circadian rhythm, which is mediated by the suprachiasmatic nucleus of the hypothalamus². It is linked to the retina via the retino-hypothalamic tract which conveys photic information in order to synchronize the circadian rhythms with the light-dark cycle².

Brain activity alternates between wakefulness and sleep². Sleep is further divided into two distinct states, non-rapid eye movement (NREM) and rapid eye movement (REM) sleep. During the night, a person alternates between NREM and REM sleep. At the start of the night, the person experiences more NREM sleep which is the deep, restful slow wave sleep after being awake for many hours². REM sleep occurs in episodes that occupy approximately 25% of the sleep time in young adults and normally tends to

recur every 90 minutes². Each state has distinct anatomic, electrophysiologic, biochemical, and behavioral characteristics which allows them to be studied independently.

The electroencephalogram (EEG) is used to study the various stages of consciousness and sleep². Electrodes are placed on the scalp but in some special cases they are inserted subdurally or even in the cerebral cortex to measure the electrical activity of the brain. The electrical activity reflects the electrical signals (postsynaptic potentials) from a large number of neurons³. Electrical currents are not directly measured but rather voltage differences from various parts of the brain are used. EEG is a useful method of studying brain activity since it is generally non-invasive and highly sensitive³. EEG can detect changes in electrical activity in the brain in a millisecond. It is a useful tool for studying patients with neurological conditions such as epilepsy, dementia, brain death and coma³.

Wakefulness

The neuronal areas of the brain involved in promoting wakefulness are primarily found in the reticular formation⁴. These neurons constitute a system located in the reticular formation of the brainstem, thalamus, posterior hypothalamus, basal forebrain, and subthalamus⁴. The tonic activity in the reticular activating system is reinforced by sensory input via collaterals in order to maintain wakefulness⁴. Reticular system activation ascends via the brainstem reticular formation into the thalamic system from where it is transmitted to the cortex of the forebrain. There is also an alternative extrathalamic route which originates in the subthalamus, posterior hypothalamus,

and basal forebrain that eventually projects to the entire cortex⁴.

NREM Sleep

NREM sleep is characterized by slowing of the electroencephalograph (EEG) rhythms, high muscle tone, and absence of eye movements. There are four stages which are summarized in Table 1.

Sleep appears when the sleep promoting neurons become active and the wakefulness-maintaining mechanism fades². Synchronized sleep is an expression of the unified activity of many different neural networks. EEG findings are summarized in Table 1 and serves to reflect the activity of these networks. Neurons involved in generating synchronized sleep are found in the anterior hypothalamus, preoptic area, solitary tract nucleus of medulla, raphe nuclei of the brainstem, reticular thalamic nuclei, basal forebrain, and orbitofrontal cortex².

Before synchronized sleep occurs, it is preceded by light transitional sleep⁴. Both the light transitional sleep and synchronized sleep form the NREM state. During the light transitional sleep, which occurs before Stage 1 of NREM, it is common for people to experience an involuntary muscle twitch known as a hypnic or hypnogagic jerk⁴. This is completely normal, especially when people are very tired or not sleeping comfortably. Stage 1 sleep is characterized by the disappearance of alpha waves (8-12Hz) which are characteristic of wakefulness, and appearance of theta waves(4-7Hz). This stage only lasts for a few minutes and may recur briefly during the night after body movements⁴.

Stage 2 sleep appears five to seven minutes later⁴. Stage 2 sleep, which is the longest stage of sleep, is characterized by sleep spindles (7-14Hz). The functional significance of sleep spindles are unknown, but they are associated with the blockade of synaptic transmission of afferent impulses through the thalamus when there is a loss of consciousness. Spindle frequency potentials and spike discharges in the neocortical neurons are recorded on the EEG when there are bursts of activity in the thalamocortical networks⁴. K complexes are also seen randomly in this stage of sleep and are thought to occur in response to auditory stimuli. For example, when researchers knocked on the door when people were in stage 2 sleep, K complexes appeared, followed by sleep spindles.

Stage 3 sleep appears 15 to 30 minutes later and is known as slow wave sleep or delta sleep (due to delta waves (<2Hz) on EEG). Serotonergic neurons located in the raphe nucleus in the brainstem promote the emergence of slow wave sleep 4. In this stage of sleep it is hard to arouse an individual and it is also virtually nonexistent in the elderly⁴. Stage 4 is the maintenance of the delta waves on the EEG. Essentially, stages 3 and 4 sleep last 30 to 45 minutes and are followed by a reversal to stage 2 and the onset of the first REM episode⁴. This marks the end of the first sleep cycle.

