# Sleep-related movement disorders and disturbances of motor control

*Panagiotis Bargiotas and Claudio L. Bassetti*

**Purpose of review**
Review of the literature pertaining to clinical presentation, classification, epidemiology, pathophysiology, diagnosis, and treatment of sleep-related movement disorders and disturbances of motor control.

**Recent findings**
Sleep-related movement disorders and disturbances of motor control are typically characterized by positive motor symptoms and are often associated with sleep disturbances and consequent daytime symptoms (e.g. fatigue, sleepiness). They often represent the first or main manifestation of underlying disorders of the central nervous system, which require specific work-up and treatment. Diverse and often combined cause factors have been identified. Although recent data provide some evidence regarding abnormal activation and/or disinhibition of motor circuits during sleep, for the majority of these disorders the pathogenetic mechanisms remain speculative. The differential diagnosis is sometimes difficult and misdiagnoses are not infrequent. The diagnosis is based on clinical and video-polysomnographic findings. Treatment of sleep-related motor disturbances with few exceptions (e.g. restless legs/limbs syndrome) are based mainly on anecdotal reports or small series.

**Summary**
More state-of-the-art studies on the cause, pathophysiology, and treatment of sleep-related movement disorders and disturbances of motor control are needed.

**Keywords**
nocturnal (sleep-related) movement disorders and disturbances of motor control, nocturnal epilepsy, parasomnias, sleep

## INTRODUCTION

Rapid eye movement (REM) and non-REM (NREM) sleep are associated with profound neurophysiological and neurochemical changes in the brain, which lead to changes in the control of motor functions [1]. This explains why movement disorders and disturbances of motor control sometimes appear only or preferentially during sleep. This review will discuss literature pertaining to clinical presentation, classification, epidemiology, pathophysiology, diagnosis, and treatment of sleep-related movement disorders/disturbances of motor control (SRMD/DMC).

## DEFINITION/CLASSIFICATION

SRMD/DMC are typically characterized, with the exception of sleep paralysis, by involuntary, excessive motor activities (hyperkinesias), meaning positive motor symptoms. On rare occasions (e.g. in the context of REM sleep behavior disorder, RBD) voluntary movements may also be affected during sleep differently than during the day [2]. Interestingly, changes in muscle tone are not a relevant feature of SRMD/DMC (as it is, conversely, during daytime), with the exception of RBD.

These disorders/disturbances are commonly age-dependent [1]. Epidemiological data of the most relevant disorder/disturbances are summarized in Table 1 [3–21].

No classification system is universally accepted. Table 2 presents a possible classification of motor phenomena during sleep in terms of causes, clinical features, and sleep stages in which they occur.

Department of Neurology, Sleep-Wake-Epilepsy Center (SWEZ), University Hospital (Inselspital) and University of Bern, Bern, Switzerland

Correspondence to Dr Panagiotis Bargiotas, Department of Neurology, Inselspital, Bern University Hospital, Freiburgstrasse 18, 3010 Bern, Switzerland. Tel: +41 0 31 632 30 66; fax: +41 0 31 632 96 79; e-mail: panagiotis.bargiotas@insel.ch

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## KEY POINTS

- Sleep-related movement disorders/disturbances of motor control are frequent and may lead to significant sleep disturbances and consequent daytime symptoms.
- Sleep-related movement disorders/disturbances of motor control often represent the first or main manifestation of an underlying disorder of the central nervous system.
- For the majority of sleep-related movement disorders/disturbances of motor control, pathophysiological mechanism remain speculative.
- International diagnostic or therapeutic criteria have been developed only for a few disorders (e.g. RLS).

## CLINICAL MANIFESTATION

The key-features of the main SRMD/DMC are presented in the following:

### Hypnic jerks (sleep starts, predormital myoclonus)

Hypnic jerks are sudden, brief contractions of the body or limbs occurring spontaneously or after a stimulus, typically at sleep onset [22]. The contracts can be accompanied by a cry and hallucinations (flashes, feeling of falling) and dreams [23]. Hypnic jerks are described as a benign movement phenomenon [24]; however, they are frequent in neurological disorders such as parkinsonian syndromes resulting in a further cause of sleep disruption [25].

