Motor Control and Dyscontrol in Sleep

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Introduction

Motor control in humans is the end result of a complex, intricate interplay between several central and peripheral loci, including the cerebral cortex, basal ganglia, brain stem motor centers, cerebellum, spinal cord, and the peripheral neuromuscular system [1–3]. The delicate balance of excitatory and inhibitory influences, created through the coordination of these systems, determines the occurrence of volitional movements and the suppression of unwanted ones. As an individual progresses from drowsiness to light sleep, slow-wave sleep (SWS), and rapid eye movement (REM) sleep, several additional factors come into play to further modulate motor activity. In recent years, there has been growing interest and a lot of research into normal and abnormal motor control in sleep. Disorders of motor control that occur in sleep may be those that are present during the day (diurnal movement disorders) but that impact sleep, either directly through their motor effects or indirectly through a variety of other mechanisms. Alternately, some motor disturbances are exclusive to sleep or the sleep–wake transition period. Motor disturbances in this latter group are generally classified as *sleep disorders*; the third edition of the International Classification of Sleep Disorders (ICSD-3) includes them in a specific category of sleep disorders called *Sleep-Related Movement Disorders* [4], and the American Academy of Sleep Medicine has elaborated on rules for recognizing them during polysomnography (PSG) [5].

This chapter discusses how motor control in sleep differs from that in wakefulness, classifies and describes disorders of motor control that intrude into sleep, including recommended treatment options, and discusses the investigative techniques employed in the evaluation of motor disorders in sleep. Non-motor symptoms in hypokinetic and hyperkinetic movement disorders that impact sleep are also briefly discussed. The main purpose of this chapter is to provide an overview of the various motor disturbances that impact sleep and to demonstrate a usable approach to the diagnosis and management of these disorders. This chapter should be useful to sleep medicine practitioners who deal with patients presenting with abnormal movements in sleep; however, readers are referred to several excellent volumes that discuss movement disorders in greater depth [6, 7].

Motor Control in Wakefulness and Sleep

The motor system is organized in a functional hierarchy at three levels: the forebrain, brain stem, and spinal cord (Fig. 39.1a, b). These three levels are under the control of two subcortical systems, the cerebellum and basal ganglia, and receive sensory inputs. The spinal cord is the lowest level in the scheme of the motor organization and contains neuronal circuits mediating reflexes and rhythmic movements. The motor neurons and interneurons of these circuits receive inputs both segmentally and supraspinally from higher centers. All motor commands ultimately converge either directly or indirectly (through the descending brain stem pathways) on the motor neurons in the anterior horn cells of the spinal cord, which Sherrington called

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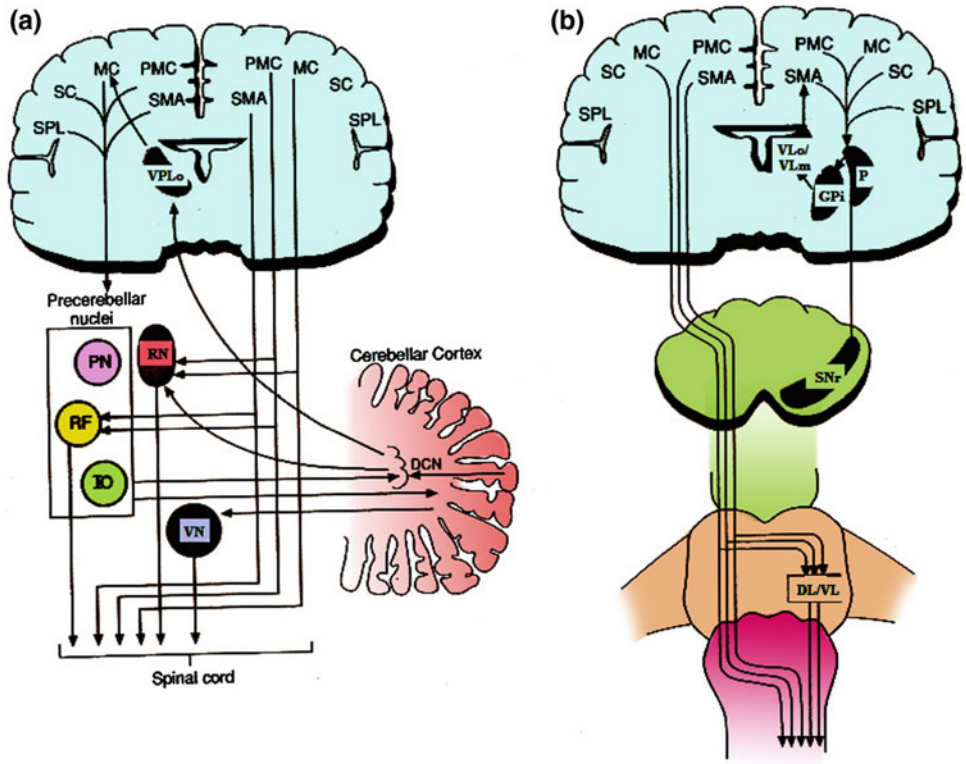

Fig. 39.1 **a** Showing schematically the principal relationships between cerebellum and other components of the motor system. *PMC* Premotor cortex, *SMA* Supplementary motor area, *MC* Motor cortex, *SC* Somesthetic cortex, *SPL* Superior Parietal Lobule, *DCN* Deep Cerebellar Nuclei, *VN* Vestibular Nucleus, *RN* Red Nucleaus Magnocellular portion, *PN* Ponitine Nuclei, *IO* Inferior Olive, *RF* Reticular formation, *VPLo* The oral portion of the ventral posterolateral nucleus of the ventrolateral thalamus. **b** Schematic diagram to show the basal ganglia-thalamocortical motor circuit. PMC, SMA, MC, SC, SPL: As in figure **a** *GPi* Globus Pallidus, internal segment, *SNr* Substantia Nigra pars reticulata. *VM* Ventromedial group of brain stem descending pathways (see text). *DL* Dorsolateral group of brain stem descending pathways (see text). *VLo/VLm* The nucleus ventralis lateralis pars oralis and ventralis lateralis pars medialis of the thalamus

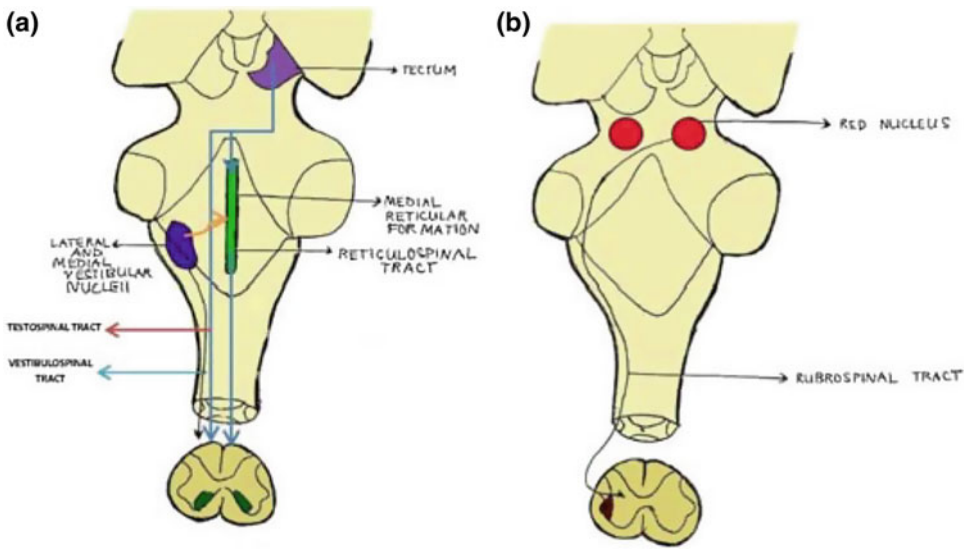

Fig. 39.2 Schematic diagram showing brain stem motor control. **a** Medial motor control pathway in the brain stem. **b** Lateral motor control pathway in the brain stem. (Modified from Ref. [8])

the "final common pathway" for motor actions [1]. In the next higher level at the brain stem, there are two descending systems: the medial descending systems consisting of the reticulospinal, vestibulospinal, and tectospinal tracts controlling posture and the lateral descending system consisting mainly of the rubrospinal system, controlling more distal limb muscles (Fig. 39.2a, b). The highest level, located in the cerebral cortex, controls spinal motor neurons directly through the corticospinal tracts and the brain stem motor neurons through the corticobulbar pathways. The cerebral cortex also controls spinal motor neurons indirectly through its influence on the descending brain stem systems. The major subcortical inputs to the motor cortex originate from the cerebellum and basal ganglia controlling the cerebral cortex through their projections to the thalamic nuclei.

The prefrontal cortex is responsible for the planning and initiation of voluntary movement. The premotor cortex and the supplementary motor cortex are involved in the programming of voluntary movement. Other parts of the cerebral cortex (e.g., somatosensory and association cortices including those responsible for tactile sensations, vision, and hearing) send their projections to the motor cortex for the coordination of skilled movements. Two subcortical circuits, the thalamocorticostriate and dentatorubrothalamocortical circuits, play a significant role in controlling coordination, posture, and muscle tone.

Muscle Tone, Posture, and Reflexes

In addition to voluntary targeted activity, motor control includes the control of muscle tone and posture directed by central generators and spinal stretch reflexes [1]. Phasic muscle contractions producing movements occur on a background of constant muscle tone, which can be defined as a state of mild contraction due to the firing of a few motor units of the muscle (i.e., due to asynchronous sustained firing of motor neurons). Clinically, muscle tone is perceived as the resistance offered by the muscle to stretch as a result of passive movement (flexion or extension) of a joint. The resting muscle tone is produced by viscosity and elastic properties of the muscle. Muscle tone is related to posture, state of alertness, and the degree of muscle stretch. Reticulospinal and vestibulospinal tracts influence the alpha and, to an extent, also the gamma motor neurons to maintain muscle tone.

Movements can be divided into three categories: voluntary, rhythmic, and reflexive. Reflexes are involuntary movements elicited by peripheral stimuli. Voluntary movements are goal-directed. The circuits for rhythmic movements lie in the spinal cord and brain stem. Alterations of muscle tone and movements may be *negative* (atonia and paralysis) or *positive* (hypertonia and abnormal movements). Central pattern generators responsible for locomotion are located in the mesencephalic and spinal locomotor centers. Central pattern generators in the midbrain and pons drive spinal locomotor generators. The mesencephalic locomotor region is under the control of the cerebral and limbic cortex (Fig. 39.3). The nature, however, of pattern generators is uncertain because the exact connection of interneurons is not known.

Motor Control in Wakefulness

In wakefulness, several circuits are involved in the generation and modulation of voluntary movement. These include the cortico-basal ganglionic-thalamo-cortical circuit, cortico-ponto-cerebello-thalamo-cortical circuit, descending brain stem motor pathways, brain stem, and spinal segmental

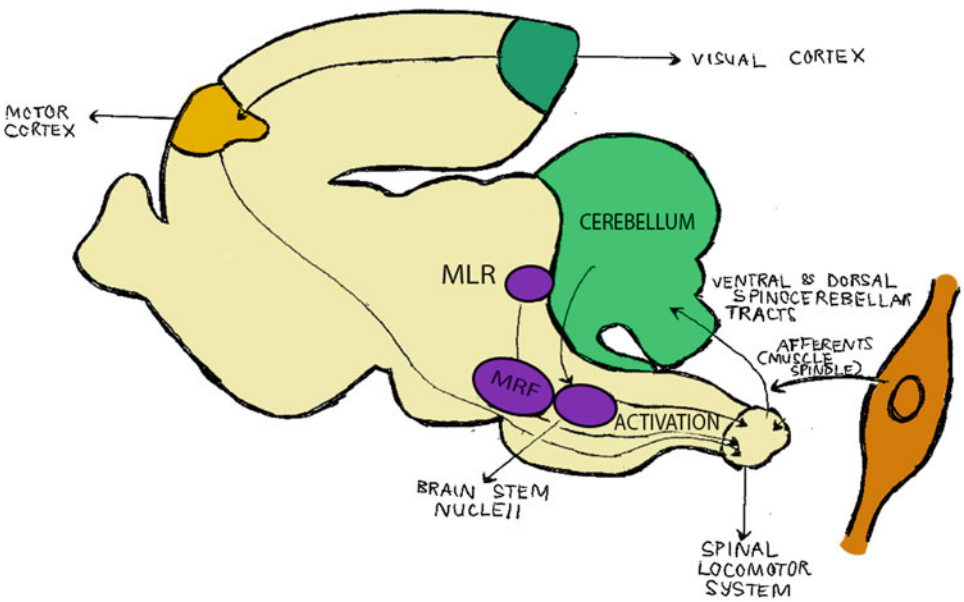

Fig. 39.3 Schematic diagram showing brain stem motor control: Mesencephalc locomotor ergion (MLR) and medial reticular formation (MRF) activating spinal locomotor region after receiving inputs from cerebellum, visual and motor cortices. (Modifed from Fig. 36.10 in "Locomotion." Ref. [8])

circuits. All these circuits are influenced by peripheral afferent inputs. To summarize, the cerebellum participates in the initiation, timing, and coordination of the movements; the basal ganglia help in influencing the direction, force, and amplitude of the movements, as well as the internal generation and assembly of movements; and the cerebral cortex selects, plans, programs, and commands the movement. The corticospinal system then distributes the commands, and the segmental spinal motor apparatus drives the muscles to execute the movements.

Changes in Motor Control in Sleep

In the simplest sense, it can be said that sleep causes a progressive decrease in muscle tone and inhibits gross movements. However, motor control in sleep is far more complex than this simple statement suggests. As in wakefulness, organized movements during sleep are the result of intricate checks and balances at multiple levels of the central nervous system—cerebral cortex, basal ganglia, thalamus, brain stem, cerebellum, and spinal cord. Sleep in general is dominated by central inhibitory drive, but the excitatory mechanism intermittently breaks through the inhibitory phase in normal individuals giving rise to physiologic motor activities during sleep (e.g., gross body shifts and hypnic jerks). It is the breakdown of this delicate mechanism of organized movements during non-rapid eye movement (NREM) sleep and REM sleep, due to a number of inciting factors and diseases, that causes abnormal motor events in sleep. In particular, lower centers (e.g., mesencephalic locomotor region and spinal locomotor generators) are released from controls by forebrain mechanisms as a result of a variety of conditions causing abnormal jerks, shakes, and screams during sleep. It is notable that Pakhomov in 1947 first observed a reduction in muscle tone in finger flexors during sleep [1]. The discovery of REM sleep associated with phasic eye movements and desynchronized EEG in 1953 by Aserinsky and Kleitman [9] paved the way to intense research into motor control during sleep. In 1959 Jouvet and Michel [10] observed muscle atonia in cats during REM sleep. This was followed by Berger's [11] observations of similar atonia in laryngeal muscles during human REM sleep, thus completing the description of REM sleep phenomena. Fundamental contributions to understanding motor control and muscle tone during sleep were subsequently made by Pompeiano [12], Chase and Morales [13], and Morrison [14] and Siegel [15]. To paraphrase Chase and Morales, "motor control landscape" in sleep is characterized by "storms of inhibition" coupled with brief "whirlwinds of excitation" directed toward the "final common pathway" [16, 17].

Modulation of Neuronal Firing

During wakefulness, most central neurons fire irregularly, at different frequencies in different brain regions. In NREM sleep, and especially during SWS, they fire more slowly compared to wakefulness (lower frequency) but tend to fire in bursts. During SWS, for example, thalamic cells fire slowly and are less responsive to afferent activity. These changes are related to the greater synchronization of surface electrical activity as measured by electroencephalography (EEG) during sleep. In REM sleep, by contrast, cellular activity is increased in many motor regions of the brain such as the primary motor cortex [18], thalamus, red nucleus, and cerebellum [19]. This increased firing in the motor centers of the brain is presumably balanced by the increased descending drive that occurs during REM sleep.

Motor Neuronal Modulation

More focused studies have examined motor neurons in the brain stem and spinal cord and traced backward some of the descending influences which modulate them depending on state. Recent studies have begun to establish the brain stem centers whose altered activity is related to the various stages of sleep and wake causing alterations in motor activity [20]. Particular information has been obtained about the control of REM sleep [21]. Neurons located near the border between the pons and midbrain such as the pedunculopontine nucleus (PPN) and laterodorsal tegmental (LDT) nuclei [22] appear to release acetylcholine into the more central reticular formation of the pons and medulla. These neurons can be divided into two classes: REM-on cells are selectively active during REM, while wake/some REM-on cells are also activated during wake. The REM-on cells are selectively inhibited by serotonin [23]. Various, as yet poorly defined, centers or cell groups in the reticular formation are then stimulated [24] to exert descending influences that act upon motor neurons. One current model suggests that cholinoceptive cells in a pontine inhibitory area project to the medulla where they release glutamate to stimulate inhibitory neurons in the medullary reticular formation [25]. Some of this modulation may also occur through suppression of the orexinergic system, which appears to cause arousal and increased motor activity in wake [26].