Table 1. Stages of Non-REM Sleep

Stage	EEG Findings	Distribution	Fact(s)
Stage 1	Disappearance of the alpha wave (8-12Hz) and appearance of theta wave (4-7Hz)	5%	
Stage 2	Sleep spindles (7-14Hz) and k complexes	45%	Longest stage of all the sleep stages.
Stage 3	Appearance of delta waves (<2Hz)	12%	Also called slow wave or delta sleep. Hardest to arouse. Tends to vanish in elderly.
Stage 4	Continuation of delta wave	13%	Same as for Stage 3
REM	Bursts of sawtooth waves	25%	Easiest to arouse. Lengthens in time as night progresses. Increased during second half of the night.

REM Sleep

REM sleep is also known as paradoxical sleep or desynchronized sleep. It generally lasts 5 to 30 minutes and on average appears every 90 minutes⁵. When a person is over-tired, the bouts of REM sleep tend to be short and possibly even absent. REM sleep is considered paradoxical because the brain is quite active but the person is not fully aware of his or her surroundings. It is difficult to arouse patients from REM sleep with sensory stimuli, as opposed to deep slow wave sleep, yet people usually awaken spontaneously in the morning during an episode of REM sleep. Overall, the brain's metabolic activity is increased by as much as 20% and EEG shows that the pattern of brain waves is similar to those occurring during wakefulness⁵. The cortical EEG rhythms are desynchronized due to the activation of large nerve cells in the central midbrain reticular formation⁵. The latency to REM is shorter in sleep deprived subjects, neonates, patients with narcolepsy, and subjects withdrawing from alcohol and REM suppressant medications⁵.

There are two main components in REM sleep: *tonic* and *phasic*. In the *tonic* phase, muscle activity is suppressed and the EEG shows low-voltage mixed frequency activity. Also, no phasic REM components are observed and the respiratory rate is regular⁵. In the *phasic* component of REM sleep the muscles twitch, rapid eye movements occur, and heart rate as well as respiratory rate become irregular. It is also characterized by the appearance of sawtooth waves, runs of 2-6Hz notched waves, which may be seen in the frontotemporal region, usually in association with bursts of eye movements⁵.

REM sleep is generated by a set of unrelated phenomena produced by different areas of the pons and caudal midbrain⁵. Although it is not the unique area for the production of REM sleep, the nucleus reticularis pontis oralis is the region of the brain most critical for the production of REM sleep. This nucleus is located in the pons and provides input to the entorhinal cortex of the hippocampus to produce highly synchronized theta rhythms, which are present continuously during REM sleep⁵. This EEG finding resembles that of stage 1 sleep⁵.

REM sleep stage is associated with active dreaming and extreme inhibition of muscle tone throughout the body, except in the diaphragmatic muscles and eye movement muscles⁶. The inhibition is mediated by cells in the perlocus coeruleus area. These cells become active and stimulate the inhibitory nerve cells of the magnocellular reticular nucleus via the tegmento-reticular tract⁶.

However, despite inhibition of the motoneuron activity during REM sleep occasionally brief clonic contractions of facial and distal extremity muscles do occur. This is part of the phasic component of REM sleep and is due to excitatory potentials reaching motoneurons at irregular intervals⁶.

The rapid eye movements are saccadic, conjugate eye movements in the horizontal, vertical, and oblique planes. Ponto-geniculo-occipital (PGO) spike generation is associated with generation of rapid eye movements both in the waking state and in REM sleep⁷. The PGO spike originates in the dorsolateral pontine tegmentum and projects to the lateral geniculate nucleus. Each half of the pons functions independently in the generation of PGO spikes and, therefore, each pathway for propagation can be interrupted independently⁷. PGO waves are speculated to eventually reach cortical areas and trigger fragmentary imagery that we consider dreams. PGO spikes can be triggered by cholinergic activation or inhibited by serotonin⁷.