**Table 1.** Epidemiology of sleep-related movement disorders

| Sleep-related movement disorders/disturbances of motor control | Frequency in the general population | Specific features |
|---|---|---|
| Sleep-related bruxism (SB) [3,4] | 10–20% | Highest frequency in children (14–20%)<br>The prevalence is not associated with sex and decreases with age<br>Parental history of SB predicted SB severity |
| PLMS [5] | 5–20% | Rare below the age of 30–40 years<br>Common in sleep disordered breathing and narcolepsy<br>Very common (70–90%) in RLS |
| Sleep paralysis [6] | 5–15% | More common in narcolepsy (50%) and in psychiatric patients (30%) |
| Sleepwalking [7–11] | 5–15% | Typically affects children (peak age 10–12 years) but it can persist or appear *de novo* in adulthood<br>Lower frequency (1–5%) in adults<br>The prevalence of childhood sleepwalking increases with the degree of parental history of sleepwalking.<br>Among adult sleepwalkers 13% report an onset in adulthood |
| RLS [12,13] | 1–10% | Rare in children<br>More common in uremia, iron deficiency, pregnancy (10–30%)<br>Variable prevalence in the general population among countries |
| Sleep terrors [7] | 1–5% | Typical age-of-onset during the early childhood (peak of prevalence at 1.5 years).<br>Lower frequency in adults<br>Parental history of sleepwalking predicts the incidence of sleep terrors in children and the persistent nature of sleep terrors. |
| RBD [14,15] | 1% | The prevalence of RBD is about 0.5–1% in the general population and 2–8% in the older adult population<br>More common (25–50%) in synucleinopathies (e.g. M. Parkinson) |
| Sleep-related (nocturnal) eating disorders [16] | 1% | The age of onset is typically in adulthood, women are more frequently affected than men.<br>More common in sleepwalkers and in patients with RLS/PLMS |
| Rolandic epilepsy [17,18] | – | Typically starts around the age of 10 years<br>It is thought to be among the more frequently occurring childhood epilepsy (14% of childhood epilepsies)<br>However, definite epidemiological data are lacking<br>Prevalence between 10–25% in children under 15 years |
| Panayiotopoulos syndrome [19] | – | Starts around the age of 5<br>Around 13% of children aged 3–6 years who have had one or more afebrile seizures |
| SHE [20] | – | Definite epidemiological data are lacking (around 2%) |
| Sleep related rhythmic movement disorders [21] | – | Typical onset in early infancy, rarely persisting in adulthood in patients with a positive family history, mental retardation or associated sleep disorders<br>Familial forms have been described |
| Sleep related dissociative disorders | – | typically appearing in patients with known, underlying psychiatric disorders |

PLMS, periodic limb movements in sleep; RBD, REM sleep behavior disorder; RLS, restless legs/limbs syndrome; SHE, sleep-related hypermotor epilepsy.

**Table 2.** A possible classification of motor activities during sleep which take into account: clinical features: simple vs. complex (meaning those leading to behavioral manifestations); etiology: physiological vs. pathological (movements disorders (sensu strictu), epileptic disorders, psychiatric disorders, others); sleep stage of occurrence (when pertinent)