Reflex Modulation

Since much of motor behavior is generated, at least in part, by reflexes, studying reflexes can be quite relevant to examining changes of the motor system with state. The most commonly studied reflex has been the Achilles tendon reflex or its electrical counterpart, the H reflex. This reflex is diminished in NREM sleep, especially SWS, and then almost completely abolished in REM sleep, especially during rapid eye movements (REMs) [27]. Polysynaptic

spinal reflexes are similarly depressed in NREM and REM sleep [28]. A somewhat related bulbar reflex, the response of the genioglossus muscle to negative pressure in the airway, is decreased in NREM sleep [29] and may be further reduced in REM sleep [30, 31]. This reduced response has significant consequences, because reduced reflex gain may contribute to airway collapse and respiratory difficulties in sleep, especially obstructive sleep apnea (OSA). It has been noted that some brain stem reflexes, such as vestibular reflexes and the blink reflex, show decreased gain in NREM sleep but may then recover partially in REM sleep [32–34]. This recovery of some brain stem reflexes during REM sleep parallels the relatively greater activity of the eye muscles, compared to trunk and limb muscles at that time, and reinforces the mixed picture of excitation and inhibition characteristic of REM. Even drowsiness, short of actual sleep, can attenuate some reflexes, such as the vestibulo-ocular reflex, which has two outputs: quick restorative jerks to head rotation and slower smooth compensatory eye deviations [35]. The more polysynaptic quick jerks are more easily suppressed by even modest drowsiness. While all these various changes in reflex gain indicate altered excitability, they do not indicate where in the reflex arc the changes occur.

The basis for much of the reduced reflex gain during sleep is most likely inhibition of motor output, rather than decrease of sensory response. In one supportive study, Morrison et al. [36] created pontine tegmental lesions in cats that caused REM sleep without atonia. They found that both orienting to tone stimuli and acoustic startle responses were evident in REM sleep in the lesioned cats, but rare or absent throughout sleep in intact cats. Since the same tones elicited brain stem generated ponto-geniculo-occipital (PGO) waves in both normal and lesioned cats, it seems likely that the block to the further responses of orienting and startle reflexes is on the motor side of the reflex arc. PGO waves were also identified in the human pons, recorded during placement of a pedunculopontine nucleus stimulator [37]. On the other hand, sensory transmission may itself be altered by sleep. Studies have indicated that in primary afferent neurons located both in the spinal cord [38] and in the brain stem [39] there is a significant, presynaptically mediated decrease in responsiveness during REM sleep but not NREM sleep.

Reflexes can also change their characteristic motor output in sleep [40] indicating that sleep is not merely a general change in activity levels but a rearranged organization of responsiveness. Sensory stimulation, which would cause motor neuron excitation in waking, can cause additional inhibitory potentials in sleep [41]. In addition, certain reflexes which would be abnormal during waking, such as the Babinski sign, may be elicited in sleep [42, 43].

Effect of NREM Sleep on Motor Control

Progressive muscle hypotonia is a cardinal feature of sleep. In NREM sleep, motor activity is less than in the waking or resting state. At the onset of NREM sleep, intracellular microelectrode recording of motor neurons by Chase et al. [44] clearly showed either no change in membrane potential or a slight hyperpolarization. This, as well as disfacilitation of brain stem motor neurons controlling muscle tone, likely explains the mild muscle hypotonia seen in NREM sleep. Postural shifts, which may signal stage changes (into or out of wake or REM), occur. There are also small flickering movements, called sleep myoclonus, which may cause no apparent movement and are associated with very brief, highly localized electromyography (EMG) potentials seen on PSG [45, 46]. In some cases, these movements may have a greater amplitude and be of increased frequency, at which point they are called excessive fragmentary myoclonus, (EFM, discussed later in this chapter) but the significance of these movements, if any, is unknown [47]. The frequency of all movements decreases with depth of sleep, being least in SWS [48–50]. Postural shifts rarely occur before entrance into SWS. A number of abnormal motor activities such as somnambulism or periodic limb movements of sleep (PLMS) occur predominantly during NREM sleep. In infants, who move more in sleep, most NREM movements are generalized, full body movements or jerks, while REM movements tend to be more focal and uncoordinated [51].

Effect of REM Sleep on Motor Control

REM sleep is dramatically different from NREM. During REM sleep there is tonic reduction in muscle tone, even below that of SWS, in the presence of a highly active forebrain (paralyzed body with activated brain) with inhibition of the mesencephalic locomotor region. This is a protective mechanism to prevent abnormal movements during REM sleep in the presence of highly active cerebral cortex and forebrain regions. However, bursts of small movements ("phasic twitching"), similar to those seen in NREM sleep but more clustered, occur in REM sleep in association with bursts of REMs. During REM there is a close balance between strong upper motor center excitation and inhibition at the level of the motor effecter. When the inhibitory influences break down, significant motor activity may be released. Infants lack this inhibition and have more movement during REM. Inhibition can also be disrupted by lesions in the brain stem of animals which destroy the

inhibitory centers [52, 53] or, it is believed, in human sleep disorders such as REM Sleep Behavior disorder (RBD). The resulting movements may represent an "acting out" of dreams, which characteristically have a motoric component [54, 55].

The mechanism of muscle atonia during REM sleep includes an activation of a polysynaptic descending pathway from the perilocus coeruleus alpha region in the pons to the lateral tegmentoreticular tract, nucleus gigantocellularis, and magnocellularis in the medial medulla (the inhibitory area of Magoun and Rhines), ventral tegmentoreticular, and reticulospinal tracts to the alpha motor neurons, causing hyperpolarization and thus giving rise to muscle atonia (see Fig. 41.5) (see also Chap. 41). Immunocytochemical techniques detected an increased number of C-Fos (a nuclear protein synthesized during neuronal activation) labeled cells in the inhibitory region of Magoun and Rhines [56] during REM sleep. A key element in the REM sleep-generating mechanism in the pons is the activation of GABAergic neurons located in a subgroup of pontine reticular formation, as well as GABAergic neurons in the ventrolateral periaqueductal gray. An activation of GABAergic neurons causes an activation or disinhibition of cholinergic neurons and inhibition of noradrenergic and serotonergic neurons in the pons. The cholinergic neurons, in turn, excite pontine glutamatergic neurons projecting to the glycernergic pre-motor neurons in the medullary reticular neurons, causing hyperpolarization of the motor neurons and motor paralysis during REM sleep. Disfacilitation of motor neurons as a result of a reduction of the release of serotonin and norepinephrine partially contribute to muscle atonia. While many interneuronal regions of the brain stem show increased activity in REM sleep, motor nuclei (masseter, facial, and hypoglossal nuclei) show depressed activity. This is consistent with studies that have shown glycinergic inhibition of hypoglossal neurons in REM [57], perhaps contributing to the difficulties with airway patency in this sleep stage.

Motor neuron control at the cellular level results from synaptic transmission as manifested by the presence of excitatory post-synaptic potentials (EPSPs) or inhibitory post-synaptic potentials (IPSPs). During REM sleep, motor neurons are hyperpolarized by 2–10 mv (Fig. 39.4). There is post-synaptic inhibition causing a decrease in 1a monosynaptic EPSPs resulting in motor neuron hyperpolarization. During wakefulness and NREM sleep, there are a few spontaneously occurring low amplitude IPSPs, but during REM sleep, in addition to an increase of these low amplitude ISPSs, there are additional high amplitude sleep-specific IPSPs noted. These are generated by sleep-specific inhibitory interneurons located mainly in the brain stem (immunocytochemical techniques are used to prove this observation), which send long projecting axons to the spinal and short axons to the brain stem motor neurons. Glycine, the major inhibitory neurotransmitter, is the driving force for these IPSPs. The REM-specific IPSPs are abolished after strychnine (a glycine antagonist) administration [58] by microiontophoretic application into the ventral spinal cord but not after application of bicuculline or picrotoxin (GABA antagonists), thus proving that it is glycine and not GABA which is responsible for these IPSPs. Intermittently during REM sleep

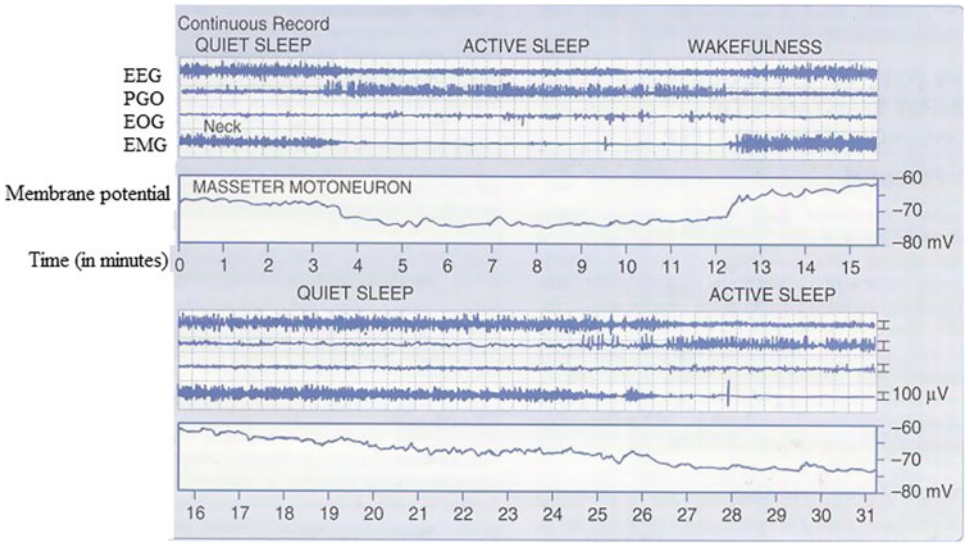

Fig. 39.4 Intracellular recording from a masseter motoneuron of a cat showing membrane potential and state changes during wakefulness, active (REM), and quiet (NREM) sleep. Note abrupt membrain hyperpolarization during active sleep accompanied by neck muscle hypotonia in the eletromyagram (EMG) and depolarization during wakefulness. In quiet sleep, membrane potential resembles that in wakefulness. Electroencephalogram (EEG); EOG, electro-otulogram: PG0, ponto-geniculo.occipital potential. (From Ref. [59])

there are excitatory drives causing motor neuron depolarization shifts as a result of EPSPs [28]. Glutamate is the excitatory amino acid for the REM EPSPs as these EPSPs are abolished by kynurenic acid (a glutamate antagonist) application near the ventral horn cells but not by NMDA antagonists. Muscle movements caused by these excitatory drives during REM sleep are somewhat different from the movements occurring during wakefulness. These are abrupt, jerky, and purposeless. EPSPs during REM sleep reflect increased rates of firing in the motor facilitatory pathways during REM sleep and enhanced IPSPs during REM sleep check these facilitatory discharges thus balancing the motor system during this activated state; otherwise the blind, unconscious subject will jump out of bed, as may happen in RBD (see below) [14]. Facilitatory reticulospinal fibers are responsible for transient EPSPs (phasic discharges) causing muscle twitches in REM sleep. Corticospinal or rubrospinal tracts are not responsible for these twitches because destruction of these fibers in cats [12] does not affect these twitches.

There are several additional factors that dictate the nature of motor control during sleep.

Circadian Activity Cycles

In humans, as in most animal species, the motor system's level of activity is dependent on an underlying circadian rhythm, even in the absence of a day–night light cycle (i.e., under constant conditions). As discussed in Chap. 6, circadian regulation of sleep, like many other important physiologic variables such as temperature, also shows circadian periodicity. While there may be a number of supplementary oscillators which control these rhythms [60–62], the suprachiasmatic nucleus (SCN) is thought to contain the most important oscillator [63] and to be the center which is responsible for the circadian variation of motor activity. The basic mechanism is a transcription–translation feedback loop [64, 65], elements of which are widely distributed in peripheral tissues [66]. Another mediator may be an expression of clock genes, such as the period gene, rPer2, which are widely distributed in different tissues and controlled by the SCN, and a large amount of SCN output is channeled through the subparaventricular zone of the hypothalamus (SPZ), which contains a specific region specialized in modulating motor activity [67, 68]. The SPZ also acts as an integrating center for various environmental influences that can impact on circadian rhythm, such as food availability, ambient temperature, and social interactions. Some of the hypothalamic regulation of motor activity is via the hypocretin system, which stimulates activity at the end of the activity period (the evening for humans) [69, 70]. In humans, activity is concentrated during the daytime hours and sleep at night; decreased movements in sleep may in fact be a marker of better quality sleep [71]. Movements in sleep are associated with autonomic surges, which may have long-term cardiovascular implications [72]. Therefore, this circadian periodicity of movement may be a protective factor. The clear separation of these periods begins to break down in normal aging and in cases of poor sleep or sleep-related disorders as well as in many movement disorders and degenerative conditions.

Development and Aging

The nature and occurrence of movements in sleep are affected by age. Movement frequency during sleep is greatest in infants, then decreases with age, even within the first few months of life [73, 74]. This is most likely due to the immaturity of regulatory mechanisms that maintain motor control in sleep. For instance, in one study, Kohyama [75] found that younger infants appear to lack the profound motor inhibition during phasic REM that is seen in older children and adults. Perhaps as a result of such immaturity, parasomnias such as somnambulism, or soliloquy are present with a greater prevalence during childhood, tending to decrease with age from early childhood on [76, 77]. Rhythmic movement disorder (RMD, see below) is also primarily a disorder of early childhood but may persist into adolescence or even adulthood in patients with significant cerebral injury or with autism [78]. With age, movements in sleep decrease; one study showed that position shifts during sleep decreased from 4.7 per hour in 8–12 year old subjects to 2.1 per hour in those 65–80 years old [79]. With aging, excessive motor activity may emerge again [80], including PLMS, RBD, and increased instability in NREM sleep manifesting as an increase in cyclic alternating pattern (CAP) [81]. In fact, these changes in CAP (see below) at various ages are increasingly being seen as a factor in age-related variation in the frequency and nature of motor dysfunction in sleep.

Drowsiness and the Sleep–Wake Transition Period

Even before sleep onset, the motor system reduces its level of activity. The sleep–wake transition period, a period of relative repose, has been called the *predormitum* by Critchley [82]. The subsequent transition to sleep is signaled by a variety of behavioral and EEG features [83]. The transition to sleep is a frequent inciting factor for a variety of jerks, jumps, and starts that may be a cause of concern to patients and their bedpartners. The most common of this is the "sleep start" or hypnic jerk. Another movement disorder activated in the transition to sleep is a form of propriospinal myoclonus [84]. These conditions are discussed in greater detail below. It is also during the sleep–wake transition period that the symptoms of restless legs syndrome (RLS) become prominent (see Chap. 40). RLS is relatively distinctive in that, unlike almost all other movement disorders, it is activated by rest.

Arousals, brief periods of interrupted, lighter sleep that may or may not lead to full awakening, are often associated

with movements. Arousals may both follow and lead movements such as body shifts. Abnormal movements, such as parkinsonian tremor [85] may recur during arousals. Sleep-related movements, such as PLMS, may provoke frequent arousals or even awakenings and may also continue during periods of arousal from sleep.

Metabolically, physiologically and behaviorally the period just after awakening, or "*postdormitum,*" is distinctly different from the predormitum [86–88]. Sleep offset occurs with abrupt changes in the EEG activity, unblocking of the afferent stimuli and restoration of postural muscle tone accompanied by a reduction of cerebral blood flow with concomitant decrement of cerebral metabolism as compared with that in presleep wakefulness [89]. This is in contrast to sleep onset with gradual changes in the EEG, blockade of the afferent stimuli at the thalamic level (essentially converting an "open" brain into a "close" one) and a reduction of postural muscle tone [90]. Because of these differences between the two states certain motor or other disorders preferentially occur in either predormitum (e.g., propriospinal myoclonus at sleep onset, hypnic jerks, RMD, hypnagogic imagery, and exploding head syndrome) or postdormitum (e.g., sleep inertia, awakening epilepsy of Jang, and sleep benefit in some Parkinson's disease patients). Sleep paralysis and hallucinations may occur in both states (hypnagogic and hypnopompic). Many of these conditions are discussed in greater detail below.

