CENTRAL HYPERSOMNIA AND REM BEHAVIORAL SLEEP DISORDER: MAKING SENSE OF THE SLEEP STUDY REPORTS

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1. Sleep Studies

PSG[1]

Sleep-related movements are commonly observed on polysomnography (PSG) and are often benign. However, certain movements warrant further investigation when they negatively impact sleep quality, resulting in daytime symptoms or injury. Technical points —PSG consists of the simultaneous recording of multiple physiologic variables during sleep:

- Electrooculogram (EOG) captures eye movement.
- Electroencephalography (EEG) captures brain wave activity.
- Electromyography (surface EMG) captures muscle activity/movement.
- Electrocardiogram (ECG) captures electrical activity from one or two heart leads.
- Respiratory airflow channels (nasal cannula and thermistor) measures the number and depth of respirations and whether there are episodes of shallow breathing (hypopneas) or episodes of breathing cessations (apneas).
- Respiratory effort channels capture the excursions of the chest and abdomen.
- Pulse oximetry continuously monitors oxyhemoglobin saturation in the blood.
- Video monitoring uses infrared-sensitive cameras and nonvisible infrared lighting during the study to capture abnormal movements or behaviors.

Multiple sleep latency test (MSLT)[2]

- The MSLT consists of 5 nap opportunities performed at two hour intervals.
- The conventional recording montage for the MSLT includes central EEG (C3-A2, C4-A1) and occipital (O1-A2, O2-A1) derivations, left and right eye EOGs, mental/submental EMG, and ECG.
- The MSLT report should include the start and end times of each nap or nap opportunity, latency from lights out to the first epoch of sleep, mean sleep latency (arithmetic mean of all naps or nap opportunities), and number of sleep-onset REM periods (defined as greater than 15 sec of REM sleep in a 30-sec epoch).
- The MSLT must be performed immediately following PSG recorded during the individual's major sleep period.
- Sleep logs should be obtained for 1 week prior to the MSLT to assess sleep-wake schedules.
- Stimulants, stimulant-like medications, and REM suppressing medications should ideally be stopped 2 weeks before MSLT.

2. REM Behavioral Sleep Disorder (RBD)

Definition - RBD is a parasomnia manifested by vivid, often frightening dreams associated with simple or complex motor behavior during REM sleep.[3]

Screening for parasomnias generally involve a clinical interview and overnight sleep study (polysomnography) at a sleep center/hospital setting.[4] Self-administered questionnaires, such as the RBD screening questionnaire (RBD[5]SQ) and the Munich Parasomnia Screening (MUP[6]S), have also been developed and validated to identify parasomnias, particularly RBD.

Parasomnias such as sleepwalking and sleep terror episodes often emerge within 2 hours after sleep onset and are not usually associated with rapid alertness; in adults, there can be associated dreaming, but dreams are usually more fragmentary and lack plot development, in comparison to RBD dreams.[7] Pseudo-RBD as a result from obstructive sleep apnea presents with severe respiratory event induced arousals with dream-enactment together with loud snoring and daytime sleepiness, and responds to CPAP therapy.[7,8] Sleep-related seizures involving dream-enacting behaviors are also in the differential for RBD.[9]

Although the history may be diagnostic, PSG is sometimes needed to distinguish between a sleep related movement disorder and a parasomnia. In these cases, it is necessary to add all-night video recording to the polysomnographic recording and to correlate the documented movements with the technician's description of the patient's behavior and level of consciousness in order to establish a diagnosis. For RBD, a PSG-RDB protocol can be performed.

Clinical and Polysomnographic (PSG) Findings in RBD

The *International Classification of Sleep Disorders, 3rd Edition (ICSD-3)*[10], published in 2014, diagnostic criteria for RBD:

The *International Classification of Sleep Disorders* diagnostic criteria for RBD
A. Repeated episodes of sleep related vocalization and/or complex motor behaviors. B. These behaviors are documented by PSG to occur during REM sleep or, based on clinical history of dream enactment, are presumed to occur during REM sleep. C. Polysomnographic recording demonstrates REM sleep without atonia. D. The disturbance is not better explained by another sleep disorder, mental disorder, medication, or substance use.
• Criterion B can be fulfilled by observation of repetitive episodes during a single night of video PSG. • The observed vocalizations or behaviors often correlate with simultaneously occurring dream mentation, leading to the frequent report of “acting out one’s dreams.” • The diagnosis of RBD does not require dream-enactment.[10] • Approximately 30% of reported RBD cases do not have dream-enactment.[11] • Upon awakening, the individual is typically awake, alert, coherent, and oriented. • On occasion, there may be patients with a typical clinical history of RBD with dream-enacting behaviors, who also exhibit typical RBD behaviors during video-PSG, but do not demonstrate sufficient REM without atonia, based on the current evidence-based data, to satisfy the PSG criteria for diagnosing RBD. Such patients may be provisionally diagnosed with RBD, based on clinical judgment. The same rule applies when video polysomnography is not readily available.

Clinical Impact -

Safety - The prevalence of sleep-related injuries in RBD ranges 33-96%.[1] “Diving from bed” has resulted in facial hematoma, head laceration, and subdural hemorrhage.[12] It is important to recognize the severity of immediate injury and long-term neurological changes in RBD.