| | **Pathological activities** | | | | |
|---|---|---|---|---|---|
| | **Simple motor activities/behaviors** | | | | |
| **Physiological activities** | **Diurnal movement disorders** | **Nocturnal (sleep-related) movement disorders (nonepileptic)** | **Nocturnal (sleep-related) movement disorders (epileptic)** | **Others** | **Complex motor activities/behaviors** |
| Hypnic jerks/sleep starts<br>Hypnagogic (sleep onset) foot tremor<br>Alternating leg muscle activation<br>NREM myoclonus (physiologic fragmentary myoclonus)<br>REM myoclonus/ twitches<br>Postural shifts<br>Sleeptalking | **Frequently persisting during sleep**<br>Palatal myoclonus/ tremor<br>Hemifacial spasm<br>Spinal myoclonus<br>Tics<br>**Sometimes persisting during sleep**<br>Tremor<br>Chorea<br>Dystonia<br>Hemiballism | Sleep related bruxism<br>Nocturnal groaning (catathrenia)<br>Faciomandibular myoclonus<br>Neck myoclonus during REM sleep<br>Sleep related leg cramps<br>Excessive NREM (fragmentary) myoclonus<br>Excessive REM myoclonus (twitches)<br>RLS<br>PLMS<br>Propriospinal myoclonus at sleep onset<br>Sleep paralysis | **Nocturnal epilepsy with simple motor manifestations**<br>Idiopathic focal epilepsy with centrotemporal spikes and variants (benign rolandic seizure, Landau–Kleffner syndrome, Epilepsy with CSWS)<br>SHE with paroxysmal arousals<br>Panayotopoulos syndrome<br>Others (e.g. temporal lobe seizures)<br>**Epilepsy with diurnal and nocturnal simple motor manifestations** | Arousal reactions secondary to sleep-disordered breathing | **Nocturnal (sleep-related) movement disorders (nonepileptic)**<br>Sleep related rhythmic movement disorders<br>NREM parasomnias (arousal disorders)<br>Confusional arousals<br>Sleep terror (pavor nocturnus)<br>Sleepwalking<br>REM sleep behavior disorder/overlap parasomnia/status dissociatus<br>**Nocturnal (sleep related) movement disorders (epileptic)**<br>SHE with complex motor manifestations<br>Paroxysmal dystonic seizures<br>Epileptic wandering<br>Hypermotor seizures (also of nonfrontal origin)<br>Epilepsy with diurnal and nocturnal complex motor manifestations<br>**Sleep-related (nocturnal) eating disorders (SRED)**<br>**Nocturnal (sleep-related) psychiatric disorders**<br>Nocturnal panic attacks<br>Sleep related dissociative disorders<br>Sleep related psychogenic nonepileptic seizures |

CSWS, continuous spike waves during slow wave sleep; NREM, non-REM; PLMS, periodic limb movements in sleep; REM, rapid eye movement; RLS, restless legs/limbs syndrome; SHE, sleep-related hypermotor epilepsy with paroxysmal arousals.

Diagnosis usually does not require any ancillary tests [26].

### Sleep-related bruxism

Sleep-related bruxism consists of rhythmic tooth grinding or tapping. Typically occurs in light NREM and REM sleep. Diurnal jaw muscle discomfort is often reported, and masseter hypertrophy and alterations to the teeth and surrounding structures can be observed [27]. In a recent study, sleep-related bruxism was associated with pain and reduced sleep quality [3].

Primary and secondary forms (associated with sleep-disordered breathing, dystonia, or psychiatric disorders, e.g. anxiety, depression, and attention-deficit/hyperactivity disorder, ADHD [28]) are known.

Diagnosis is suspected clinically and can be confirmed by typical electromyography (EMG) artefacts during video-polysomnography [26].

### Nocturnal groaning (catathrenia)

It consists of repetitive expiratory respiratory (groaning, moaning) monotonous sounds occurring in clusters (mainly but not exclusively in REM sleep) and lasting for up to 30–50 s [29]. A recent study reported that the occurrence of catathrenia is associated with anatomical abnormalities of the mouth [30]. An association with (other) parasomnias is known and differential diagnosis include snoring, stridor, sleep talking, and central sleep apnea [31,32]. The diagnosis is made clinically.

### Facio-mandibular myoclonus

This refers to nocturnal myoclonic jerks involving the jaw and facial musculature which can lead to diurnal jaw discomfort and teeth alterations [33]. The diagnosis is based on specific EMG activity of oro-facial, masticatory and cervical muscles during polysomnography.

### Excessive fragmentary myoclonus

Excessive fragmentary myoclonus (EFM) refers to the presence of excessive, nonrhythmic, and nonperiodic limb twitches with no or only minimal movement effect [34]. Although EFM is described as a benign movement phenomenon [24], recent studies suggest an association with Parkinson's disease [35] and with peripheral nerve pathologies [36▪]. The diagnosis is based on the presence of characteristic EMG pattern of at least 150 ms, in at least 20 min of NREM sleep, and a rate of five EMG EFM potentials per minute, during polysomnography.

### Restless legs/limbs syndrome

The restless legs/limbs syndrome (RLS) is a common, today still underdiagnosed, sensorimotor disorder. The disease can appear in childhood, its course is usually chronic with rare periods of remission. The severity of symptoms varies largely but usually enhances with age. The following international RLS diagnostic criteria have been suggested [37]:

(1) An urge to move, usually accompanied by unpleasant (or painful) sensations in the legs.
(2) The symptoms begin or worsen during periods of rest or inactivity (sitting/lying).
(3) The symptoms are partially or totally relieved by movement (walking/stretching).
(4) The symptoms are worse or occur only in the evening or at night.