Effects of Sleep Stage on Motor Control

Changes in motor activity are dependent on the sleep state (i.e., wake, NREM sleep, and REM sleep). As discussed above, there is an orderly progression of loss of muscle tone as an individual proceeds through these stages, with muscle hypotonia being most pronounced in REM sleep, where only the diaphragm and extraocular muscles (as well as the middle ear muscles) are spared from almost complete paralysis. This is the underlying principle in measuring chin EMG during PSG. During wake, chin muscle tone is high and a tonically active chin EMG is interrupted by phasic contractions (facial expressions, tension, chewing, etc.). With relaxation and drowsiness, the level of EMG activity decreases. It further decreases as NREM sleep is achieved and deepens to SWS levels. Then, during REM sleep, EMG activity becomes minimal or even inapparent, although it may be occasionally interrupted with brief, irregular bursts of activity in phasic REM sleep, including the tongue [91]. These changes mirror, to a fair degree, the changes undergone by much of the motor system during sleep.

Any discussion on the effects of sleep stages, as determined by PSG, on motor control needs to be tempered by the fact that sleep staging in 30-second epochs, as is standard [5] (see Chap. 24) is based on rules that are arbitrary and are subject to a great degree of interscrorer variation. Physiologic processes are unlikely to adhere to these convenient timescales. For example, Mahowald and Schenck [92] reported on six patients with marked admixture of features from the different sleep–wake states (i.e., wake, NREM sleep, and REM sleep). These patients showed abnormal distribution of motor activity with relation to sleep features. Motor events, although typical of one sleep stage or state, may less commonly occur in other stages. For example, although PLMS are primarily a sleep phenomenon, these movements may also occur during arousals or periods of wakefulness after sleep onset (periodic limb movement in wake, PLMW), often as part of a periodic sequence of movements that span the sleep–wake divide [93]. PLMS occur primarily in NREM sleep but may also occur in REM sleep [94], especially in disorders of disturbed REM sleep such as narcolepsy and RBD [95, 96]. Patients with somnambulism, which typically occurs in NREM sleep, may show REM sleep motor abnormalities suggestive of RBD [97], and confusional arousals have been reported in REM sleep [98]. Even dream-enacting behavior, traditionally thought of as a REM parasomnia seen in RBD, has been reported in NREM sleep [99].

Table 39.1 summarizes the frequency of normal and abnormal motor activities that occur during the various phases of sleep and waking.

Cyclical Alternating Pattern and Movements in Sleep

The evaluation of periodic alternations in EEG activity represents an important additional means of scoring that may be more meaningful than the traditional, AASM mandated epoch-by-epoch scoring of sleep stages from a physiological perspective [5]. In NREM sleep, especially stage N2, this periodicity is common and designated the cyclical alternating pattern (CAP) [100]. First described by Terzano et al. [101], this pattern shows an alternation between bursts of both slow and fast activity (A phase) alternating with a medium frequency, lower amplitude activity (B phase). The burst-like activity (A phase) is associated with autonomic activation (Fig. 39.5). The A phases can include greater or lesser amounts faster frequencies: A1 has the least and A3 the most fast frequencies. A2 and A3 phases are often associated with arousals that can disrupt sleep [102, 103]. A number of different abnormal sleep-related movements are found to be associated with specific phases of the CAP cycle, especially the A phase. These include: PLMS [104] parasomnias or other sleep-related abnormal movements, such as bruxism [105], somnambulism [106, 107], or alternating leg movement activity during sleep (ALMA) [108], and nocturnal paroxysmal dystonia (NPD) [109]. CAP, especially phases A1 and A2, occurs more in early childhood [110], decreases during school age [111], may transiently increase during the adolescent period [112],

Table 39.1 Persistence of various movements in sleep

Motor activity	Awake/active	Drowsiness/sleep onset	Arousal/awakening	Stage 1 NREM	Stage 2 NREM	Stage 3 NREM	REM sleep
Normal motor activity							
Postural shifts	Very frequent	Frequent	Frequent	Common	Occasional	Rare	Occasional
Sleep myoclonus	Unreported	Rare	Rare	Common	Occasional	Rare	Frequent
Hypnic jerk	Unreported	Frequent	Occasional	Occasional	Rare	Rare	Unreported
Sleep paralysis [1]	N.A.	Common	Common	Rare	Unreported	Unreported	Frequent
Movement disorders							
Bobble headed doll syndrome	Frequent	Diminished	Diminished	None?	None?	None?	None?
Chorea	Very frequent	Frequent	Common	Occasional	Rare	Very rare	Rare
Dystonia	Very frequent	Common	Common	Occasional	Rare	Very rare	Rare
Fasciculations	Present	Present	Present	Present	Present	Present	Present
Hemiballismus	Very frequent	Common	Common	Occasional?	Occasional?	Very rare	Occasional?
Hemifacial spasm	Very frequent	Frequent	Frequent	Common	Common	Occasional?	Common
Hiccups—chronic	Frequent	Frequent	Frequent	Common	Common	Common	Common
Myoclonus: cortical/subcortical	Very frequent	Common?	Occasional?	Occasional?	Occasional?	Rare	Rare
Myoclonus: spinal	Very frequent	Frequent	Common	Common?	Common?	Occasional	Common?
Palatal tremor	Constant	Frequent	Frequent	Frequent	Frequent	Common?	Common?
Parkinsonian tremor	Very frequent	Common	Common	Occasional	Rare	Very rare	Occasional
Tics	Very frequent	Common	Common	Occasional	Occasional	Rare	Common
Sleep disorders							
Benign infantile myoclonus	N.A.	Unreported	Unreported	Common	Common	Common	Common
Bruxism	Common	Occasional?	Occasional?	Frequent	Frequent	Occasional	Frequent
Fragmentary myoclonus	Unreported	Unreported	Unreported	Frequent	Frequent	Common	Occasional
Mandibular myoclonus	Unreported	Unreported	Occasional?	Frequent	Frequent	Uncommon	Common
Npd	N.A.	Unreported	Common?	Frequent	Frequent	Occasional	Rare
PLMS: isolated or with RLS	N.A	Occasional	Occasional	Frequent	Common	Rare	Occasional
PLMS: narcolepsy, RBD	N.A.	Occasional?	Occasional?	Frequent	Common	Rare	Common
Propriospinal myoclonus at rest	N.A.	Frequent	Occasional	Rare	None	None	None
REM behavior disorder	N.A.	Unreported	Occasional?	Rare	Rare	Rare	Frequent
Rhythmic movement disorder	Common	Very frequent	Common?	Common	Common	Rare	Occasional?
RLS: restlessness	Rare	Very frequent	Frequent	Occasional	N.A.	N.A.	N.A.
Sleep terrors	N.A.	Unreported	Common? [2]	Rare	Uncommon	Usual	Occasional?
Somnambulism	N.A.	Unreported	Common?	Occasional	Common	Frequent	Occasional
Somniloquy	N.A.	Occasional	Common	Common	Usual	Uncommon	Occasional?

N.A. = Not Applicable
? = Limited Information
(1) In narcolepsy, presents as cataplexy in wake state
(2) Occurs together with incomplete, confusional arousal
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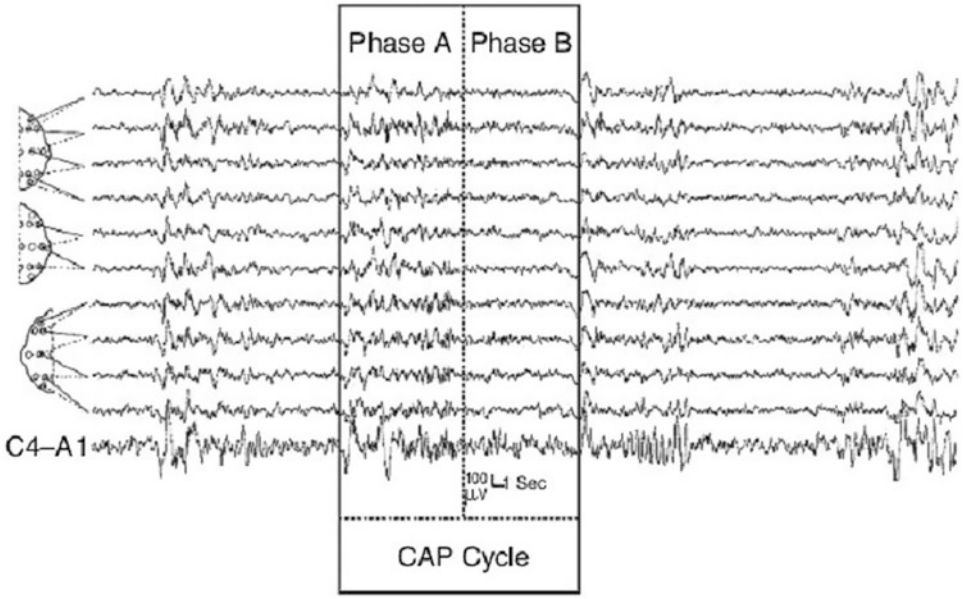

Fig. 39.5 Shows a cyclic alternating pattern (CAP) as part of a CAP sequence in Stage N2 sleep. The CAP cycle (highlighted) is defined by a Phase A (classified into threee subtypes A1, A2, A3 [subtype A2 is shown here] depending on the amount of high amplitude slow waves and low amplitude fast rhythms) followed by a phase B (relatively inactive) [each phase is 2–60 s in duration]. Bipolar EEG derivation (international electrode placement). Channels 1-6 from top: FP2-F4; F4-C4; C4-P4; P4-O2; F8-T4; T4-T6. Channels 7-11 from top: FP1-F3; F3-C3; P3-O1;C4-A1. (Reproduced with permission from Ref. [114])

decreases again in young adulthood, and then finally increases again in older ages [104]. CAP is a normal pattern, but deviations from normal amounts, especially excessive CAP can be abnormal [113].

Classification of Motor Disorders in Sleep

Motor disorders of sleep can broadly be classified into (1) diurnal movement disorders persisting into sleep and (2) primary sleep motor disorders (exclusive to sleep). The latter category can be further subclassified into disorders of motor control as the subject lays in bed trying to get to sleep, immediately before and at sleep onset, during NREM sleep, during REM sleep, during both NREM and REM sleep, and at sleep offset. These are listed in Box 39.1, and the individual motor disorders are discussed in detail in the following sections.

Box 39.1: Disorders due to Failure of Motor Control in Sleep

I. Diurnal Movement Disorders Persisting in Sleep

- Usually persisting in sleep
  - Symptomatic palatal tremor
- Frequently persisting in sleep
  - Spinal and propriospinal Myoclonus
  - Tics in Tourette's syndrome
  - Hemifacial spasm
  - Hyperekplexia
- Sometimes persisting in sleep
  - Tremor
  - Chorea
  - Dystonia
  - Hemiballismus

II. Disorders of Motor Control Unique to Sleep

A. Failure of motor contol while resting in bed trying to get to sleep

- Restless legs syndrome (myoclonic-dystonic movement in quiescence)

B. Failure of motor control at NREM sleep onset (including predormitum, an ill-defined stage between sleeping and waking)

- *Physiological*
  - Physiological body movements and postural shifts
  - Physiological hypnic Myoclonus

  - Hypnic jerks
  - Hypnagogic foot tremor
  - Alternating leg muscle activity
  - Rhythmic limb movements
- *Pathological*
  - Intensified hypnic jerks
  - Rhythmic movement disorder
  - Propriospinal Myoclonus at sleep onset

C. Failure of motor control during NREM sleep

- Partial Arousal Disorders
  - Confusional arousals
  - Sleepwalking
  - Sleep terrors
  - Sleep-related eating disorder (SRED)
- Others
  - Periodic Limb Movements in Sleep

D. Failure of motor control during REM sleep

- *Physiological*
  - Phasic muscle bursts (Myoclonus) including fragmentary hypnic myoclonus
  - Phasic tongue movements
  - Phasic rapid eye movements
  - Periorbital integrated potentials (PIPs)
  - Sleep paralysis
- Pathological
  - REM Behavior Disorder (RBD)
  - Sleep paralysis with narcolepsy
  - Familial sleep paralysis

E. Failure of Motor Control in both NREM and REM sleep

- Rhythmic movement disorder
- Catathrenia
- Excessive fragmentary Myoclonus
- Sleep bruxism
- Upper airway obstructive sleep apnea

F. failure of Motor Control during Sleep offset

- Sleep paralysis
- Hypnopompic hallucinations
- Sleep inertia ("sleep drunkenness")

Description of Individual Motor Disorders of Sleep

A. Diurnal Motor Disorders Persisting into Sleep

As a general rule, most abnormal movements seen during the daytime show a markedly decreased frequency, amplitude, and duration in sleep and tend to be limited to light NREM sleep (stages N1 and N2) [115]. Much less commonly, they will be reactivated during REM sleep as well. Only tardive dyskinesias and primary palatal tremor may show complete cessation of movements during sleep.

The degree of persistence of various abnormal daytime movements into sleep varies greatly (Table 39.1). In one of the most informative studies on the topic, performed using EMG, accelerometry, and split screen video recording. Fish et al. [85] examined the relationship of motor activity not only to conventional sleep staging, but also to epochs with transitions (to lighter or deeper sleep stages or to wakefulness). They also monitored the 2-second periods before onset of dyskinesias in patients with Parkinson's disease, Huntington's disease, Tourette syndrome, and torsion dystonia (both primary generalized and secondary) and scored them for presence of arousals, REMs, sleep spindles, and slow waves. They compared these dyskinesias to normal movements both in patients and in normal subjects. Forty-one of 43 patients had characteristic movements that persisted in sleep. In every disorder, both normal movements and dyskinesias followed the same general plan: most common in wakeful epochs followed by lightening, in stage N1 sleep, REM sleep, then stage N2 sleep, with no movements in SWS. Only Tourette patients had dyskinesias during transition from wake to sleep. The 2-second period before both normal and abnormal movements showed arousals most commonly, followed by REMs, with spindles and slow waves rarely. These results support prior speculation [116] that both dyskinesias and normal movements are likely to be modulated by sleep in a similar fashion. This may be due either to the general suppression of centers for both normal and dyskinetic movements or suppression of some common descending path, such as the pyramidal tract.

It should be noted that all of the abnormal motor activities described in the experiment above, which tended to become attenuated and repressed by sleep, are thought to be generated in higher motor centers, most of them located above the brain stem. On the other hand, movement disorders associated with

abnormalities of the lower motor centers, specifically the brain stem and spinal cord, have a greater tendency to persist during sleep [117]. Perhaps the best example is acquired (rather than primary) palatal myoclonus or palatal tremor (see below), which persists in sleep, although the frequency or persistence of these movements may vary with sleep stages [118]. In addition, spinal myoclonus will often persist during sleep [119]. Similar persistence may be seen in hemifacial spasm [120, 121], which is thought to involve damage either in the brain stem facial nucleus or in the peripheral nerve (cross talk due to ephaptic transmission) or both. Also, fasciculations due to damage to the lower motor neuron, whose generator lies at the spinal cord level, may persist in sleep [122].

In addition to the impact of the movements in sleep themselves, many disorders in which abnormal movements are a prominent feature impact sleep in other ways, including by causing changes in sleep architecture, mood, and level of daytime alertness, and medications treating the primary condition may equally affect the above domains, decreasing the patient's quality of life. These aspects are discussed below.

i. Sleep-Associated Problems of the Hypokinetic Disorders

Parkinson's Disease

Sleep impairment is a cardinal feature of Parkinson's disease. The original quotes from James Parkinson are worthy of note [123].

> But as the Malady proceeds …. (P.6)
>
> In this stage (stooped posture with "unwillingly a running pace"… most likely stage 3), the sleep becomes much disturbed. The tremulus motion of the limbs occur during sleep and augment until they awaken the patient, and frequently with much agitation and alarm. (P.7)
>
> …. and at the last (advanced bedridden stage), constant sleepiness, with slight delirium, and other marks of extreme exhaustion, announce the wished-for release. (P.9)

A spectrum of sleep dysfunction occurs in Parkinson's disease (see Fig. 39.6). Many studies have confirmed the fact that sleep is a major issue for patients with Parkinson's disease and their quality of life [124, 125]. Sleep disturbances also appear to impact cognition in Parkinson's disease, although the mechanisms and exact relationships remain unclear [126]. Many studies have shown sleep architectural disturbances in Parkinson's disease, including shorter total sleep time, lower sleep efficiency, and increased REM latency [127]. There have been conflicting reports on whether dopaminergic therapy improves sleep architectural changes [128, 129]. Early reports do seem to suggest that deep brain stimulation in Parkinson's disease appears to improve NREM sleep, abnormalities of REM sleep, and improve daytime sleepiness [130]. Compared with controls, there appears to be disruption of a number of circadian processes in parkinson's disease; including a sustained elevation of serum cortisol levels, reduced circulating melatonin levels, and altered peripheral clock gene expressions, and sleep disturbances, at least in part, may be related to this mechanism [131]; however, recently published data also suggest that dopaminergic therapy, while increasing melatonin levels (thus theoretically promoting sleep), may also show a delayed sleep onset relative to dim light melatonin onset (DLMO), suggesting that it may uncouple circadian

Fig. 39.6 Schematic diagram showing the spectrum of sleep dysfunction in Parkinson's Disease

and sleep regulation [132]. In recent years, several questionnaires have been developed and validated that can be used to assess sleep-related problems in Parkinson's disease, and liberal use of these instruments helps detect sleep issues [133–137]. Poor sleep in patients with Parkinsons's disease is multifactorial but can broadly be divided into being due to motor and non-motor symptoms.