Given disruptive motor movements associated with RBD, it is recommended that the bedroom environment be clean and uncluttered.

RBD has been associated with neurodegeneration disorders (Parkinson’s disease and Lewy Body disease),[13] neurologic disorders (e.g., brain tumors and stroke), other primary disorders (narcolepsy and periodic limb movement disorder), and medications (antidepressants and β-blockers;).[14,15]

There is now direct evidence that certain prodromal symptoms, such as anosmia, (RBD), constipation, and depression can be present in the prodromal phase of PD.[16]

RBD may be one of the earliest signs of and/or a long-term predictor for neurodegenerative disorders, Particularly, PD.[17]

RBD and stage 2 of PD (i.e., the stage of disease when PD symptoms are bilateral, affecting both limbs and both sides of the body), both show pathomorphological similarity by way of demonstration of alpha-synuclein pathology in the brain, suggesting that RBD is a pathway to PD.[17]

Patients with RBD have up to a 65% risk of developing PD[18] at 10 years, making RBD a specific clinical marker of premotor PD.

RBD has been reported to be present in 42.6% of all PD patients.[19]

PD patients with RBD symptoms had worse motor findings than those unlikely to have RBD. This association provides further evidence for the relationship between RBD and PD.[20]

Pharmacological treatment, particularly the use of Clonazepam, is commonly used to treat RBD.[21] However, this medication should be used with caution for older adults with a dementia diagnosis, gait disorders, and obstructive sleep apnea (OSA) because the common side effects include sedation, confusion, memory dysfunction, and earning morning motor incoordination.[14] Melatonin is an alternative medication treatment that appears to alleviate some of the RBD symptoms and has fewer side effects.

3. <u>Central hypersomnias</u>

The MSLT is a well-validated and extensively published objective measure of the tendency of a patient to fall asleep under standardized laboratory conditions. The MSLT involves 4 or 5 nap periods, each 2 hours apart, with sleep-study monitoring to objectively assess the degree of sleepiness and evidence of decreased REM latency during daytime naps. It is conducted using a standardized protocol22 in which the patient is given a set of directions before undergoing each nap trial in order to maintain reliability and optimize interpretability of the results. Prior to performing the MSLT, patients should be weaned from all medications that may affect sleep architecture (for at least 2 weeks).

Diagnostic Criteria
Both must be met:
A. Daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months.
B. The presence of one or both of the following:

-Cataplexy (as defined under Essential Features) *and* a mean sleep latency of ≤ 8 minutes and two or more sleep onset REM periods (SOREMPs) on an MSLT performed according to standard techniques. A SOREMP (within 15 minutes of sleep onset) on the preceding nocturnal polysomnogram may replace one of the SOREMPs on the MSLT.[2]

-CSF hypocretin-1 concentration, measured by immunoreactivity, is either ≤ 110 pg/mL or <1/3 of mean values obtained in normal subjects with the same standardized assay.

Narcolepsy type 1 is a disorder primarily characterized by excessive daytime sleepiness and signs of REM-sleep dissociation, the most specific of which is cataplexy. Narcolepsy type 1 is caused by a deficiency of hypothalamic hypocretin (orexin) signaling.
Narcolepsy affects more than 1 in 2,000 Americans. In most cases, the syndrome is presumed to develop sporadically, but there is a 1% to 2% chance that a patient with narcolepsy will have an affected child.

Narcolepsy commonly begins near adolescence, suggesting a precipitating role for the hormonal changes surrounding puberty.

Aging can affect symptom severity, as many patients with narcolepsy experience improvement in cataplexy with advancing age.
The peak incidence of narcolepsy is seen in patients aged 15 to 30 years. Narcolepsy manifests before age 25 years in 70% to 80% of patients. Interestingly, approximately 5% of cases have an onset after age 50 years.
There are two types of Narcolepsy (1 and 2)

4. Idiopathic Hypersomnia[10]

Diagnostic Criteria
Must have all the following:
A. The patient has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least three months.
B. Cataplexy is absent.
C. An MSLT performed according to standard techniques shows fewer than two sleep onset REM periods or no sleep onset REM periods if the REM latency on the preceding polysomnogram was less than or equal to 15 minutes.[2]
D. The presence of at least one of the following:
-The MSLT shows a mean sleep latency of ≤ 8 minutes.
-Total 24-hour sleep time is ≥ 660 minutes (typically 12–14 hours) on 24-hour polysomnographic monitoring (performed after correction of chronic sleep deprivation), *or* by wrist actigraphy in association with a sleep log (averaged over at least seven days with unrestricted sleep).
E. Insufficient sleep syndrome is ruled out (if deemed necessary, by lack of improvement of sleepiness after an adequate trial of increased nocturnal time in bed, preferably confirmed by at least a week of wrist actigraphy).
F. The hypersomnolence and/or MSLT findings are not better explained by another sleep disorder, other medical or psychiatric disorder, or use of drugs or medications.

IH is characterized by excessive daytime sleepiness that occurs in the absence of cataplexy, is accompanied by no more than one SOREMP on MSLT and preceding PSG combined, and is not adequately explained by another disorder.

Prevalence and incidence of IH are not known.

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