Diagnosis is usually made clinically. The sensory discomfort may involve the arms (30–50% of patients) or other body parts, as well [38]. Supportive criteria include the detection of periodic limb movements in sleep (PLMS) during polysomnography or leg actigraphy [37] (in 70–90% of RLS patients [39]), response to dopaminergic treatment and positive family history. In addition, supportive criteria may be helpful to differentiate RLS from RLS mimics [40].

The disorder is chronic and associated with multiple comorbidities. Patients often present with insomnia, psychiatric symptoms, and occasionally with daytime excessive sleepiness and fatigue [41]. Primary and secondary forms (associated with iron deficiency, pregnancy, uremia, spinal cord diseases, parkinsonian disorders, spinocerebellar atrophies) are known [13,42–45,46▪].

### Periodic limb movements in sleep

PLMS are repetitive, periodic/pseudoperiodic, stereotyped movements, usually consisting of a toe extension with a dorsiflexion of the ankle and a flexion of the knee and hip. The contractions last 0.5–10 s, the episodes consist of at least four consecutive contractions/movements, the intervals between the episodes ranges from 5 to 90 s (on average 20–40 s).

PLMS may result to increased arousability during the night or daytime symptoms such as fatigue, suggesting the presence of a periodic limb movements disorder (PLMD) if no other sleep disorder is diagnosed. Recently, severe PLMS have been reported to be associated with abnormal sleep behaviors, mimicking dream enacting behavior [47▪] and with greater cognitive decline among non-demented individuals [48▪]. The detection of PLMS

is made by leg actigraphy and video-polysomnography.

### Propriospinal myoclonus at sleep onset

Propriospinal myoclonus refers to repetitive axial jerks slowly spreading rostral and downward during the sleep–wake transition period and may leading to insomnia and falls out of the bed [49]. Differential diagnosis include Hypnic jerks, RLS, PLMS, or epileptic myoclonus [50].

### Sleep paralysis

Sleep paralysis (recently reviewed by Sharpless [51]) refers to short-lasting (typically <10 min [52]) episodes of inability and struggle to move and speak while in the process of falling asleep or awakening [53]. Its frequency can vary from a few life events to daily episodes. Stress, excessive sleepiness, irregular sleep–wake cycle and sleep deprivation, jet lag, and uncomfortable sleeping may increase its frequency [54–56]. Anxiety, hallucinations [sensed presence; sensation of a pressure on the chest with shortness of breath (incubus); and sensation of floating/flying (out-of-body experience)] and lucid dreaming [54] are often experienced. Primary (sporadic and familial) and secondary forms (associated with narcolepsy, other sleep or psychiatric disorders [57,58]) are known. Diagnosis is usually made clinically.

### Sleep-related rhythmic movement disorders

These are stereotyped, repetitive movements such as head rolling/banging, body rolling/rocking, occurring commonly at sleep onset with a frequency of 0.5–2 Hz and duration of seconds up to several minutes. The diagnosis is suspected clinically and made by video-polysomnography.

### Sleep terror (pavor nocturnus)

It consists of spells characterized by sudden onset of fear, loud screaming, and autonomic symptoms arising from deep NREM sleep and usually lasting only few minutes. Patients are difficult to be awaken and have no recall of the episodes [26]. Frequently co-occurs with other parasomnias (e.g. sleepwalking) and in combination may lead to a consequent significant daytime sleepiness [59]. The diagnosis is suspected clinically and made by video-polysomnography.

### Sleepwalking (somnambulism)

Sleepwalking refers to an ambulatory activity arising (in most cases) from deep NREM sleep [26,60,61]. Patients wake up suddenly, look around with a confused stare, leave the bed, and deambulate. Movements can be repetitive and purposeless, on other occasions the appear complex and meaningful [62]. Sleepwalkers are difficult to be awakened and there is usually no recall of the episodes. Self-injuries [63,64] and rarely even homicidal, filicidal, and suicidal episodes are possible [65]. Sleepwalkers have a higher frequency of other parasomnias (sleep terrors, confusional arousals, enuresis, sleeptalking, bruxism), nocturnal eating (somnophagia), and abnormal sexual behavior during sleep [66]. More recently specific reward-related personality traits [67] have been associated with sleepwalking.