Motor Symptoms Impacting Sleep

The persistence of the parkinonian tremor into sleep, and its reoccurrence during periods of sleep–wake transition, is a major cause of sleep fragmentation. Parkinsonian tremor decreases in amplitude and duration in early NREM sleep and may lose its alternating aspects and is rarely seen in Stage N3 and often disappears in REM sleep [138]. Bradykinesia often causes trouble turning in bed, which is an additional source of discomfort and may contribute to poor sleep quality.

On the other hand, sleep can also influence these motor symptoms in a positive way; in some patients, sleep can reduce Parkinsonian disability and alleviate symptoms [139–141], perhaps due to the circadian peak of dopamine in the morning [142]. Sleep benefit may last from 30 min to three hours. This may be particularly true of patients suffering from early onset Parkinsonism such as that due to the most common recessive Parkin (PARK2) mutation. Sleep benefit is less consistent in those with the recessive Pink1 (PARK6) mutation [143, 144]. Sleep benefit in this group of early onset patients is often associated with some degree of dystonia.

A major parasomnia that causes motor dysfunction occurring in patients with Parkinson's disease is RBD, which can disrupt sleep and be potentially injurious to the patient and the bedpartner. RBD may precede the diagnosis of Parkinson's disease or other extrapyramidal disorders by several decades. This association may be due to the Parkinsonian degeneration affecting brain areas and systems responsible for sleep–wake regulation [145]. A recent scheme postulates that the synuclein pathology of Parkinson's disease (Lewy Body pathology) ascends from the brain stem to the basal ganglia and finally to the cortex [146, 147], with early involvement of sleep regulatory nuclei before development of motor symptoms [148]. The combination of RBD with olfactory dysfunction may be a strong predictor for later development of Parkinson's disease [149]. In general, RBD patients show subtle motor, cognitive, autonomic, olfactory, and visual changes that are associated with Parkinsons's disease [150, 151], as well as brain perfusion changes determined by single photon emission computerized tomography (SPECT) imaging [152]. A recent finding is that of markedly reduced cardiac I-metaiodobenzylguanidine (MiBG) uptake, consistent with the loss of sympathetic terminals, in idiopathic RBD similar to the deficit seen in Parkinson's disease [153]. One recent study suggests that RBD occurs primarily in Parkinson's disease patients who have the non-tremor form [154]. The authors also suggest that RBD will not precede early onset Parkinson's disease, an observation supported in cases of PARK6 (PINK1) early-onset familial PD [155]. RBD later in the course of Parkinson's disease may be associated with additional complications such as hallucinations [156, 157], which may represent REM intrusions and cognitive decline [158]. A detailed analysis of movements in five patients with Parkinson's disease and RBD found that they had many more movements in sleep than controls, but that most movements were brief and restricted in scope [159]; 3.6 % of all movements were violent while 10.5 % involved vocalizations. It has also been proposed that RBD-related movements may show "normalization" of motor control in Parkinson's disease, with reduction in bradykinesia and vocal hypomimia [160]. Diagnosis and management of RBD is discussed in detail in Chap. 49 and 50.

There has been much research into the association between Parkinsons's disease on the one hand, and RLS and PLMS on the other. Recent studies have suggested that the prevelance of RLS is increased in patients with Parkinson's disease [161–163], including association in one family with a parkin mutation [164]. But this association is only poorly understood [165–167]. Some studies report that most RLS symptoms develop after onset of Parkinson's disease and initiation of dopaminergic treatment. This suggests that RLS may be provoked by such treatment rather than the disease itself; indeed, such treatment has been shown to induce RLS through a process of "augmentation," even in those who do not have RLS [168]. In one communication, subthalamic deep brain stimulation was reported to have induced RLS [169], but this may have been due to decreased medication doses. Similarly, some studies have found increased PLMS in patients with Parkinson's disease [170, 171], but one small study of de novo patients found no such elevation [172]. Thus, while it remains unclear if RLS and PLMS truly occur more frequently in patients with Parkinson's disease outside of dopaminergic treatment, when they do occur, they represent another factor that fragments sleep. Both RLS and PLMS are discussed in greater detail in Chap. 40.

Nonmotor Symptoms Impacting Sleep

Excessive Daytime Sleepiness and Irresistable Sleep Attacks

Excessive daytime sleepiness (EDS) is a common symptoms in Parkinson's disease and has been found to be more frequent in patients than in controls (15.5 % vs. 1 %) [173]. More advanced disease, higher frequency of cognitive decline and co-occurrence of depressive symptoms, more hallucinations,

and longer time on levodopa are predictive factors [174]. This daytime somnolence can exist even without evidence for or complaints of severely disrupted sleep [175, 176]. A related condition is the occurrence of Parkinson's disease-related "irresistable sleep attacks," sudden episodes of sleep that appear without warning on a background of normal alertness [177]. These attacks are much rarer than pervasive daytime sleepiness that the patient is aware of [178, 179]. Genetic variants of the preprohypocretin [180] and dopamine D2-receptor genes [181] have been associated with predisposition to sleep attacks. Some patients with Parkinson's disease have a narcoleptic phenotype, including a finding of sleep onset REM periods (SOREMPs) [182, 183]. This can be seen as 2 or more SOREMPs on multiple sleep latency test (MSLT; 4 or 5 naps scheduled during the day at 2 h intervals). Consistent with narcolepsy, hypocretin neurons are progressively lost with more severe Parkinson's disease [184], most likely due to Lewy Body degeneration. The picture in Parkinson's disease, however, is often more complex, while cataplexy, a key finding in narcolepsy, is generally absent [185]. Additionally, both EDS and irresistable sleep attacks can be caused by dopaminergic medication, especially at higher doses; non-ergot agonists specifically, may be more likely to cause somnolence. Treatment of daytime sleepiness may include the use of stimulants. Some recent studies have supported the use of modafinil as a relatively well tolerated stimulant [186–188], but one double-blind placebo-controlled study failed to support efficacy [189].

Sleep-Disordered Breathing

Respiratory disturbances are common in Parkinson's disease and other related neurodegenerative disorders due to changes in upper airway function or disturbed central regulation of breathing. This may be due to Lewy Body deposition leading to cell loss. Altered upper airway function may be based on weakness of respiratory and upper airway muscles or on altered muscle tone and coordination. The prevelance of SDB in Parkinson's disease has been demonstrated to be indepenedent of the degree of severity of motor and non-motor symptoms [190], but male gender and greater duration of illness are predictors [128]. Patients with Parkinson's disease may have stridor or laryngeal spasm associated with off-states or dystonic episodes [191], although this is more common in multiple system atrophy (MSA, see below). Abnormal vocal cord function with regular rhythmic movements or irregular jerky movements in the glottic area may also produce changes of airflow and contribute to intermittent airway closure [192]. Similar activity persisting during sleep can lead to OSA or upper airway resistance syndrome [193]. Snoring has occurred in the majority of subjects in some series [194]. It has not been definitely established that the prevalance of respiratory dysfunction during sleep in patients with Parkinson's disease as a whole is any higher than in healthy elderly persons [195, 196]. However, in some studies sleep-disordered breathing was more frequent and occurred in up to 50 % of patients with Parkinson's disease [197]. Trouble turning in bed may be a contributory factor in those patients with positional OSA [198]. Patients with parkinsonism and autonomic impairment more often develop sleep apnea and related respiratory abnormalities, including central and obstructive apneas and nocturnal hypoventilation. In the presence of sleep apnea, patients with autonomic impairment are probably more likely than other patients to have nocturnal cardiac arrhythmias. An interesting recent report suggested that treatment with dopaminergic agonists predisposed patients with Parkinson's disease to central sleep apnea [199] but more research on the subject is clearly needed.

Insomnia Insomnia, both sleep initiation and sleep maintenance, is a common complaint among patients with Parkinson's disease and is likely multifactorial [200]. Intrusion of motor symptoms into sleep (see above), depression and anxiety, concomitant sleep-disordered breathing and RLS, and in many cases dopaminergic treatment itself may contribute to insomnia in this population [201]. Other side-effects of medication include nightmares that may worsen underlying anxiety. Nevertheless, where motor symptoms seem to be the biggest impediment to quality sleep, appropriate therapy, including long-acting forms of dopaminergic medications to cover the night [202, 203], and, in some cases, deep brain stimulation [204, 205] may be helpful. Treatment of mood disorders with cognitive behavioral therapy and suitable antidepressants and anxiolytics is also recommended. SDB must be identified and adequately treated with continuous upper airway pressurization (CPAP) therapy.

Other Extrapyramidal Neurodegenerative Conditions

Alpha-synuceinopathies other than Parkinson's disease (the "*Parkinson's plus*" *syndromes*) have sleep disurbances as severe as those seen in Parkinson's disease itself, most likely due to the same pathology of Lewy Body-related neurodegeneration. RBD occurs in most of them and is in fact more common in MSA than in Parkinson's disease. Disturbances of sleep architecture, SDB, EDS, and insomnia are also frequent.

Progressive Supranuclear Palsy (PSP) Patients with this condition have been reported to have severe sleep disruption with reduced total sleep, marked diminution in sleep spindles, reduced REM sleep time with abnormal REMs, disordered sleep architecture, and frequent awakenings [206–212]. RBD is frequent [213, 214], although possibly less common than with Parkinson's disease [215]. As with

Parkinson's disease, sleep disruption increases with severity of the motor abnormalities [208–210]. The greater sleep abnormalities of PSP compared to Parkinson's disease may be due to the greater brain stem pathology, especially that in the pedunculopontine tegmentum, a region linked to control of REM sleep; one report also found that cerebrospinal fluid (CSF) hypocretin levels were lower in patient with PSP than in those with Parkinson's disease [216].

Multiple System Atrophy (see also Chap. 41)

Among the extrapyramidal disorders, sleep disruption appears to be worst in MSA [217–221], and these patients may be especially sensitive to the hypersomnolence induced by dopaminergic therapy [222]. Patients with severe MSA may even lack normal circadian regulation of sleep [223]. As mentioned above, RBD is very common [224], although RBD is unlikely to be seen in pure autonomic failure and provides one means of differentiating the two conditions [225]. PLMS is prevalent as well [221]. A somewhat characteristic feature of MSA is the occurrence of atrophic paralysis of the laryngeal abductor [226], or sleep-related hyperactivity of the adductors, which has been described as dystonic [227], leading to a coarse, snoring-like sound, and laryngeal stridor [228]. In fact, stridor, a potentially life-threatening condition that may cause sudden death from respiratory arrest [229, 230], has been reported as the first or even only apparent sign of MSA [231, 232]. Milder cases may be managed with CPAP [233]; more severe cases require tracheostomy. In some cases, patients with MSA may have predominantly central sleep apnea [234].

ii. Sleep-Associated Problems of the Hyperkinetic Disorders

The hyperkinetic disorders are a diverse group characterized by excessive involuntary movement, often coupled with a deficiency of voluntary movement such as bradykinesia.

Chorea

Chorea consists of movements that occur in a flowing or irregular pattern and appear to migrate from one part of the body to another. They may be increased with action and typically are seen in the face and distal limbs [6].

The best-known cause of chorea is *Huntington's disease*, an autosomal dominant disease with a known mutation of the *IT15* gene located on the short arm of chromosome 4. The mutation in Huntington's disease is the expansion of a CAG repeat in the DNA that leads to increased length of a polyglutamine tract in the protein product, now called *huntingtin*. Currently, research is directed at finding the function of huntingtin in the normal brain and the elucidation of the toxic effect of the mutated protein. Although huntingtin is widely distributed in the brain, the pathology of Huntington's disease is more restricted. Patients also have prominent psychological symptoms, including depression, psychosis, and behavioral disorders. Onset is typically between the ages of 25 and 50, although it may occur even in the first decade or in late adult life. Progression is slow but relentless, with eventual debility, dementia, and inanition occurring in those with onset before old age.

Sleep disturbances in Huntington's disease have been the focus of considerable research. Recently, investigators found that sleep disturbances may be the earliest manifestation of Huntington's disease [235]. There appears to be no correlation between CAG repeat length and sleep disturbances [236]. Investigators have shown a variable persistence of chorea during sleep, with most chorea present in awakening, and in the lighter stages of NREM sleep (stages N1 and N2), similar to other dyskinesias [85]. One study reported an increase in overall sleep movements in Huntington's disease [237]. There has also been some research into sleep architecture in Huntington's disease, but the results have been inconclusive. Some reported deficits include prolonged sleep latency, excessive waking, decreased SWS and REM sleep, and decreased sleep efficiency, possibly correlating to caudate atrophy [238–240]. Reports of alterations in sleep spindles in Huntington's disease have been inconsistent [241, 242]. It has been suggested that nocturnal agitation and sleep disruption in Huntington's disease patients is secondary to anosognostic voluntary movements on arousals, rather than to RBD [236]. A recent study of 30 patients with Huntington's disease showed that they, compared to controls, had shorter sleep duration, reduced sleep efficiency, increased arousals and awakenings, and higher PLMS index in both NREM and REM sleep, but were not at increased risk for RBD or SDB. Greater clinical disease severity predicted decreased REM sleep percentage and greater daytime sleepiness [243]. Other studies have confirmed that unlike patients with parkinsonism, patients with Huntington's disease have not been found to have a significant number of sleep apneas contributing to impaired sleep [244].

Sleep has not been well-studied in other conditions with predominant chorea. Broughton et al. [245] reported that four patients with *Sydenham's chorea*, which follows a streptococcal infection, had reactivation of their movements during REM sleep. Neuroacanthocytosis or chorea-acanthocytosis, is an often inherited movement disorder with chorea, tics, vocalizations, and self-mutilation together with frequent seizures, associated with elevated acanthocytes (spiked red cells) in blood smears [246–248]. Silvestri et al. [249, 250] reported that in this condition, abnormal movements persisted during sleep, but with decreased amplitude, duration, and frequency. Patients frequently vocalized during REM sleep. Sleep was

fragmented and of poor quality. Two siblings with neuroacanthocytosis showed EEG slowing (predominantly delta) both while awake and during REM sleep [251], indicating abnormal cerebral function. RLS has been reported to occur in this condition [252].

Dystonia

Dystonia is a condition characterized by sustained distorted or twisting postures and contorting movements, often mixed with a variety of jerk-like or oscillatory movements [253]. Dystonia can be primary or secondary and can be of variable extent, focal, segmental, or generalized, depending on the area of involvement. Dystonia includes a number of different conditions, some of which, such as early onset torsion dystonia, have a single-gene basis. The protein for early-onset torsion dystonia, torsin A, has been found to bind adenosine triphosphate, but how it causes dystonia itself remains unresolved [254–258]. Not all idiopathic dystonia patients have been shown to have a genetic mutation, however, and there are many cases of secondary dystonia that do not appear to depend on common dystonia genes [259]. One problem in evaluating sleep complaints in dystonia is that the studies so far have often examined a fairly heterogeneous collection of patients with different distributions of dystonia and different etiologies.

Although they usually subside significantly, dystonic movements may persist during sleep at a reduced frequency and amplitude. They are maximally reduced during SWS and may be partially reactivated during REM sleep episodes [260]. In the study by Fish et al. [85] of dyskinetic movements, both primary and secondary dystonic patients followed the general pattern of more frequent dyskinetic movements during wakefulness, fewer movements in stage N1 sleep, only infrequent movements in stage N2, REM, and SWS, and no movements during epochs of deepening sleep. In a study including focal and segmental dystonias, Silvestri et al. [249] found that Meige's syndrome (oromandibular dystonia), blepharospasm, and tonic foot syndrome all showed persistent abnormal activity during sleep, with reduced amplitude, duration, and frequency of EMG bursts. The greatest suppression was in SWS and REM sleep.

Inhibitory mechanisms are postulated to be defective in dystonia. This prompted Fish et al. [261] to study both primary and secondary dystonics to determine whether REM inhibition is intact. They found that all dystonics had normal chin EMG atonia. No patients had complex abnormal activity during REM sleep. In an attempt to analyze motor excitability, the authors successfully stimulated three normals and seven primary dystonics with a magnetic coil over the vertex to evoke a motor response in the fifth finger abductor, the abductor digiti minimi. Whereas response amplitudes were highly variable, dystonics, like controls, showed a decrease in the mean response during REM sleep relative to responses obtained before and after the sleep study in relaxed wakefulness. Latencies were prolonged on average in all groups. The findings of decreased amplitude and prolonged latency were consistent with REM motor inhibition. Occasional high-amplitude responses may have corresponded to periods of phasic excitation. These results indicate that, whatever may be the decreased inhibitory processes in dystonia, they do not involve the descending inhibitory pathways of REM sleep.