During REM sleep several physiologic changes occur. The heart rate is accelerated, blood pressure is variable, the respiratory rate increases due to the phasic (intermittent) activation of the medial and lateral parabrachial nuclei in the pons⁵. These nuclei appear to exert a modulatory effect over the bulbar neurons (cranial nerves of the lower brain stem). The respiratory fluctuations in REM sleep are controlled directly by the pneumotaxic centers of the brainstem and are independent of peripheral metabolic changes (oxygen saturation, pH of blood etc.)⁵. Other changes which have been observed include increased intracranial pressure, decreased cardiac output and urine flow, increased cerebral blood flow and sympathetic tone is loosely coupled with phasic changes in parasympathetic tone⁵.

Dreaming

Dreams are the subject of much interest in neurology and psychiatry. While there has been some interesting research, it is hard to elucidate the exact nature of dreams. Dreaming can occur in any stage of sleep, but it is most common in REM sleep⁷. Dreams do occur in slow wave sleep, and sometimes night terrors as well, but they are not usually remembered⁷. Dreams in NREM are associated with somatic muscle activity (due to the high muscle tone) as opposed to REM sleep (due to muscle atonia)⁷. This is the stage where night terrors are experienced. Usually seen in young children (but can be seen in any age group), night terrors are characterized by the awakening from Stage 4 sleep with a strong sense of fear and panic⁸. It is often impossible to completely awaken the subject and eventually he or she settles back to sleep. However, when the subject is asked about the episode, he or she is more than likely not to be able to recall the events⁸.

When subjects are awakened from REM sleep they report dreaming 85% of the time. EEG evidence shows high levels of PGO waves that originate in the pontine area travel to the lateral geniculate nuclei in the thalamus providing excitation to the forebrain. Autoradiographic experiments during REM sleep have shown increases in glucose metabolism in the visual cortex which may be the input for the dream visual experiences⁷. Sensory system activation during the dreaming experience always involves

the visual system and auditory experiences appear in about 65% of dreams⁷. Less commonly, spatial experiences such as floating or flying occur but these are most likely associated with the vestibular system. Rarely experiences involving tactile, taste or smell perceptions occur. Pain is almost never incorporated in dreams⁷.

Despite motor system excitation during dream mentation, motor commands are not executed because of the powerful inhibition of motoneurons present in REM sleep⁷. Experimental evidence indicates that cortical and subcortical motor structures, which mediate complex organized movements, are activated during the dream state⁷.

There are two main proposed theories regarding dreaming - the activation synthesis theory and continual activation theory. The activation theory, proposed in 1977 by J. Hobson, asserted that sensory experiences were due to PGO spikes⁹. Essentially PGO spikes originate in the pons and stimulate higher midbrain and cortical structures leading to rapid eye movements. This internally generated information is thought to lead to the synthesis of dreams⁹. It was assumed that the same structures producing REM sleep also led to the generation of sensory information. Since neurotransmitters such as norepinephrine and serotonin are present in decreased concentrations during REM sleep this leads to memory, attention and lack of orientation⁹.

Later on, further research on dreaming was done on patients with various brain injuries by M. Solms¹⁰. He discovered, as he questioned patients about their dream experiences, that patients with parietal lobe damage stopped dreaming (this was also shown in Hobson's theory). Patients, however, with brain stem damage did not lose the dream experience, so this raised doubts that the brain stem was the source of dreams (this was contrary to Hobson's theory)¹⁰. Solms viewed dreaming as a complex function involving several brain structures and felt that REM sleep and dreaming were not directly related¹⁰.

In 2001, a study showed that dreams may serve to help the brain consolidate memories by illogical locations, characters, and dream flow¹¹. These conditions may occur in REM sleep because there is a decreased flow of information between the hippocampus and neocortex¹¹. This lack of communication may be linked to increased levels of cortisol which generally occurs during REM sleep¹².

Neurotransmitters and Sleep

The key neurotransmitter systems involved in controlling the sleep-wake cycle are monoaminergic (noradrenaline, dopamine), cholinergic and histaminergic neurons¹³. Gamma-aminobutyric acid (GABA) neurons located in the

anterior hypothalamus and basal forebrain play an important role in sleep control. While most neurons have a very minimal role in NREM sleep, GABAergic neurons are the most active during this state compared with REM sleep or the awake state. These neurons discharge at increasing rates during sleep and maintain high levels of GABA. The main function of GABAergic neurons is to inhibit cells involved in arousal in order to induce sleep. For example, the GABAergic neurons inhibit cholinergic neurons in the basal forebrain¹³. These cholinergic neurons are one of the key forebrain arousal systems of the brain, so when they are inhibited the cortical activity diminishes. However, cholinergic neurons are active during the REM state and are involved in generating PGO spikes which are linked to dreaming¹³.