Typically, sleepwalking occurs once per night (first part) and lasts several minutes. The frequency can range from few episodes in a lifetime up to several (five to six) episodes per night [9]. Sleepwalking usually appears in the context of a sporadic or familial NREM parasomnia, less frequently also in the context of a more complex NREM/REM overlap parasomnia (e.g. in neurodegenerative diseases), of a nocturnal epilepsy (epileptic wandering), or of dissociative disorders [68–70].

Diagnosis is usually made clinically. Video-polysomnography may be needed for the correct interpretation of frequently reported nocturnal deambulatory activities.

### Rapid eye movement sleep behavior disorder

REM sleep behavior disorder (RBD) is a disorder characterized by an abnormal behavior arising from REM sleep which is accompanied by (oft frightening) vivid dreaming [26,71]. The patients 'act out their dreams' exhibiting a variety of motor activities ranging from talking and twitching of the limbs extremities to screaming, kicking, punching, grabbing, and even complex violent and nonviolent behaviors [2]. Injuries are typical and may involve the patients or their bed partners. Autonomic activation is limited/absent. Typically, RBD occurs repeatedly in the second part of the night.

RBD appears more often in elderly males and commonly in the context of synucleinopathies [72,73]) but also in narcolepsy [74]. Recently, motor complex behaviors, mimicking dream-enacting, have been reported in children with type 1 narcolepsy as well [75▪▪], further highlighting the relation between the two disorders.

The onset of RBD may precede the appearance of daytime manifestations (e.g. cognitive, motor symptoms) by up to decades [76]. Parkinsonian patients may exhibit during REM sleep/RBD in comparison to wakefulness a paradoxical improvement of speech, facial, and extremity motor control. RBD

in parkinsonian patients has been associated with psychiatric manifestations, hallucinations, cognitive decline, and sleepwalking [2,77].

Rarely, RBD occurs also in the context of a NREM/REM overlap parasomnia and its extreme form of a wake–sleep state breakdown (status dissociatus) [78–80].

International diagnostic criteria have been developed [81]. Diagnosis is confirmed by video-polysomnography documenting a loss of motor atonia, an increase of phasic muscle activity during REM sleep, and corresponding behaviors.

### Sleep-related epilepsy with simple motor manifestations

The most common syndrome is that of rolandic epilepsy (also called benign epilepsy with centro-temporal spikes, BECTS), which is characterized by infrequent nocturnal (often at sleep onset or before awakening) simple, hemifacial motor seizures lasting 1–3 min. Postictal amnesia is not always present.

Panayiotopoulos syndrome refers to an idiopathic epileptic syndrome with (typically nocturnal) short episodes of disturbed autonomic functions (e.g. nausea, retching, vomiting) and occasionally with syncope-like epileptic seizures [82].

Others: typically temporal lobe epilepsy and occasionally sleep-related hypermotor epilepsy (SHE) with paroxysmal arousals, may manifest with nocturnal simple motor manifestations [33,83].

### Sleep-related epilepsy with complex motor manifestations

SHE and hypermotor seizures of nonfrontal origin (e.g. insula, temporal, or occipital cortex) are characterized by a wide spectrum of stereotyped manifestations, mostly occurring during NREM sleep. The short-lasting (10–30 s) episodes present a sudden onset of motor behaviors including repetitive patterns (hand clenching, arm raising/lowering, knee bending), more complex patterns (hypermotor/hyperkinetic seizure) such as body rocking, kicking, pedaling, hitting, boxing, screaming, and episodic nocturnal/epileptic wandering, and occasionally asymmetric tonic posturing of the extremities (nocturnal paroxysmal dystonic seizures) [33,84–88]. The amnesia can be incomplete.

For the diagnosis of SHE, a video-polysomnography is needed. The features differentiating SHE from motor parasomnias and dissociative sleep related disorders are: several attacks per night at any time during the night, brief duration of the attacks, and stereotyped motor pattern [85,86].