Studies of sleep in dystonia have not been systematic; studies have involved small numbers of patients on diverse medications, some of whom had prior thalamic surgery [262]. In these studies, sleep has been found to be inconsistently disrupted, with more severe fragmentation seen in more advanced cases [263]. A number of studies have reported the presence of exaggerated sleep spindles in dystonia [264, 265]. The major therapeutic effort in these patients is the attempt to reduce the dystonic movements. Successful therapy of the movements should also improve sleep.

It is not known that to what degree different forms of dystonia—early- versus late-onset, focal versus generalized—differ in their relationships to sleep, although one striking form of dystonia, variably called *hereditary progressive dystonia with marked diurnal fluctuations* (HPD), *dopa-responsive dystonia* (DRD), and the *Segawa variant*, often shows distinct circadian variability [266–268]. These patients typically present at a young age, often in the middle of the first decade, with postural dystonia, usually affecting one leg and sparing the trunk and neck. Thereafter, the dystonia spreads and parkinsonian signs, which are present at onset in a minority of patients, become more prominent. The condition is usually inherited in an autosomal dominant mode with a mutation in GTP cyclohydrolase I (GCHI) [269, 270]. A number of different mutations in GCHI have been described, but, less commonly, it seems that the condition can be inherited recessively with a mutation in tyrosine hydroxylase [271]. Some studies have found that even patients thought to have more typical idiopathic torsion dystonia may harbor a mutation in the *GCHI* gene [272]. A number of these patients may obtain significant symptomatic relief from sleep, similar to the sleep benefit seen in Parkinson's disease, and therefore are minimally impaired early in the day, and even some dystonic patients unresponsive to L-dopa may have similar benefit from sleep. These patients do show abnormal movements in sleep. Segawa et al. [273] obtained movement counts from PSG with multiple EMG channels (8–12 surface recordings on trunk and limbs) and found that in DRD, there is a decrease in gross body movements in stage I sleep, an increase in stage II sleep, and a decrease in REM sleep. In

contrast, localized twitch movements were depressed in all sleep stages, but followed the normal relative distribution between stages.

Patients with diurnal dystonia or the nocturnal sleep abnormalities of DRD are responsive to low doses of L-dopa, often as little as 50–200 mg per day with decarboxylase inhibitor [274]. Some patients can maintain a stable therapeutic effect with doses every other day. Patients with long-standing disease (24–45 years before treatment) may benefit as well as those with recent onset. DRD patients can use L-dopa without the development of the dyskinetic side effects that are so prominent in juvenile parkinsonism. A few patients may develop "wearing off" phenomena, the re-emergence of symptoms several hours after an oral dose of L-dopa. Older family members may present with a "parkinsonian picture," but still show the same persistent, positive response to L-dopa. This finding is consistent with the idea that a single underlying disease has different manifestations that vary with age, dystonia being prominent in early and late parkinsonism [275–278].

With fluorodopa positron emission technology (PET) scanning, it has been shown in a number of families that patients with DRD have normal to modestly reduced striatal uptake of fluorodopa, including those who present with parkinsonian features later in life [276]. Because of this finding, it can be concluded that these patients have relatively intact dopamine uptake, decarboxylation, and storage systems in the striatum. The genetic abnormalities so far uncovered are involved with the dopamine synthetic system. It has also been speculated that the diurnal fluctuations that characterize DRD may be due to the circadian variation in dopamine production, with greater synthetic activity possible at night. One study found that acute dystonia secondary to neuroleptic medication also shows a circadian pattern [279], with maximal dystonia present between 12:00 noon and 11:00 PM. This could not be accounted for by sleep, fatigue, or time since the last dose of medication (in this case, injections twice daily). Some of this circadian variability may be accounted for by circadian variations in the dopamine system, which seem to show the least activity in the evening hours with maximal activity in the morning [280].

Nocturnal Paroxysmal Dystonia

Nocturnal Paroxysmal Dystonia (NPD) was first described by Lugaresi's group as a condition which might be considered analogous to diurnal paroxysmal movement disorders [281]. Although it is now established that this and related conditions are variants of frontal lobe epilepsy, their atypical presentation often makes the diagnosis quite challenging. The characteristically short lasting attacks of NPD begin with arousal, including an abrupt autonomic activation that can include substantial tachycardia, followed by dystonic choreo-athetoid or ballismic movements and large-scale semi-purposive movements of all limbs. Vocalizations are common. The attacks are quite diverse if considered between patients but appear to be stereotyped in a single patient. Attacks are brief, last about a minute (range 15 s to 2 min for typical attacks) and may be vaguely remembered. Neither tongue biting nor urinary incontinence is common and tend to resolve without a significant period of post-ictal confusion, which is one of the reasons that it was not appreciated early on that at least the brief attacks are a form of epilepsy. In some patients, the attacks are decidedly unilateral The epileptiform nature of these attacks, together with two other conditions, paroxysmal arousals (in which patients awake abruptly from NREM sleep, perhaps with a start or cry, and have fleeting dyskinetic movements, then fall back to sleep) [282] and episodic nocturnal wanderings (attacks of sudden motor activity, including violent ambulation, loud vocalizations, and a variety of forceful gestures commonly occuring in stage 2 NREM sleep [283–285] is now clearly established [286, 287]. Therefore, the diagnosis and treatment of these disorders is discussed in detail in Chap. 44.

However, it is worth mentioning that there have been reports in the literature of attacks similar to NPD that did not respond to antiepileptic treatment. In the original description, two cases had longer duration (2–50 min) attacks, with no epileptic associations [281]. In one case, a patient afflicted with such attacks for 20 years developed Huntington's disease. There are a number of more recently described disorders of at least uncertain etiology. Lugaresi's et al. [288] described a periodic form of NPD which recurs every 30 s to 2 min with usually quite brief attacks (2–13 s in duration) and associated arousals which they called atypical periodic movements in sleep. While showing overlap with the short-lasting NPD, this condition was unresponsive to seizure medications, even though one patient in the original series had a vascular orbital frontal tumor on computerized tomography (CT) scanning and spikes on depth recording. Other such disorders include dystonic attacks provoked both by sleep and exercise [289], apnea-associated paroxysmal dyskinetic movements [290, 291], and post-traumatic nocturnal hemidystonia [292]. Thus, when the diagnosis is in doubt, it is prudent to order a PSG with an extended seizure montage as well as extra EMG channels to distinguish between a motor disorder and an epileptic phenomenon; in our laboratory, we employ a hybrid montage for this purpose (Table 5 from Chap. 18).

Myoclonus

The myoclonias [293] are a diverse group of conditions with abnormal movements generated at various levels of the neuraxis, from cortex (cortical reflex or epileptic myoclonus) to spinal cord (spinal or segmental myoclonus). The basic abnormal movement is a single, repeated, or periodic jerk,

most typically abrupt and "lightning-like." Most of the studies of myoclonus and sleep have focused on the persistence of myoclonic movements during sleep. Whether myoclonus persists in sleep or not appears to be related to the source of the discharge; elegant experiments have shown that myoclonus with a cortical source shows suppressed movements during sleep while (as in epilepsy) cortical discharges persisted, myoclonus of presumed subcortical origin is rapidly suppressed during sleep, and myoclonus of lower-level origins (spinal cord or secondary to peripheral damage) persists during sleep [294]. Thus, cortical and subcortical myoclonus tends to be attenuated by sleep, whereas myoclonus of peripheral origin, such as spinal myoclonus, and propriospinal myoclonus, shows persistence into sleep in varying degrees [295, 296]. Myoclonic jerks associated with startle disease also persist during sleep, although with diminished intensity [297].

Palatal Myoclonus (Palatal Tremor) Palatal myoclonus (more accurately described as palatal tremor) is characterized by rhythmic movements of the soft palate and pharynx at a rate of 1–3 Hz. It is sometime associated with rhythmic ocular, buccal, lingual, laryngeal and diaphragmatic movements, and occasionally also movements of the upper limbs [298]. Two types have been described as follows: a primary or essential type (idiopathic) due to contraction of the tensor veli palatini muscle presenting with a clicking noise in one or both ears, and an acquired or secondary due to contraction of the levator veli palatini muscle [299]. When acquired, it is usually secondary to brain stem damage within Mollaret's triangle (dentatorubroolivary pathways, with damage most common in the central tegmental tract which runs from the region of the red nucleus to the ipsilateral olive). While primary palatal tremor may be completely abolished by sleep, electrophysiologic studies in a small number of patients demonstrated that palatal contractions persist during sleep, albeit with shifts in amplitude and frequency or even altered rhythmicity [300–302]. The range of such cyclic motor dyskinesias may be broader than currently known: a similar tongue movement was reported to persist largely unchanged in sleep [303]. The finding of persistent rhythmicity suggests a relatively autonomous oscillator consistent with the idea that these segmental myoclonias may represent release of a primitive rhythmic center. In contrast to other forms of myoclonus, these dyskinesias appear to arise at a segmental level and to be associated with decreased motor control from higher centers. This dissociation may explain their resistance to modulation by descending inhibitory influences during sleep. The dyskinesias are not completely removed from higher motor centers or the periphery, however, because they may disappear in sleep, change with state, and be influenced by attention [304–306]. In one interesting case, palatal tremor was associated with time-locked respiration, suggesting a coupling of these two rhythms [307].

Palatal tremor is generally refractory to treatment. There are reports of occasional response to anticholinergics, botulinum toxin injections, baclofen, valproic acid, lamotrigine, tetrabenazine, and carbamazepine [308].

Tics

Tics are typically brisk, stereotyped, complex, often repetitive movements [309]. Usually, any given patient has a somewhat limited repertoire of movements that may change over a period of months to years. The prototypical tic disorder is Gilles de la Tourette's syndrome, a condition involving multiple motor tics with vocalizations that usually begins in childhood or adolescence but may subside in later adult life [310]. Tics may be associated with a sensory penumbra and an urge to move. Tourette's patients also have a number of commonly-associated behavioral abnormalities, especially obsessive-compulsive disorder [311, 312]. Of all tic disorders, sleep disorders have been best studied in patients with Tourette's syndrome.

Tics in Tourette's syndrome have been found to persist during sleep in most cases, mostly in stages I and II of NREM sleep, with fewer during SWS or REM sleep [313, 314]. Also observed is increased frequency of disorders of arousal (e.g., somnambulism and pavor nocturnus) and parasomnias in general, as well as poor quality and fragmented sleep [315, 316] in children with Torette's syndrome. Bodily movements in general are increased in Tourette's syndrome; Hashimoto et al. [317] found that both twitch-like and gross body movements were increased over controls during all stages of sleep, with total movements in tic patients markedly increased during REM sleep. Those authors did not attempt to analyze such movements in detail, so it is not clear what fraction of them were actual tics. In one study, patients were monitored after successful treatment of their movements with tetrabenazine, and it was found that sleep also improved [318].

Hemifacial Spasm

Hemifacial spasm consists of intermittent contraction of one side of the face that can be repetitive and jerk-like or sustained. It is believed to arise from irritation of facial nerve or nucleus. Both central and peripheral (ephaptic transmission between adjacent nerve fibers without synapses) factors are responsible for the spasms. EMG recording shows highly synchronous discharges in upper and lower facial muscles. Montagna et al. [319] studied 16 patients, recording from upper and lower facial muscles during sleep studies. In most patients, the dyskinesias decreased during sleep, being approximately 80 % less frequent in SWS and REM

sleep. One patient showed almost no change in the prevalence of spasms. Current therapy for hemifacial spasm includes medications such as carbamazepine, botulinum toxin injection into the affected muscles, or varied surgical treatments, such as vascular decompression of the facial nerve. Combined treatment with pregabalin and botulinum toxin injections has been reported [308].

Other Hyperkinetic Disorders

In *hemiballismus*, there are proximal flinging movements of one side of the body, which may be of a violent nature, associated with damage to the contralateral subthalamic nucleus [320]. In most cases, hemiballismus is a transient phenomenon after local injury to the subthalamus, usually ischemic, although it may be transformed into a chronic choreiform disorder. It was initially thought that the movements totally subsided in sleep. Askenasy [321], however, reported a patient whose movements persisted in sleep, and Silvestri et al. [115] found that the movements were present during stages N1 and N2, as well as during REM sleep, although diminished in intensity and frequency. Puca et al. [322] reported one case in which spindle density and amplitude were greater ipsilateral to the damaged subthalamic nucleus. There was also disrupted sleep, with prolonged latency and an absence of both SWS and REM sleep. Successful treatment with haloperidol improved the sleep and decreased the spindling.

In *athetoid cerebral palsy*, abnormalities of REM sleep have been noted. Hayashi et al. [323] reported on a group of severe adolescent and young adult patients. The significant motor abnormalities were associated with REM sleep: three patients had decreased numbers of REM, two had increased chin muscle tone, and seven had reduced numbers of muscular twitches. The authors suggest this may be related to brain stem pathology in these birth-injured patients. One family with five generations affected by *paroxysmal dystonic choreoathetosis* with dominant transmission was found to show substantial benefit from even brief periods of sleep [324]. In a Serbian family with mutations in the Myofibrillogenesis regulator 1 gene, sleep was reported to be the most effective means of terminating attacks [325].

Sleep-Associated Problems of the Ataxic Disorders

Relatively little research has been done on sleep disturbances in the ataxic disorders. Today, a large number of different genetically based variants of spinocerebellar ataxia have been described and some of these have been examined with respect to sleep. Patients with Machado–Joseph disease (Spinocerebellar atrophy type 3, SCA3) may have both RLS and RBD as common sleep-related problems. Patients with SCA2 can have reduced REM-sleep atonia. One report suggests increased PLMS and RLS in SCA6. SCA6 patients also have impaired subjective sleep quality and tend to have greater daytime sleepiness. It seems likely that the paucity of associations reported to date is more due to the lack of studies than the absence of sleep problems in these disorders [326–331].

B. Motor Disorders Exclusive to Sleep

i. Failure of motor control while resting in bed trying to get to sleep.

This category includes RLS and PLMW, which are discussed in Chap. 40.

ii. Failure of motor control immediately before and at sleep onset

Since normal individuals enter the sleep cycle through NREM sleep, these disorders can also be considered failures of motor control in NREM sleep. Many of these are of unclear clinical significance and require no treatment.

Physiological Hypnic Myoclonus

The term physiological hypnic myoclonus (PHM) was first coined by De Lisi [332] to describe brief asynchronous, asymmetric, and aperiodic muscle twitches during sleep in all body muscles of man and domestic animals resembling fasciculations seen prominently in face and distal body parts (e.g., face, lips, fingers and toes). PHM is also known as physiological fragmentary hypnic myoclonus and is seen prominently in babies and infants. Quantitative study by Dagnino et al. [333] and Montagna et al. [334] in 1988 showed the maximum occurrence of these twitches in stage N1 and REM sleep, decreasing progressively in stages N2 and N3. Presence of PHM also during relaxed wakefulness challenges the term hypnic Myoclonus [335, 336]; however, it should be noted that propriospinal myoclonus at sleep onset and intensified hypnic jerks in many patients [336] are present in relaxed wakefulness before sleep onset. The origin of PHM remains controversial. Facilitatory reticulospinal tract, pontine tegmentum, and corticospinal tract [337, 338] have all been suggested as the generator of PHM. These movements are physiologic without disrupting sleep architecture and require no treatment.

Hypnic jerks including intensified hypnic jerks

Hypnic jerks or "sleep starts" are sudden, brief contractions of the body that occur at sleep onset and are due to excitation of motor centers. They are physiological and occur in up to 70 % of the population at some point in their adult lives. They are often accompanied by a sensation of falling [339]. The movement itself is an abrupt, myoclonic flexion movement, generalized or partial, often asymmetric, which may be accompanied by a sensation or an illusion of falling. Unless very frequent (which does occur rarely) [336, 340] this is a benign movement which has little effect on sleep and carries no negative prognosis. When it occurs, it is

usually a single event, which causes a brief arousal. EMG records show relatively brief EMG complexes (<250 ms in duration) that may be simultaneous or sequential in various muscles. The earliest mention of this phenomenon is credited to Mitchell [341], who described insomnia occurring as a result of hypnic jerks in 1890. Oswald [339] first described the EEG correlates of hypnic jerks. In 1965, Gastaut and Broughton [342, 343] performed the first polygraphic study of hypnic jerks. It was not until 1988 that Broughton [340] coined the term "intensified hypnic jerks" to describe the clinical phenomenon of sleep onset insomnia caused by accentuated and disruptive hypnic jerks occurring at sleep onset. More recently, Chokroverty et al. [336] performed a polysomnographic and polymyographic analysis of ten patients with intensified hypnic jerks and identified four patterns of propagation: synchronous and symmetrical patterned muscle bursts between the two sides and agonist–antagonist muscles similar to those noted in audiogenic startle reflex; reticular reflex myoclonus; dystonic myoclonus; and pyramidal myoclonus with rostrocaudal propagation of muscle bursts.