Histaminergic neurons, found in the posterior hypothalamus, play an important role in arousal and maintaining wakefulness¹³. Lesions in this area produce a comatose-like continuous sleep. These neurons are inhibited by GABAergic neurons during sleep in order to inhibit the awake state. Histaminergic neurons are virtually inactive during REM sleep. It is interesting to note that antihistamine medications which cross the blood brain barrier make patients drowsy¹³.

Norepinephrine, which is found in the locus ceruleus of the pons, is also inactive during REM sleep¹³. This neurotransmitter along with serotonin plays a role in maintaining muscle tone and motor activity during the wakeful state. Serotonergic neurons are located in the raphe nuclei which extends in the midline from the midbrain to the medulla. These neurons are also inhibited by GABAergic neurons during sleep¹³. They may play an important role in regulating the phasic events of REM sleep in that if the serotonergic neurons are destroyed, the inhibition on the phasic events would be released. Essentially, when GABA is applied to adrenergic and serotonergic neurons, REM sleep is triggered¹³.

Another substance that plays a role in sleep is adenosine¹³. The adenosine neurons are found in the hypothalamus and the receptors are blocked by caffeine and xanthines. CSF (cerebrospinal fluid) borne factors and opiate peptides, such as enkphalin, b-endorphin, and dynorphins, could play an important role in initiating and maintaining sleep¹³. These neuromodulators are crucial for sensory modulation and analgesia¹³. Several blood borne factors, such as insulin and cholecystokinin, which are released from the gut after meals, tend to promote sleep¹³.

Recently, another peptide and its variants, hypocretin I and II (also named orexin A and B) were discovered in the posterior and lateral hypothalamus¹³. Hypocretin has an unusual relationship with amino acid neurotransmitters such as glutamate and GABA¹³. In the locus ceruleus, hypocretin was shown to release both glutamate and GABA producing an excitation and inhibition which may

stabilize the electrical polarization of the membranes¹³. Absence of hypocretin is considered as the basis of the behavioral and physiologic instability which occurs in narcolepsy¹³.

REM Sleep Behavior Disorder

Definition

The key feature characterizing REM Behavior disorder (RBD) is the loss of muscle paralysis during otherwise intact REM sleep¹. REM sleep is the stage of sleep where the most vivid dreaming occurs and patients with RBD have a tendency to act out their dreams¹. This behaviour can be violent in nature and distressing to the patient, as well as their bed partner. Despite the complex pathophysiology behind RBD, it is an easy illness to diagnose and treat appropriately¹⁴.

Animal Model

The defining features of REM sleep are rapid eye movements, desynchronized EEG, and muscle atonia. The key clinical feature of RBD is loss of REM atonia with behavioral release during REM sleep. This leads to serious clinical risk of sleep related injuries because dreams crash into reality.

When bilateral dorsolateral pontine tegmental lesions in cats were introduced, the REM atonia was lost permanently¹⁵. This was the only lesion in the brainstem which produced such effects. These cats always displayed hallucinatory behaviors during unequivocal REM sleep which resembled dream enactment¹⁵. The behaviors were always stereotypic and repetitive without any external influence or provocation. It was almost always an attack behavior that was displayed, but sexual and feeding behaviors were never observed in these cats¹⁵. Also, these cats were never inappropriately aggressive during wakefulness¹⁵. This model most closely resembles the findings seen in human RBD.

Researchers identified four levels of dream-enactment behavior in the cat model of RBD¹⁵. The level of the behavior depended on the location and size of the pontine tegmental lesion. The levels are shown in Table 2.

Table 2. *Dream-Enactment Behavior as seen in Cats*

Level of behavior	Behaviors experienced by cats
1	Minimal syndrome with limb or trunk jerking. Intermittent violent behavior.
2	Exploratory behaviors – head raising and turning, grasping, searching
3	Stalking imaginary prey. Episodic attack behavior
4	Locomotion

Brain mechanisms originating in the peri-locus ceruleus alpha nucleus of the pons are responsible for the REM atonia⁶. Neurons from this region have excitatory projections to the nucleus reticularis magnocellularis in the medulla. These neurons in the medulla have an inhibitory descending projection, more powerful than the competing excitatory projections, to the spinal alpha motoneurons. This produces the hyperpolarization and muscle atonia leading to REM-atonia⁶.