### Nocturnal sleep-related eating disorders

Nocturnal sleep-related eating disorders (NSRED) present with an evening hyperphagia and/or nocturnal awakening and ingestion of food. Awareness of the night eating is inconstant/absent. When awareness is present the term of night eating syndrome (NES) is preferred.

NSRED comorbidities include depression, insomnia, RLS, and sleepwalking [16,89]. Recent studies reported associations of nocturnal eating with anxiety and obsessive–compulsive symptoms [90,91].

### Sleep-related dissociative disorders/psychogenic nonepileptic seizures

These disorders manifest typically after awakening from sleep with nocturnal episode of complex motor behaviors (e.g. vocalization, screaming, crying, deambulation/sleepwalking, violence, self-mutilation) and are common in patients with known, underlying psychiatric disorders [70,92]. Episodes may last for several minutes up to hours. Amnesia is typically present for the episodes. A coexistence of 'true' epileptic seizures and parasomnias in a single patient is possible and can complicate the diagnosis. In these cases video-polysomnography/telemetry is necessary.

## ETIOLOGY

Several etiologic factors, not uncommonly in combination, of SRMD/DMC have been identified, suggesting for some of them an underlying continuous spectrum of disorder (for RLS reviewed by Trenkwalder *et al.* [93▪]).

Genetic factors are known to be relevant for RLS [reviewed recently by Winkelman *et al.* [94▪]), sleepwalking (positive family history in 25–50%), bruxism, SHE (25% of cases), rolandic epilepsy [84,95,96], and for RBD [97,98] including the susceptibility of individuals with RBD to develop synucleinopathies [99,100] (although negative for APOE e4 allele [101]). More recent studies reported an association of PLMS [102] and of sleep paralysis [103] with specific single-nucleotide polymorphisms.

Neurodegeneration probable RBD is associated with neurodegenerative disease markers such as hyposmia and nonmotor symptoms [15] and over 50% of patients with idiopathic RBD develop within 5–10 years a neurodegenerative parkinsonian disorder (typically a synucleinopathy) [72,73,104▪,105▪▪,106▪,107].

Focal brain damage is mainly related to nocturnal epilepsy (e.g. in the context of cortical dysplasia [108]), RBD (limbic encephalitis, brainstem stroke,

demyelinating disorders [109,110]), and RLS (e.g. spinal cord demyelination, subcortical stroke).

Psychiatric factors/disorders is an underlying stress or psychiatric disorder is often found in (particularly adult) patients with sleepwalking, bruxism, sleep-related dissociative disorders, nocturnal eating disorder, and sleep paralysis [111–113]. A number of studies highlighted the association of RLS with psychiatric disturbances (recently reviewed by Mackie *et al.* [114]) mainly with depression and anxiety and with ADHD [115]. Interestingly, patients with RLS with augmentation are at high risk of developing impulsive behavior, suggesting that impulse control disorder and augmentation may share a common pathophysiology [116▪▪].

Drug effects: Benzodiazepine may trigger/exacerbate sleepwalking, occasionally also NSRED; antidepressants may exacerbate RBD, RLS, sleepwalking, and bruxism; neuroleptics can exacerbate RLS and bruxism; dopaminergic drugs may trigger/aggravate NSRED and bruxism [117,118].

Others: Alcohol has been shown to exacerbate RBD, PLMS, bruxism, and sleepwalking [119]. A deficient iron transport/metabolism and content, recently highlighted also in quantitative magnetic susceptibility [46▪], may underlie RLS.

## PATHOPHYSIOLOGY

Motor control requires afferent, integrating, and efferent systems involving the spinal cord, the brainstem, the cerebellum, the basal ganglia, and the cerebral cortex.