Hypnagogic Foot Tremor and Alternating Leg Muscle Activation

Hypnagogic foot tremor (HFT) (Fig. 39.7) and ALMA (Fig. 39.8) rarely come to clinical attention, being discovered as incidental findings on PSG. Both occur during lighter sleep and in transitional states into and out of sleep. ALMA has also been documented in wakefulness, all stages of NREM and also, though less frequently, in REM sleep in patients with a variety of sleep disorders [344]. Another feature of ALMA is its occurrence, in addition to the traditional tibialis anterior EMG, in gastrocnemius and sometimes in quadriceps muscles alternating between two sides. Because variant patterns are reported in each, and there is at least some plausible degree of overlap between HFT and

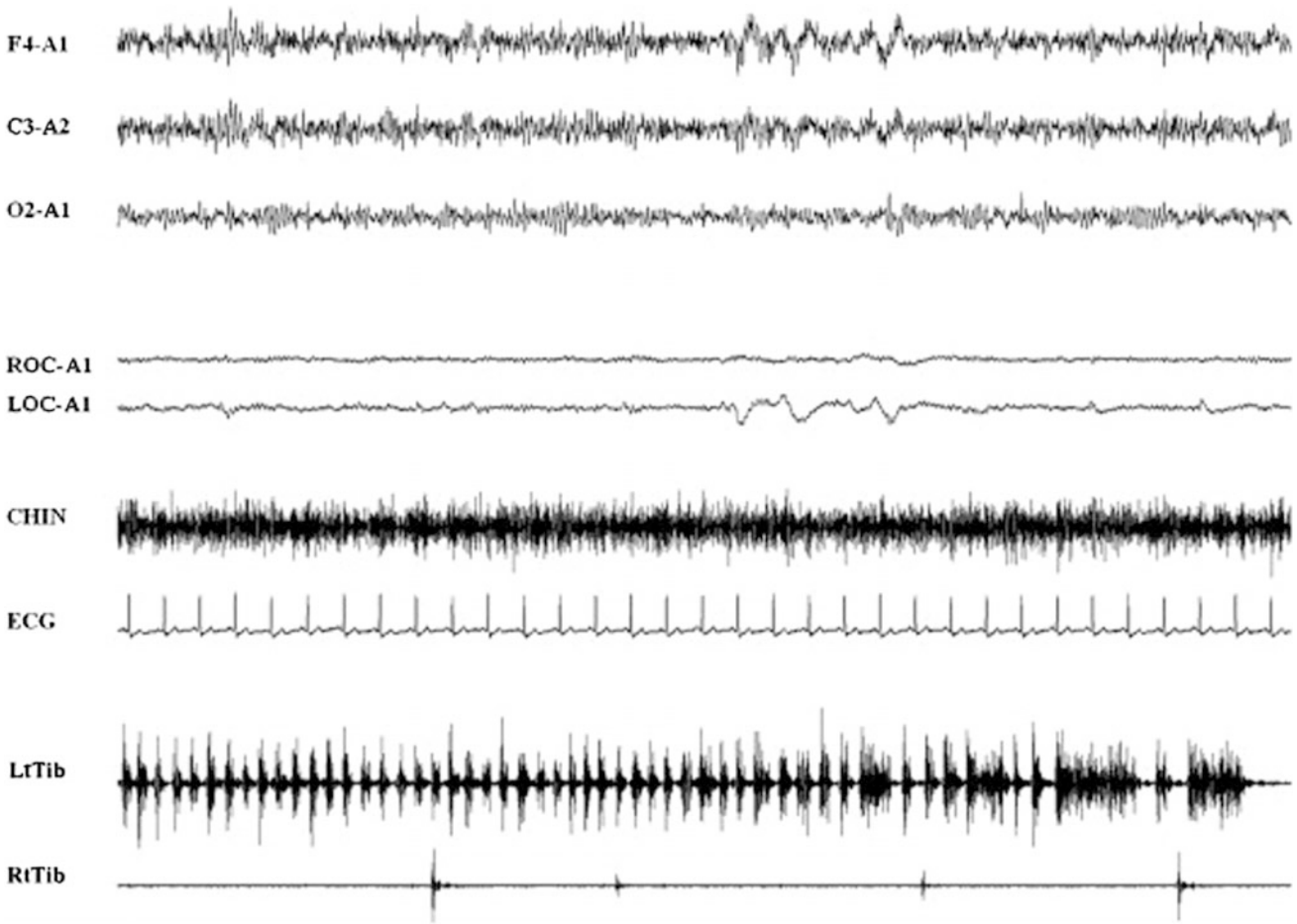

Fig. 39.7 Hypnagogic foot termor. A 30-s epoch of relaxed wakefulness from the polysomnogram of a 69-year-old man affected by snoring and nonrestorative sleep. Note the occurrence of a series of rapid tibialis anterior activations longer than 30 s, with single burst durations of 200–300 ms. Top three channels, electroencephalography. ROC and LOC: electrooculogram channels. ECG, electrocardiogram. LtTib and RtTib, tibialis anterior electromyography channels. (Reproduced with permission from Ref. [114])

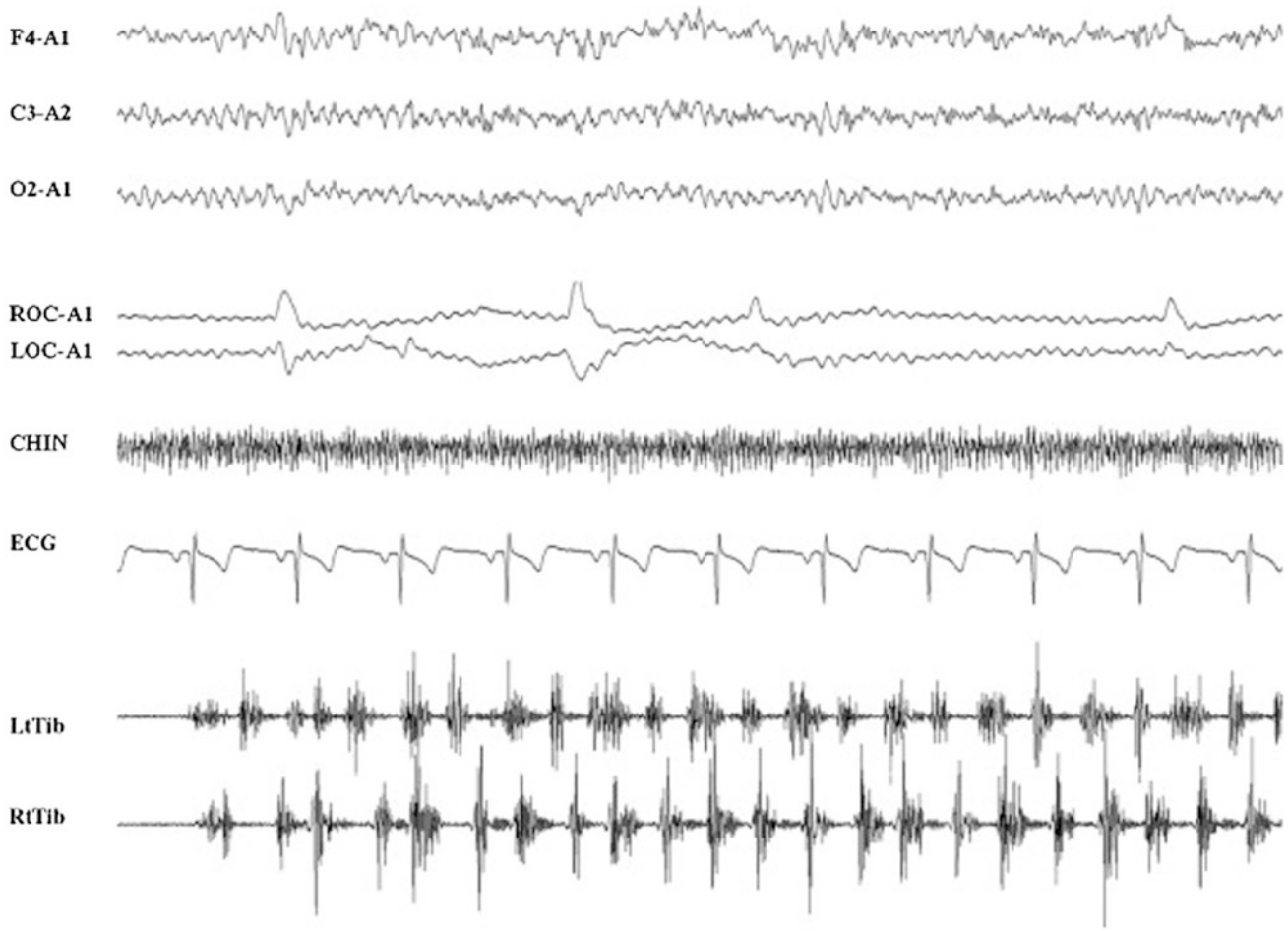

Fig. 39.8 Alternating leg muscle activation. A 10-s epoch of relaxed wakefulness transitioning to N1 sleep from the polysomnogram of a 32-year-old man with chronic insomnia and no comorbid history of restless legs syndrome, affected by snoring and nonrestorative sleep. Note the occurrence of a series of alternating tibialis anterior activations longer than 10 s, with single burst durations of 200–300 ms. Top three channels, electroencephalography. ROC and LOC: electrooculogram channels. ECG, electrocardiogram. LtTib and RtTib, tibialis anterior electromyography channels. (Reproduced with permission from Ref. [114])

ALMA (and also PLMS) further investigation may be required to ascertain whether they are distinct or merely variant conditions. It has also been suggested that both may be variants of RMD (see below). HFT is defined by the AASM Manual for the Scoring of Sleep and Associated Events as rhythmic contractions of foot and leg occurring during sleep onset generally bilaterally but asynchronously at a frequency of 0.5–4 Hz [5] and was first described by Broughton [340]. Wichniak et al. [345] later performed polysomnography on 375 consecutive subjects and found HFT (which they called "rhythmic feet movements while falling asleep" and described as rhythmic, oscillating movements of the whole foot or toes) in 7.5 %. Per the AASM Manual for the Scoring of Sleep and Associated Events, ALMA consists of EMG bursts that occur alternately in each leg in a rhythmic pattern of 0.5–3 Hz and was first described by Chervin's et al. [346], who found it in just over 1 % of reviewed PSGs; most of those showing the phenomena were taking anti-depressants. The duration of an individual movement varies between 100 and 1000 ms. For both HFA and ALMA, at least 4 movements must be present in a row to make the diagnosis [5]. ALMA requires the presence of alternating activity and has been suggested to be an equivalent of a locomotor rhythm [347]. Diagnosis of either requires a PSG recording. Convincing evidence of any definite clinical consequence of these movements is yet to be presented. In one patient, pramipexole-reduced ALMA and improved sleep [347], together with a reduction of associated CAP. The clinical significance of both HFT and ALMA remains undetermined requiring no treatment.

Rhythmic Movement Disorder

RMD (Fig. 39.9) is characterized by repetitive, stereotyped, rhythmic movements involving large muscle groups,

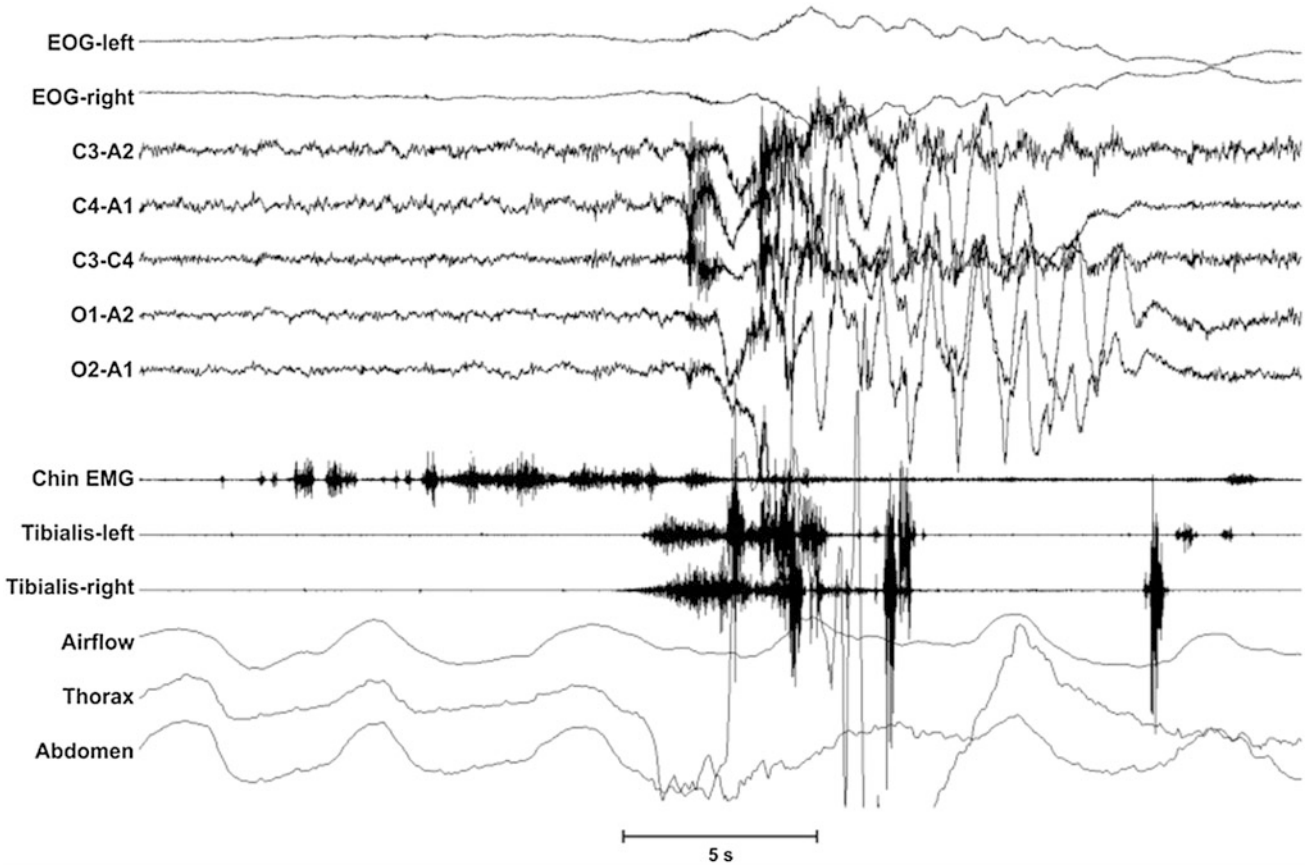

Fig. 39.9 Rhythmic movement disorder. Polysomnographic recording of a rhythmic movement disorder (RMD) episode. RMD typically consists of repetitive stereotyped and rhythmic motor behaviors, such as head banging, body rolling, and body rocking. These movements generally occur at sleep–wake transitions and after arousals from sleep but may also occur in wakefulness, and rarely during REM sleep. These episodes may also occur at the termination of a respiratory event in obstructive sleep apnea syndrome. (Reproduced with permission from Ref. [114])

occurring predominantly during sleep onset or during sleep–wake transitions, at a frequency of 0.5–2 Hz. It can take many forms, including head banging ("jactatio capitis nocturna"), body rocking, body rolling, and leg rolling. Reports of events matching the current description of RMD have been abundant in the literature [348, 349] and even reported as early as in 1880 [350] although the term *jactatio capitis nocturna* was first used by Zapert [351]. According to the AASM Manual for the Scoring of Sleep and Associated Events, in addition to the above frequency criterion, the minimum number of individual movements to make a cluster of rhythmic movements is 4 movements and the minimum amplitude of an individual rhythmic burst must be at least 2 times the background EMG activity [5].

RMD generally presents before 18 months of age and tends to occur immediately before sleep during relaxed wakefulness continuing into stage N1 and sometimes into stage N2. Rare case may show a REM predominance [352, 353]. Bouts of movements may be related to CAP [354]. While RMD is most common in pre-pubertal children, there are older children [355] and also adults [356–361] who will show persistent or emergent rhythmic movement. Most older children with persistent disorder are usually suffering from organic brain dysfunction (cerebral palsy, autism or attention deficit disorder). In developmentally normal children, however, RMD is generally benign and the child usually outgrows the movements by the second or third year of life.