However, these animal experiments reveal that the loss of atonia during REM sleep is not sufficient in itself to generate RBD¹⁵. In fact, it is interesting to note that unlike the animal model, the pons are rarely involved in the pathogenesis of RBD in humans, as shown with extensive neuroanatomical and neurophysiologic testing¹⁵. It is not completely certain which area of the brain is linked to the pathogenesis of RBD in humans. The manifestations are still similar in both humans and cats.

Aetiology and Epidemiology

Although the disorder was identified as earlier 1966, RBD was not formally recognized and classified until 1986-87 by the International Classification of Sleep Disorders. RBD can be either an acute or chronic disorder. The acute form is generally seen during withdrawal from ethanol or sedative-hypnotic abuse, as well as anticholinergic medications¹⁶. REM behavior disorder can also be drug-induced by tricyclic antidepressants, MAOIs and SSRIs¹⁶. It is difficult to study the acute form of REM behavior disorder since it is transient and often associated with the symptoms of withdrawal¹⁶.

The chronic form is most often presented to physicians for evaluation. Generally, the disorder affects older individuals (over age 50) and has a male predominance (80%)¹⁷. Approximately a quarter of the patients have a prodromal phase, which is often lengthy and involves subclinical behavioral release during sleep. Some patients report a history of childhood sleepwalking or sleep terrors¹⁸. The chronic form is associated with other neurodegenerative conditions such as Parkinson's disease and related disorders, such as Lewy body disease. There is also a link between RBD and narcolepsy as well as cerebrovascular disease^{19,20}.

The neurologic disorder may precede or follow the appearance of REM behavior disorder. Extensive neurological investigations are only required if patient has a history or clinical exam suggestive of CNS pathology¹⁹. In several studies, it is shown that REM behavior disorder is possibly the first manifestation of parkinsonian disorder, which is otherwise considered in many cases idiopathic¹⁹. In one case series report, 38% of patients further went on to develop parkinsonism with 3.7 years of diagnosis and 12.7 years after initial onset of REM behavior disorder symptoms¹⁷. There is also an association with narcolepsy and when patients are treated with TCAs or SSRIs it may

induce or aggravate the REM behavior disorder²⁰.

Clinical Features

The key complaint in RBD is that of violent dream-enacting behaviors that are potentially harmful to the patient, as well as their bed partner. Bed partners report that the patients generally have recurrent dream enacting behaviour ranging from laughing, talking, yelling, gesturing, grabbing, punching, kicking, crawling, and jumping out of bed. Generally, the dream enacting behaviors do not begin until 2 hours after sleep onset which generally coincides with typical REM onset (sleep cycles last 90 minutes and end with REM sleep)¹⁷. However, most of the time these dream enacting behaviors occur in the early morning hours when REM sleep predominates¹⁷. The frequency of these RBD episodes range from several episodes nightly, to one episode every 2-3 weeks¹⁷.

These behaviors occur within REM sleep but are not accompanied by tachycardia and do not occur during arousal from REM sleep. Complex behaviors are generally aggressive and exploratory, but never appetitive (feeding, sexual)¹⁷. It is important to note that patients do not reenact customary dreams but distinctly altered dreams usually involving violence and aggression.

Unless the RBD is linked to narcolepsy, daytime multiple sleep latency testing rarely documents objective daytime sleepiness²⁰. The explanation for this phenomenon is obscure, but one clue provided in research is RBD patients appear to have a higher percentage of restful slow wave sleep. This may be a compensatory mechanism in the body after tremendous energy expenditure in agitated REM sleep²⁰. Patients with RBD generally spend 75% of their time in slow-wave sleep²⁰.

Diagnosis

The diagnosis of RBD is made clinically, based on the history elicited from the patient and usually their bed partner. There are several important questions a physician should ask during the history about their sleep behaviours¹⁴. Patients should be asked about limb or trunk movement during sleep and if it is linked to them trying to enact their dreams. It should also be noted if the patient injured themselves or their bed partner during sleep and if they ever fell out of bed during sleep¹⁴. Also, patients should be asked if they were ever talking loudly or screaming during sleep¹⁴.