Nocturnal/sleep-related motor manifestations arise from a disruption of such mechanisms, often in form of the abnormal activation and/or disinhibition of motor circuits. However, he exact

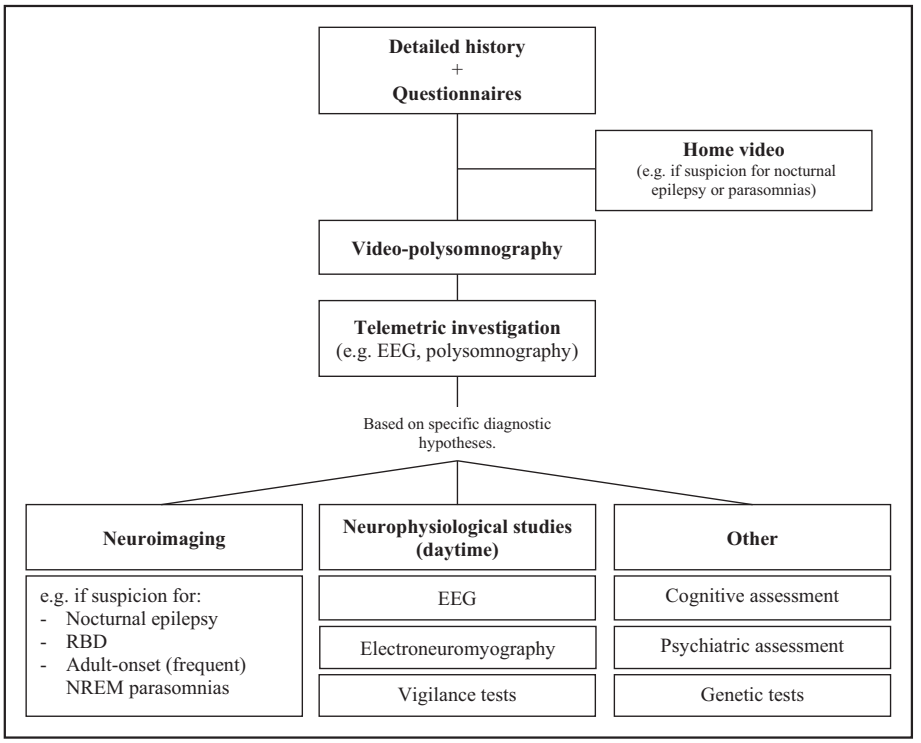


**FIGURE 1.** The flowchart shows important steps and tools for the diagnostic work-up of sleep-related movement disorders and motor control disturbances. Detailed history: whenever possible including an interview with bed partners. International diagnostic criteria have been develop only for a few disorders including RLS and RBD [37,81]. Questionnaires: Few scales have been suggested to estimate the severity of some of these disorders (e.g. RLS and RBD), others to differentiate between epileptic and nonepileptic disorders [77,130,131]. Home video: it may be helpful as a first step before performing more sleep or telemetric investigations, especially if suspicion for nocturnal epilepsy or parasomnias. Video-polysomnography including multiple EEG and EMG derivations: In some situations (e.g. NREM parasomnias, nocturnal epilepsy) sleep deprivation may be used to trigger motor events. Neuroimaging: it should be considered especially in patients with suspicious nocturnal epilepsy, REM sleep behavior disorder (RBD) and adult-onset (frequent) NREM parasomnias. Based on specific diagnostic hypotheses specific diagnostic including EEG (e.g. epilepsy, adult-onset parasomnias), daytime neurophysiological studies (e.g. sleepwalking, RBD) genetic tests (e.g. epilepsy), detailed cognitive (e.g. RBD) and psychiatric (e.g. sleep related dissociative disorders, nocturnal eating disorder, sleep paralysis, RLS) assessments, should be considered.

contribution of afferent or efferent systems (and corresponding neurotransmitters) in these disorders remains speculative [60,120]. In sleepwalking, autosomal dominant SHE, and nocturnal (sleep-related) panic attacks a primary dysfunction of ascending, activating systems may prevail [60,121]. In addition, in RBD a primary dysfunction of descending, inhibitory systems is currently favored [120]. In most situations, a dysfunction in both systems is probably involved [77].

In sleep paralysis, emerging hypotheses regarding the pathophysiology of the commonly reported 'bedroom intruder' hallucinations implicate the mirror neurons system and interaction between several brain region, mainly the prefrontal cortex and the sensory feedback [122].

In RLS, increasing data support the notion of a complex network disorder, involving primarily the brain iron content reduction and then the dysfunction of dopaminergic pathways in nigrostriatal and mesolimbic networks [123].