Because RMD is a benign phenomenon in itself, treatment is not always necessary. However, it may cause significant injury. In addition, RMD may be secondary to frequent arousals from another condition, commonly OSA [362]. RMD may present in a rather dramatic fashion, and so may need to be distinguished from tremor or segmental myoclonias, as well as RBD or nocturnal seizures. Given this, evaluation of a patient with suspected RMD requires careful clinical history and physical examination, viewing of a video recording of the events if possible, and occasionally PSG. PSG is always recommended for most cases of RMD in patients in whom a primary sleep disorder is being

considered and should be performed with an extended seizure montage if nocturnal epilepsy is suspected. In case of primary RMD, behavioral therapy and in severe cases with potential for inflicting injury clonazepam (0.5–1 mg nightly), imipramine (10 mg at night) or melatonin [363] maybe helpful [308]. Protective measures should be used in cases with violent movements.

Propriospinal Myoclonus at Sleep Onset

Propriospinal myoclonus is a form of spinal myoclonus in which the excitatory impulses are believed to travel through relatively slow-conducting intersegmental propriospinal pathways [364–366]. However, *propriospinal myoclonus at sleep onset* was described fairly recently by Montagna et al. [367, 368] who performed polygraphic studies that showed that the myoclonic activity began in spinally innervated muscles, propagating at low speed to rostral and caudal muscular segments, and hypothesized that a spinal generator may be facilitated by changes in supraspinal control related to vigilance levels. They identified it as a potential cause of severe anxiety and insomnia. The myoclonic movements typically involve the trunk with possible extension into the limbs. In a recently described form of this myoclonus, the myoclonic jerks are only evident during relaxation or recumbency [369], especially when the patient is drowsy. Unlike PLMS, the movements are relatively easily abolished by even light sleep. They may, however, produce a substantial difficulty with sleep induction and can therefore be a cause of significant insomnia. Cases have been described that are associated with RLS [370] and an important consideration in the differential diagnosis of propriospinal myoclonus at sleep onset is the myoclonic form of PLMW seen while sitting or lying in patients with RLS [371]. One case of propriospinal myoclonus that occurred during sleep was reported after a thoracic spine fracture that progressed to "myoclonic status" and respiratory failure [372]. The treatment of this condition is challenging and some cases respond to clonazepam, zonisamide and other antiepileptic drugs used in the classic propriospinal myoclonus [308].

iii. Failure of Motor Control During NREM Sleep

This includes PLMS (discussed in Chap. 40) and the disorders of partial arousal, such as sleep terrors, confusional arousals and sleepwalking/Parasomnias (discussed in Chap. 50).

iv. Failure of Motor Control During REM Sleep

This includes RBD (discussed in Chaps. 49 and 50). The scoring criteria for REM without atonia, an essential neurophysiological component in the diagnosis of RBD, is provided in Table 39.3.

v. Failure of Motor Control in both NREM and REM Sleep

Benign Sleep Myoclonus of Infancy

This is a transient, sometimes familial condition that begins soon after birth and resolves within months [373–377]. It may, however, persist for up to a year after birth, hence the recent change in nomenclature from "benign neonatal sleep myoclonus" to "benign sleep myoclonus of infancy." The myoclonic jerks are brief, asynchronous, and repetitive, involving primarily the distal limbs, especially the arms, but also the trunk; the jerks are often generalized. The jerks occur during all stages of sleep, with most occurring in NREM sleep, and typically do not arouse or wake the infant [378]; waking the child will cause them to cease promptly. The movements do not occur continually in sleep and, when not present in sleep, they may be precipitated by rocking the infant or by gentle restraint during sleep [379]. The exact pathophysiology is unknown, but these movements most likely represent an exaggeration of the normally greater sleep-related movements in infants [380]. Although completely benign, self-limiting and with no long-term sequelae, the clinician is often called upon to reassure frantic parents that their baby is not having seizures, which it may superficially resemble [381–383]. When in doubt, EEG or PSG may help alleviate some of the concern.

Sleep Bruxism

While bruxism or teeth grinding can occur during the day, *nocturnal bruxism* (Fig. 39.10) is to be clearly differentiated from daytime bruxism. Nocturnal, or sleep bruxism, when frequent and intense enough, can interrupt sleep and cause significant dental wear [384]. It is associated with arousals and autonomic activation during sleep [385, 386]. SPECT studies show an asymmetry in D2 dopamine receptor binding in bruxism patients at the level of the basal ganglia compared to controls suggesting that dopaminergic cell dysfunction may play a role in the pathogenesis of bruxism [387]. Bruxism tends to decrease with age, although bruxers may also have increased movements during sleep in general, and may be more common in the supine position [388]. Bruxism may also be a sign of recurrent OSA-related arousals, and thus any patient with bruxism should be screened for possible sleep-disordered breathing.

Bruxism may need to be distinguished from other dyskinetic movements which involve the jaws, including oromandibular dystonia and idiopathic myoclonus in the oromandibular region during sleep. Idiopathic myoclonus in the oromandibular region (e.g., faciomandibular myoclonus) during sleep is an apparently isolated, non-epileptic condition that occurs predominantly in stages 1 and 2 NREM sleep [389–391]. It consists of isolated or short runs of shock-like jaw movements with brief EMG bursts.

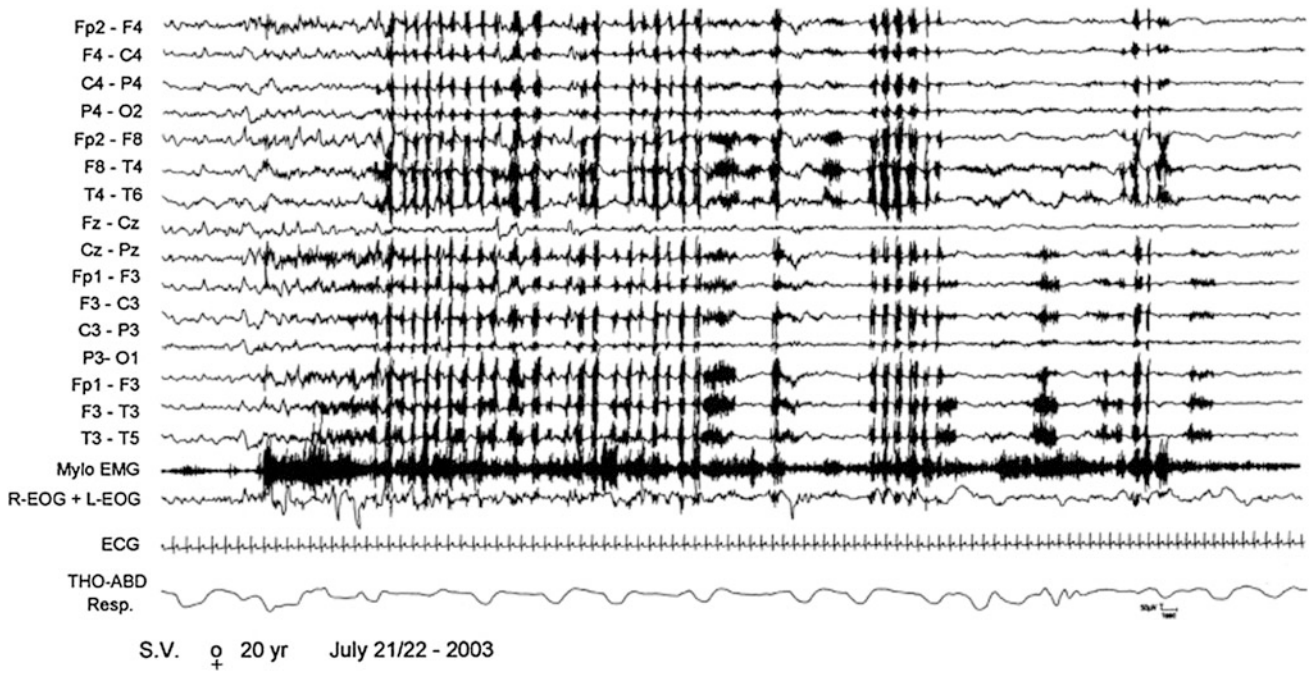

Fig. 39.10 Sleep bruxism. A 20-year-old woman referred for nocturnal awakeings with vocalization and sleepwalking. Polysomnogram shows arousal from slow-wave sleep with subsequent rhythmic masticatory muscle activation and teeth grinding (note electromyographic [EMG] artifacts on electroencephalogram [EEG] channels) typical of sleep bruxism. Top 15 channels, EEG. Mylo EMG, mylohyoid EMG activity. R-EOG + L-EOG, right and left electrooculogram; ECG, electrocardiogram; THO-ABD, thoracoabdominal respiration. (Reproduced with permission from Ref. [114])

Sleep-related bruxism has been described in every stage of sleep. While highest level of activity occurs during stage N3 and wakefulness, no difference has been described with regard to percentages of the sleep stages [392]. A close association between sleep bruxism and REM sleep has also been described [393, 394]. In 2008, Manconi et al. [395] published an interesting case report of a patient with sleep bruxism and catathrenia (see below) occurring in a synchronized fashion. They hypothesized about the presence of a common trigger mechanism for both phenomena.

According to guidelines put forth by the new AASM Manual for the Scoring of Sleep and Associated Events [5], bruxism can be identified by either brief (phasic) EMG elevations of 0.25–2 s and sustained (tonic) EMG elevations of >2 s. These EMG elevations must be at least twice the amplitude of the background EMG. Phasic bruxism events must occur in a sequence of 3 or more and this sequence can be said to comprise a bruxism episode. At least 3 s of stable EMG must be present before a new episode of bruxism can be scored. Bruxism can be reliably scored by audio in combination with polysomnography by a minimum of 2 audible tooth grinding episodes/night of polysomnography in the absence of epilepsy. In addition to chin EMG, additional masseter electrodes may be placed at the discretion of the investigator or clinician for optimal detection of bruxism. An alternate term for the phasic type of bruxism is *Rhythmic Masticatory Muscle Activity*.

The treatment for bruxism has yet to be standardized; various modalities have been employed, including dopaminergic agents [396], anticonvulsants [397], or with botulinum toxin injections [398]; dental devices may also help [399, 400] but some studies suggest caution in their use [401].

Catathrenia (see also Chap. 41)

Catathrenia, or nocturnal groaning, is a relatively newly described entity characterized by loud expiratory vocalization, whose exact pitch and timber may vary from individual to individual but is fairly stereotyped in a given patient (see Fig. 41.12). Not strictly a disorder of motor control, it may rather represent a disorder of breathing in sleep and is classifies as such according to the ICSD-3, although this is disputed by some [402]. While far more frequent in REM sleep, it may also occur in NREM sleep and alternates with normal breathing. It was actually first described by Pevernagie et al. [403] but was first named by Vetrugno et al. [404]. The same group subsequently reported in 2007 [405] that the groaning was accompanied by disproportionately prolonged expiration causing reduced tidal volume and bradypnea without oxygen desaturation, and that patients experienced no additional symptoms after a mean follow up

of 4.9 years. They speculated that catathrenia was due to persistence of a vestigial type of breathing pattern. In 2011, Ott et al. [406] performed laryngoscopy under deep sedation in a patient with catathrenia and found that while the glottis was open at inspiration, there was subtotal closure of the glottis at expiration, resulting in the characteristic groaning. The following year, Koo et al. [407] performed acoustic analysis of catathrenia and found that it had morphologic regularity, with two types of sound pitches (either a monotonous sinusoidal pattern or a sawtooth-shaped signal with higher fundamental frequency), as opposed to snoring which was distinct from catarthrenia and had an irregular signal. Several authors have reported the efficacy of CPAP in treating this benign but socially awkward condition [408–410]. The anatomical factors that predispose to catathrenia, namely broad upper airway, yet protrusive upper incisors and flat mandibular angles, have recently been described [411].

Excessive Fragmentary Myoclonus

Excessive Fragmentary Myoclonus (EFM) is essentially a variant PSG finding (Fig. 39.11), often found incidentally, that has yet to be demonstrated to be of clinical relevance. This condition may be another in which inadequate inhibitory drive fails to block descending activation from higher centers or it may represent a condition of excessive activation of higher centers during sleep. A neurophysiologic analysis by Vetrugno et al. [412] failed to disclose any cortical prepotential on EEG–EMG backaveraging suggesting a subcortical origin. The condition has been found in degenerative developmental disease (Niemann-Pick) [413] and as a consequence of brain stem lesions [414] but usually occurs in isolation [415]. Generally, EFM is not accompanied by gross visible movements; if movements are present at all they are small movements involving the corner of the mouth or small movements of the fingers or toes. In most cases no movement across a joint space occurs and the movements may resemble fasciculations, mere dimplings seen over the muscle associated with very brief EMG potentials (<50 ms). According to the AASM Manual for the Scoring of Sleep and Associated Events [5], EFM is present when at least 20 min of NREM sleep is recorded on PSG with the characteristic EMG pattern present (bursts typically <150 ms and of variable ampltude) and at least 5 EMG potentials per minute. Although classically described in the lighter stages of NREM sleep, they may occur in REM sleep, where the pattern resembles the normal phasic twitches seen in REM sleep, except they are more evenly spread throughout an individual epoch and not clustered as are phasic REM twitches. Some, [416] but not all [417] reports suggest that they are least common in slow-wave sleep. Given the lack of known clinical consequences, treatment is not required.

vi. Failure of motor control at sleep offset

Sleep paralysis

Transitions out of sleep may also be associated with *sleep paralysis,* a condition in which an individual is paralyzed while awakening from sleep. Weir Mitchell [341] is given credit for an early description of the condition in 1876 and he termed it "night palsy". Adie [418], in the 1920s observed occurrence of sleep paralysis in narcolepsy patients and Wilson in 1928 [419] introduced the actual term. There are earlier descriptions in the Chinese, Indian, Persian and Greek cultures and mythologies, as well as in famous novels such as Herman Melville's *Moby-Dick* (1851).

During episodes of sleep paralysis, breathing and eye movements are usually preserved. This condition is thought to represent a variety of REM sleep tonic motor inhibition [420]; recordings of the state can show REMs together with an electrophysiological pattern consistent with REM sleep [421]. Sleep paralysis is generally associated with arousal from a REM period (hypnopompic) or, less commonly progress into REM sleep from wake (hypnagogic) [422]. The latter would be very unusual in the normal course of events and more likely to occur with narcolepsy, though it may occur in many non-narcoleptic individuals, sometimes with a familial pattern. There are three forms of sleep paralysis, isolated or recurrent isolated sleep paralysis (physiological occurring mostly in adults up to 30–50 % of the population), familial sleep paralysis and sleep paralysis as part of narcolepsy. Several studies suggest that, at least in some populations, sleep paralysis may be quite common [423–425]. When it does occur in normal individuals, it is generally infrequent, but may cause significant anxiety, especially the first time that it occurs. A similar condition, *nocturnal alternating hemiplegia of childhood*, involves paralysis limited to one side while awakening from sleep [426]. This may be a variant of hemiplegic migraine, a complicated headache disorder with paralysis due to suppressed activity in certain brain regions.