Disruptive nocturnal behaviors should be extensively evaluated by the physician. Generally, this involves asking the patient about their sleep habits, medical and psychiatric history, and evaluating their alcohol and substance use. Patients should also undergo neurologic testing since there is a high association with RBD and parkinsonism and dementia¹⁴. If history and neurologic

examination appears positive, an MRI scan may be indicated. It is important for the physician to rule out EEG epileptiform activity during sleep¹⁴. Patients should be monitored continuously with videotaping overnight during polysomnography (PSG)¹⁴.

PSG is a multi-parametric test carried out to study sleep. It consists of monitoring the patients ECG, pulse oximetry, EEG, nasal and oral airflow, electrooculogram (EOG) and electromyography (EMG)³. EOG is used to monitor eye activity which aids in the determination of when REM sleep is occurring. Two electrodes are placed slightly out and above the outer canthus of the right eye and slightly out and below the outer canthus of the left eye. The electrodes determine the activity of the eye using the electropotential difference between the cornea and the retina (cornea has a positive charge in relation to the retina)³. EMG studies are used to measure muscle tension in the body and monitor excessive amount of leg movements during sleep³. Four leads are positioned on the body. Two leads are placed on the chin, with one above the jaw line and one below it. The other two leads are placed on the anterior tibialis of each leg to monitor leg movements. The PSG gives the physician an extensive clinical picture of what is occurring during the time the patient is asleep¹⁴.

Differential Diagnosis

RBD is one of several disorders that manifest with violent behaviors during sleep. Things to consider in patients presenting with this clinical history are nocturnal seizures, sleep walking, sleep terrors, obstructive sleep apnoea with agitated REM-related arousals, periodic limb movement disorders and malingering²¹.

The history of dream enacting behaviour does not automatically confirm the diagnosis of RBD. This behavior can appear in sleepwalking and sleep terrors²¹. In these disorders, vivid dream-like meditation can occur with precipitous arousals from slow wave sleep. Also, in nocturnal complex seizures, patients can have a peculiar dream-like aura, seizure-equivalent, or postictal experience²¹. Obstructive sleep apnoea is the most severe during the REM stage of sleep and often apnoea related arousals from REM sleep can be associated with persistent dreaming and agitated behaviors²¹. When periodic limb movement disorder persists in REM sleep, agitated dream related arousals can result in post arousal dream enactment. Nocturnal psychogenic dissociative episodes involve dream mentation related to dissociated memories of past physical and/or sexual abuse²¹.

Treatment

Clonazepam is highly effective in the treatment of REM behavior disorder, in that it controls both the behavioral and dream-disordered components²². Patients typically respond immediately to a dose between 0.5-1.0 mg at bedtime and generally relapse when they fail to take

clonazepam on a given night²². The long term use of chronic, nightly clonazepam in treatment of RBD and other parasomnias has been documented in terms of efficacy and safety²².

It is noted, however, that benzodiazepines may actually worsen sleep since patients can awaken more often during the night even though it is commonly prescribed for insomnia²². Also, another important side effect to be monitored, especially in the elderly, is dizziness which may lead to fainting and falls²². Physicians should monitor patients with RBD for side effects on a long term basis ²².

If the patient cannot tolerate clonazepam, there are several alternative therapies for RBD such as imipramine, clonidine, melatonin, gabapentin, and L-tryptophan¹⁶. Patients are treated for life for REM behavior disorder since it is a chronic problem where, if patients discontinue their medication, the symptoms will reappear¹⁶.

CONCLUSION

It is important for physicians to recognize RBD for several key reasons. RBD is commonly associated with neurological disorders and, in fact, may possibly be the first sign of a disorder. RBD onset can precede the classical signs and symptoms of the neurological disorder by several years. This is commonly seen in Parkinson's disease patients. RBD may be induced or aggravated by various medications such as SSRIs, TCAs, MAOIs, and alcohol / drug withdrawal or abuse.

Also, RBD is easy to misdiagnose unless physicians are informed about the disorder. It may be considered psychiatric in nature since the common complaint is disturbed dreaming with violent behaviors enacting them. It may also be treated as nocturnal seizures or obstructive sleep apnoea. It is important that RBD is diagnosed and treated since it can potentially cause severe harm and injury to the patient and their bed partner.