Complex nocturnal/sleep-related motor manifestations/behaviors are thought to arise from the abnormal (nonepileptic/epileptic) activation of innate (genetically determined) or learned motor patterns (central pattern generators) that are essential for survival [124,125]. The term of 'state dissociation' has been used to describe the coexistence of abnormally activated brain areas with others that exhibits features of normal sleep [126]. Such a dissociation has been documented in few patients with parasomnias and sleep-related epilepsy by means of neuroimaging and neurophysiological methods [121,127,128].

## DIAGNOSTIC WORK UP

The etiological differential diagnosis between SRMD/DMC is sometimes difficult [84] and coexistence in a single patient (e.g. nocturnal seizures and parasomnias) is frequent [33,129]. In addition, the clinical phenomenology can be observed in the context of sleep disorders of different etiology.

International diagnostic criteria have been developed only for RLS and RBD [37,81]. Few scales have been suggested to estimate the severity of some of these disorders (e.g. RLS and RBD), or to differentiate between disorders [77,130,131].

A diagnostic work-up of SRMD/DMC is presented in Fig. 1.

## TREATMENT

For most SRMD/DMC, only anecdotal reports or small series have been published on treatment. International treatment guidelines have been

**Table 3.** General principles of treatment for sleep related movement disorders

| Nonpharmacological interventions | Pharmacological interventions | Other Interventions |
|---|---|---|
| **Psychotherapy** | **Benzodiazepines** (commonly clonazepam) | **Avoidance of triggering/exacerbating situations** |
| NREM parasomnias | NREM parasomnias | **Sleep deprivation** |
| Bruxism | RBD | NREM parasomnias |
| Sleep paralysis | Sleep-related rhythmic movement disorders | Nocturnal epilepsy |
| Sleep-related dissociative disorders/ psychogenic non epileptic seizures | Excessive non-REM and REM myoclonus | Sleep paralysis |
| **Stress reducing techniques** | Intermittent RLS | **Fever** |
| NREM parasomnias | Nocturnal eating disorders | NREM parasomnias |
| Bruxism | **Dopaminergic agents** | Nocturnal epilepsy |
| Sleep paralysis | RLS | Sleep paralysis |
| Sleep-related dissociative disorders/ psychogenic non epileptic seizures | PLMS | **Drugs** (see section etiology) |
| **Cognitive-behavioral treatment** | RBD | **Treatment of underlying disorder** |
| NREM parasomnias | Nocturnal eating disorders | **Surgical intervention** |
| Bruxism | **Melatonin** | Severe nocturnal frontal lobe epilepsy |
| Sleep paralysis | RBD | Parasomnias in the context of Parkinson's disease (e.g. deep brain stimulation) |
| Sleep-related dissociative disorders/ psychogenic nonepileptic seizures | **Antiepileptic drugs** | **Injections of botulinum toxin** |
| **Safe sleep environment** | (e.g. carbamazepine, gabapentin or topiramate) | Sleep bruxism |
| Sleepwalking | Nocturnal eating disorder | **Positive Airway pressure therapy** |
| RBD | RLS | Sleep-disordered breathing |
| Nocturnal epilepsy | Nocturnal epilepsy | |
| **Oral appliances, splints** | **Antidepressants** | |
| Bruxism | Sleep paralysis | |
| | Nocturnal panic attacks | |
| | Sleep-related rhythmic movement disorders | |
| | **Opioids** | |
| | RLS | |

NREM, non-REM; PLMS, periodic limb movements in sleep; RBD, REM sleep behavior disorder; REM, rapid eye movement; RLS, restless legs/limbs syndrome.

published only for RLS [132]. General principles of treatment are presented in Table 3.

## CONCLUSION

SRMD/DMC are frequent and may lead to significant sleep disturbances (e.g. sleep fragmentation/insomnia, sleep-associated injuries/violence) and consequent daytime symptoms (e.g. fatigue, sleepiness). In addition, they can represent the first or main manifestation of an underlying disorder of the central nervous system (e.g. epilepsy, neurodegenerative disease) which requires specific work-up and treatment. In most SRMD/DMC, the pathogenetic mechanisms remain speculative. Several etiologic factors have been identified, not uncommonly in combination however the differential diagnosis is sometimes difficult. International diagnostic or therapeutic criteria have been developed only for a few disorders (e.g. RLS). More state-of-the-art studies on the treatment of these disorders are needed.

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### Conflicts of interest

*The authors have no conflicts of interest.*

## REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

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