REFERENCES

1. Culebras A. Preface. In: Culebras A (ed): Sleep Disorders in Neurological Disease. New York, Marcel Dekker, Inc., 2000
2. Jones BE, Basic mechanisms of sleep-wake states. In: Kryger M H, Roth T, Dement WC (eds). Principles and Practice of Sleep Medicine, 3rd ed. Philadelphia, W.B. Saunders Co., 2000, pp134-153
3. Haines DE: Fundamental Neuroscience. New York: Churchill Livingstone, 1997
4. Swick TJ. The neurology of sleep. *Neurol Clin.* 2005 Nov 23:967-89.

5. Siegel JM. Brainstem mechanisms generating REM sleep. In: Kryger MH, Roth T, Dement WC (eds). Principles and Practice of Sleep Medicine, 3rd ed. Philadelphia, W.B. Saunders Co., 2000, pp 112-133
6. Chase MH, Morales FR. The atonia and myoclonia of active (REM) sleep, *Annu Rev Psychol* 41:557-584, 1990
7. McCarley RW, Hoffman EA. REM sleep dreams and the activation-synthesis hypothesis. *Am J Psychiatry* 138:904-912, 1981
8. Miller G. Neuroscience Hunting for a meaning after Midnight. *Science.* 2007 Mar 9; 315(5817):1426-9
9. Hobson, J.A.; McCarley, R. "The brain as a dream state generator: An activation-synthesis hypothesis of the dream process". *American Journal of Psychiatry* 134: 1335-1348, 1977
10. Solms, M. Dreaming and REM sleep are controlled by different brain mechanisms, 23(6), *Behavioral and Brain Sciences*, 793-1121. 2000
11. R. Stickgold, J. A. Hobson, R. Fosse, M. Fosse. Sleep, Learning, and Dreams: Off-line Memory Reprocessing. *Science* 294 (5544): 1052 - 1057. 2001
12. Jessica D. Payne and Lynn Nadel. Sleep, dreams, and memory consolidation: the role of the stress hormone cortisol. *Learning and Memory*: 671-678. 2004
13. Siegel JM. Neurotransmitters in Sleep. *J Clin Psych* 2004;65[suppl 16]:4-7
14. American Sleep Disorders Association: International Classification of Sleep Disorders, revised: Diagnostic and Coding Manual. Rochester, Minn: American Sleep Disorders Association; 1997: 177-80
15. Schneck CH, Hurwitz TD, Mahowald MW: REM sleep behavior disorder: an update on a series of 96 patients and a review of the world literature. *J Sleep Res* 2;224-231, 1993
16. Gaillard JM: Biochemical pharmacology of paradoxical sleep. *Br J Clin Pharmacol* 1983; 16 Suppl 2: 205S-230S
17. Schenck CH, Bundlie SR, Mahowald MW: Delayed emergence of a parkinsonian disorder in 38% of 29 older men initially diagnosed with idiopathic rapid eye movement sleep behaviour disorder. *Neurology* 1996 Feb; 46(2): 388-93
18. Olson EJ, Boeve BF, Silber MH: Rapid eye movement sleep behaviour disorder: demographic, clinical and laboratory findings in 93 cases. *Brain* 2000 Feb; 123 (Pt 2): 331-9
19. Eisensehr I, Linke R, Noachtar S, et al: Reduced striatal dopamine transporters in idiopathic rapid eye movement sleep behaviour disorder. Comparison with Parkinson's disease and controls. *Brain* 2000 Jun; 123 (Pt 6): 1155-60
20. Schenck CH, Mahowald MW: Motor dyscontrol in narcolepsy: rapid eye movement (REM) sleep without atonia and REM sleep behavior disorder. *Ann Neurol* 32:3-10, 1992
21. Mahowald MW, Schneck Ch: REM sleep parasomnias. In Kryger MH, Roth T, Dement WC (eds): Principles and Practices of Sleep Medicine, 3rd ed. Philadelphia, WB Saunders, 2000, pp 724-741
22. Schneck CH, Mahowald MW: Long term, nightly benzodiazepine treatment of injurious parasomnias and other disorders of disrupted nocturnal sleep in 170 adults. *Am J Med* 100:548-554, 1996