Physiological sleep paralysis is generally brief, lasting for seconds to a few minutes, but sometimes may last longer, particularly *recurrent isolated sleep paralysis*. On occasions the episodes are accompanied by hypnagogic or hypnopompic hallucinations. The episodes may be triggered by sleep deprivation, stress, physical exertion or supine position. Isolated or recurrent sleep paralysis does not require any specific treatment other than reassurance, life-style changes, regularizing sleep–wake schedule but in severe cases causing anxiety and panic short-term treatment with

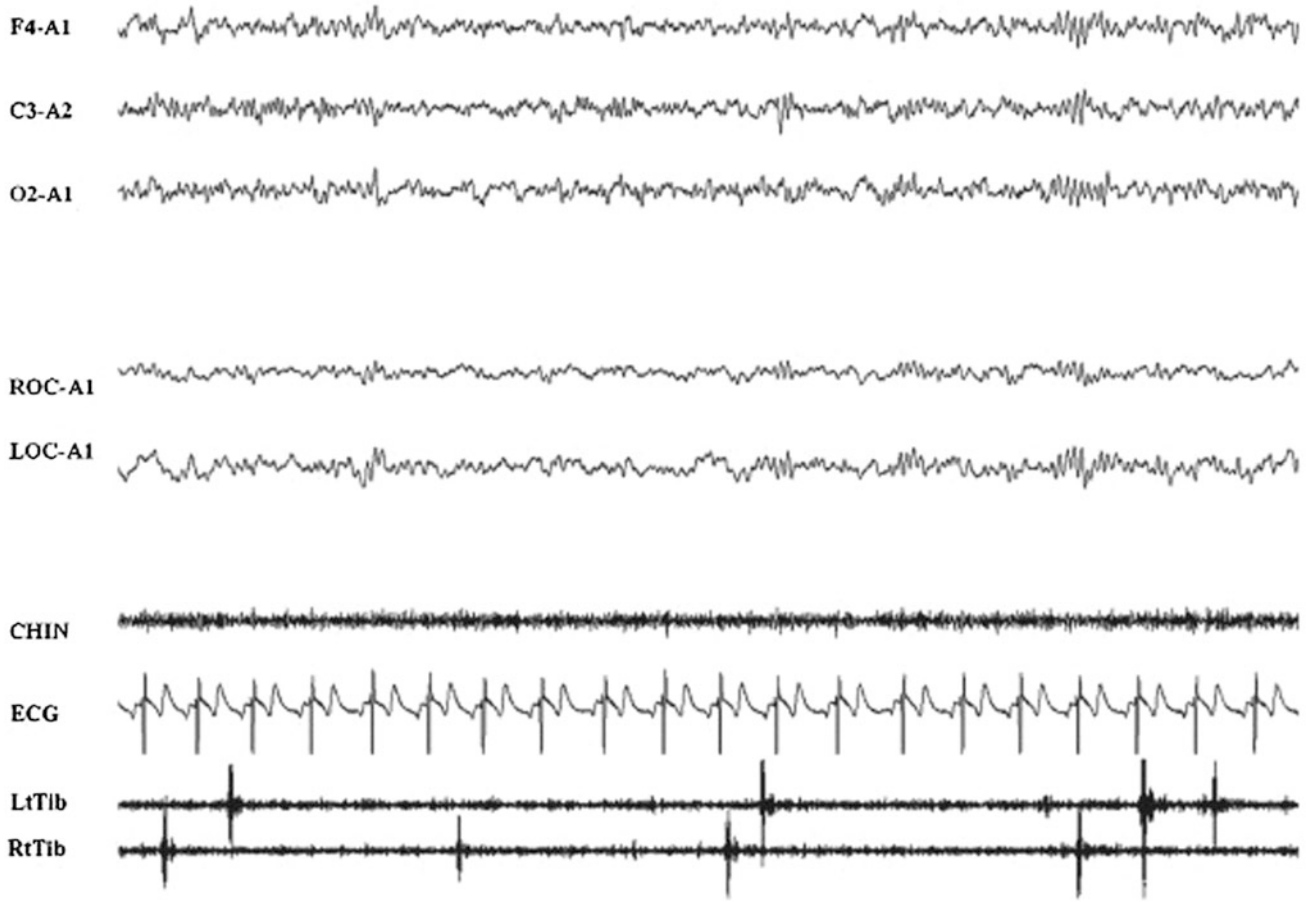

Fig. 39.11 Excessive fragmentary myoclonus. Poysomnogram epoch from the study of a 71-year-old man who presented a 2-year-history of continuous twitch-like movements of the arms and legs throughout the night, which did not wake him from sleep. Note the brief, asynchronous, asymmetric potentials in the limb electromyography (EMG) channels (RtTib and LtTib). Visually, they presented as brief twitch-like movements not causing movement of major joints. Excessive fragmenrtary myoclonus is considered a benign phenomenon with no clinical consequence. Top three channels, EEG. ROC-A1, LOC-A2, electrooculography channels. CHIN, chin EMG. ECG, electrocardiography. (Reproduced with permission from Ref. [114])

selective serotonin reuptake inhibitors (SSRIs) or tricylic antidepressants may be beneficial.

Sleep Inertia

This is most likely not a disorder of motor control in sleep in the strictest sense, but is discussed here for conveneience. Sleep inertia, also known as *sleep drunkenness* is a transient physiologic state of hypovigilance, confusion, impaired cognitive and behavioral performance, and grogginess that immediately follows awakening from sleep [427]. Put simply, the subject is physiologically awake (body awake) but cognitively asleep (brain asleep). EEG of sleep inertia is characterized by a generalized decrease of high frequency beta-1 and beta-2 EEG power but an increase of delta power in the posterior scalp region concomitant with decreased frontal delta power [428]. This state can last from minutes up to four hours, most commonly about five minutes and rarely may exceed 30 min. Prior sleep deprivation, awakening from SWS and short naps may aggravate sleep inertia. It is also more intense when awakening from near the trough rather than the peak of the circadian core body temperature rhythm. Sleep disorders, particularly idiopathic hypersomnia, as well as narcolepsy-cataplexy syndrome and obstructive sleep apnea syndrome may be associated with prolonged sleep inertia. Bedrich Roth and collaborators were probably the first to describe idiopathic hypersomnia with sleep drunkenness in the 1950s [429]. One suggestion for the pathogenesis of sleep inertia is build-up of adenosine and this state can be reversed by caffeine acting through adenosine A2a receptors, thus explaining the well-known reinvigorating effects of an early morning cup of coffee.

Table 39.2 American Academy of Sleep Medicine (AASM) polysomnography scoring criteria for sleep-related movements [5]

Movement	Criteria
Hypnagogic foot tremor	• Frequency of EMG bursts 0.5–4 Hz • Duration of each burst: 250–1000 ms • Minimum number of bursts needed to score: 4 • Occurs at sleep–wake transition, stage N1 and stage N2 sleep • Burst series duration: 10–15 s
Alternating leg muscle activation	• Frequency of EMG bursts 0.5–3 Hz • Duration of each burst: 100–500 ms • Minimum number needed to score: four • Occurs at sleep–wake transition, arousals, NREM and REM sleep • Burst series duration: 20–30 s
Rhythmic movement disorder	• Frequency of EMG bursts: 0.5–2 Hz • Episode duration variable: seconds or minutes • Series of RMD: at least 4 rhythmic movements • Occurrence mainly during drowsiness or sleep, or after sleep onset (mostly during stage N1 or N2) • Amplitude of EMG burst at least twice the EMG background
Excessive fragmentary myoclonus	• At least 5 bursts per minute during NREM sleep • Burst duration: 75–150 ms • Myoclonus index: number of 3-s mini-epochs containing at least one fragmentary myoclonus potential, included within each 30 s epoch
Periodic limb movements	• PLM sequences are identified by at least four LM • Interval between two consecutive PLM (onset-to-onset) is 5–90 s • PLMS index: number of PLMS divided by the number of hours of sleep • PLMS with arousal index: number of PLMS associated with arousal divided by the number of hours of sleep • Periodicity index: ratio of consecutive intermovement intervals, all separated by 10–90 s (at least 3 intervals) divided by the total number of movements
Sleep bruxism	Phasic or tonic increase of chin EMG signal, at least twice the amplitude of the background EMG activity (A) Tonic increase of the chin EMG signal lasting more than 2 s (B) Phasic increase of the chin EMG signal, rhythmic masticatory muscle activity (RMMA); at least 3 consecutive contractions, with a frequency of 1 Hz • Burst duration: 0.25–2 s • Interval between each episode of sleep bruxism: 3 s of stable background chin EMG signal • At least 4 episodes of sleep bruxism/hour of sleep, or at least 25 individual masticatory muscle bursts per hour of sleep associated with at least two audible episodes of tooth-grinding

Scoring Criteria for Sleep-Related Movements

These are summarized in Tables 39.2 and 39.3.

Methods for Studying Sleep-Related Movements

As with any branch of clinical medicine, there is no substitute to a well-taken history and thoroughly-conducted physical examination. Not only is this good clinical practice that ensures that the appropriate test is ordered, but in many cases where the underlying disorder is clearly benign, and reassurance and observation is desirable (such as hypnic jerks), may obviate the need for testing at all.

A. Accelerometry Based Testing

i. Actigraphy

Actigraphy is a validated, relatively cost-effective and convenient alternative to expensive, cumbersome in-laboratory procedures in the assessment of sleep–wake cycles and movements in sleep, in both clinical practice and research. Depending on the equipment and technique used, recordings can be made for many days or even months. In assessing sleep disorders, this extended recording can allow for the capture of rare events, overcoming the problem of variability which can limit the accuracy of more abbreviated studies, and repeated measurement of sleep in different conditions (evaluation of sleep patterns, disease progression or remission, therapeutic responses). In addition to the cost consideration, the small size, light weight and ease of use of most of these devices allows for its application in multiple settings; the activity monitors can be taken out of the laboratory, self-applied, and even transmitted by mail. They may be particularly useful in uncooperative patient groups with degenerative disease who would not tolerate a laboratory sleep study.

The limitations on activity monitoring result from the relatively non-specific results and the limited information monitored. All movement, even transmitted movement, is recorded. There is generally no information about cerebral

Table 39.3 Scoring criteria for REM without atonia

Criteria	Lapierre and montplaisir [95]	SINBAR	REM sleep atonia index
Muscle	Submental	Mental, FDS	Chin
EMG activity	Tonic: 50 % tonic >2 × background amplitude (or >10 μV) Phasic: >4 × background amplitude 0.1–10 s	Tonic: 50 % tonic >2 × background amplitude (or >10 μV) Phasic: >2 × background amplitude 0.1–5 s Any: >2 × background amplitude 0.1 s	Tonic: ≥1 μV
Epoch duration	20/2 s mini-epochs	30/3 s mini-epochs	1 s
Cut-off and combination	Tonic: >30 % Phasic: >15 %	Phasic chin: 16.3 % Any chin EMG (3 s): 18 % Any chin EMG + phasic FDS EMG (3 s): 32 % Any chin EMG + phasic FDS EMG (30 s): 27 %	AI <0.8

SINBAR Sleep innsbruck barcelona group; *FDS* Flexor digitorum superficialis; *EMG* Electromyography; *AI* Atonia index
Reproduced with permission from Ref. [430]

state (EEG), eye movements (too small to be reflected in a limb monitor), or breathing. Therefore, they do not provide much useful information about physiological state and crucial information about exact sleep stages.

Typically, activity monitoring devices use accelerometry to quantify movement. Several small self-contained devices currently available on the market provide a direct assessment of the amount of activity or body movement at the point of the body where they are attached. These are all derived from the work of Colburn and Smith who produced the first of these meters and documented the methods for others to use [431]. Virtually all of these use a piezoelectric sensor (usually a ceramic bender unit). The ceramic bender generates its own electric current that is directly proportional to the amount of acceleration. The activity devices usually include a volatile memory chip and a small computer or micro-controller chip. They are programmed to determine the amount of activity in a unit time and record that amount at a determined storage rate. The activity accepted by these devices is usually filtered so that they cover the dominant frequency ranges for human movement of about 0.5 to 10–15 Hz [432]. Later the data are downloaded to a computer, typically a desktop or laptop PC, usually through a special interface device. Various manipulations can then be performed on the downloaded data for further quantification or illustration. The activity data are maintained with a time-date code so that the activity can be analyzed by the time of each day recorded. The self-contained units are battery powered; current models provide batteries capable of actively recording for from 14 days to 4 years. Although shorter battery life does limit the maximum duration of the recording, battery life may increase as this technology develops. Another limitation on the duration of monitoring is the amount of computer memory available to retain the stored values. Currently, the memory size available for these monitors is 4 MB–1 GB. Duration of monitoring is inversely proportional to the rate at which values are stored. For low storage frequencies (e.g., once every minute), these capacities translate into a total monitoring period of 3–720 days. However, at high storage rates useful for examining individual movements (e.g., 10 per second), total monitoring would only be from about 7 min up to 29 h. These devices all use internal circuitry to sample the output voltage at a certain frequency (sample frequency or rate). The amount of activity can be determined by checking the number of times the voltage reaches or exceeds a minimum criteria (threshold crossing) or by some integration or summation of the total voltage from the individual samples. Integration provides the more sensitive approach, especially for examining individual movements as opposed to total activity. After a certain number of samples, the result either in total threshold crosses or integrated voltage is stored. The storage frequency or rate limits the time resolution of this technique. For assessing total activity occurring in spans of a few seconds to minutes, the digital sampling can be at relatively low rates (e.g., 4–8 Hz) and still provide an adequate measurement. But for higher storage frequencies designed to examine individual movements, a sampling frequency of 10–40 Hz is probably necessary. Storage rates of 10 Hz or more would be ideal although slower movements can be analysed with storage rates perhaps as low as 1 Hz.

In sleep–wake detection for the evaluation of various circadian rhythm disorders and in insomnia, the patient wears the device on the non-diominant wrist, and simultaneously keeps a sleep log for comparison. There have been several validation studies published, in both children and adults as well as in special populations, under a variety of conditions, evaluating a large number of wrist actigraphs from various manufacturers. Most devices show good sensitivity and specificity (of the order of 86–96 %), but low specificity (30–40 %); detection of wake is usually unsatisfactory [433–437]. These caveats should be borne in mind when interpreting data from actigraphy.

For movement disorders, the activity monitor is placed at the site of the abnormal movement. In general, the goal of such recording is to count and quantify such movements, not merely to indicate when movement occurs. Various earlier studies showed that abnormal movements associated with hyperkinetic disorders could be quantified using actigraphy [438, 439], if appropriate filtering was used to select for frequencies associated with the movements. Early studies attempted such a quantitation in PLMS. The total movement activity during sleep for patients was determined from activity monitors worn on the ankle of the affected leg, but the correlations between overall activity and the number of PLM were not high (values of about 0.6) [440]. More recently, sophisticated systems for counting movements have been developed and validated [441–443], making these systems useful for therapeutic monitoring or assistance in diagnosis of PLMD and RLS [444–446]. A much better correlation between total activity and specific abnormal movements may be obtained with a finer-grain analyses [447]. Recognizing the distinctive profile of individual movements requires matching the descriptive powers of an EMG record. To detect the onset and end of a specific movement requires sensitivity to higher-frequency components of the movement, necessitating sampling rates in the range of 10–40 Hz. Moreover, there are major data-storage problems for this condition. PLM are, by definition, greater than 0.5 s in duration (see Chap. 40). Activity measurements to detect PLM should have storage frequencies of at least 4 Hz and preferably 8–10 Hz to enhance measurement accuracy. A fine-grain analysis with 40 Hz sampling and storage at 10 Hz available from one of these monitors (PAM-RL, Respironics, Pittsburg, PA) provides a description closely matching the EMG recordings for these movements (Fig. 39.12). The recording at 10 Hz can then be saved for up to 7 days depending on the memory size in the units. In the more advanced activity meters such as the PAM-RL detections are based on sampling at 40 Hz with data stored for the activity summed over 4 samples (10 Hz data storage). The descriptive information about the movement along with total activity per 0.1 s permits a review of

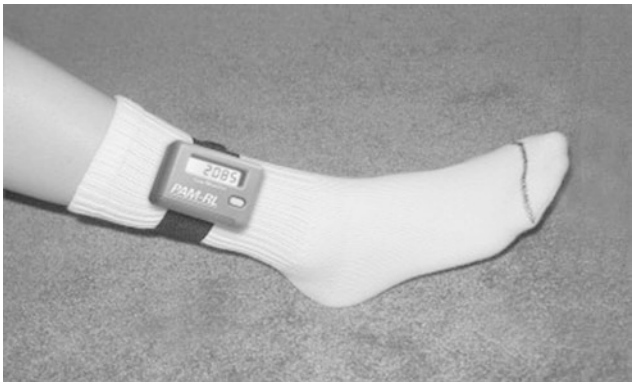

Fig. 39.12 Example of a high-precision activity monitor worn on the ankle to detect leg movements

machine scoring to determine if criteria are met for periodic movements of sleep. The data provides an excellent agreement with the nocturnal PSG for number of leg movements (Fig. 39.13) with a correlation of 0.997 and an average error for rates per hour of less than 1.0. when done in the laboratory setting with calibrated meters [448]. The monitors when used off the shelf in a standard clinical setting also have very good agreement with results from the PSG and are considered validated for this use [443]. The PAM-RL has an advantage for home recordings since it records separately the PLM rates when the legs are stretched out from when they are upright (subject sitting or standing). Thus they give the PLM rates for the sleep position (although not sleep, per se) (Fig. 39.14).

The use of the new ambulatory monitors that provide this fine-grain analyses of movements might be further extended to assess other movement disorders in sleep, such as RBD or rhythmic movement disorder. But even such a development would fail to provide relevant information about the patient's sleep–wake state. This can be approached by adding illumination or position information. To detect body position, a system has been developed [449] which requires wearing small monitors on the trunk and also on the leg just above the knee. Each monitor records position in three-dimensional space for each epoch (30 s to 1 min), and the combination of the two provides a description of the overall body position as standing, sitting, reclining, supine, prone, or lying on the right or left side. These monitors, when compared to direct observation of a subject's body position, show an excellent overall agreement (contingency coefficients C = 0.85–0.91, maximum value of C for these data = 0.913). Activity data collected at the same time as position data permits differentiating abnormal movements that occur while the patient is lying down from those while standing or sitting. It also permits the detection of events during the sleep time when the patient sits or stands up, such as occurs for sleepwalking.

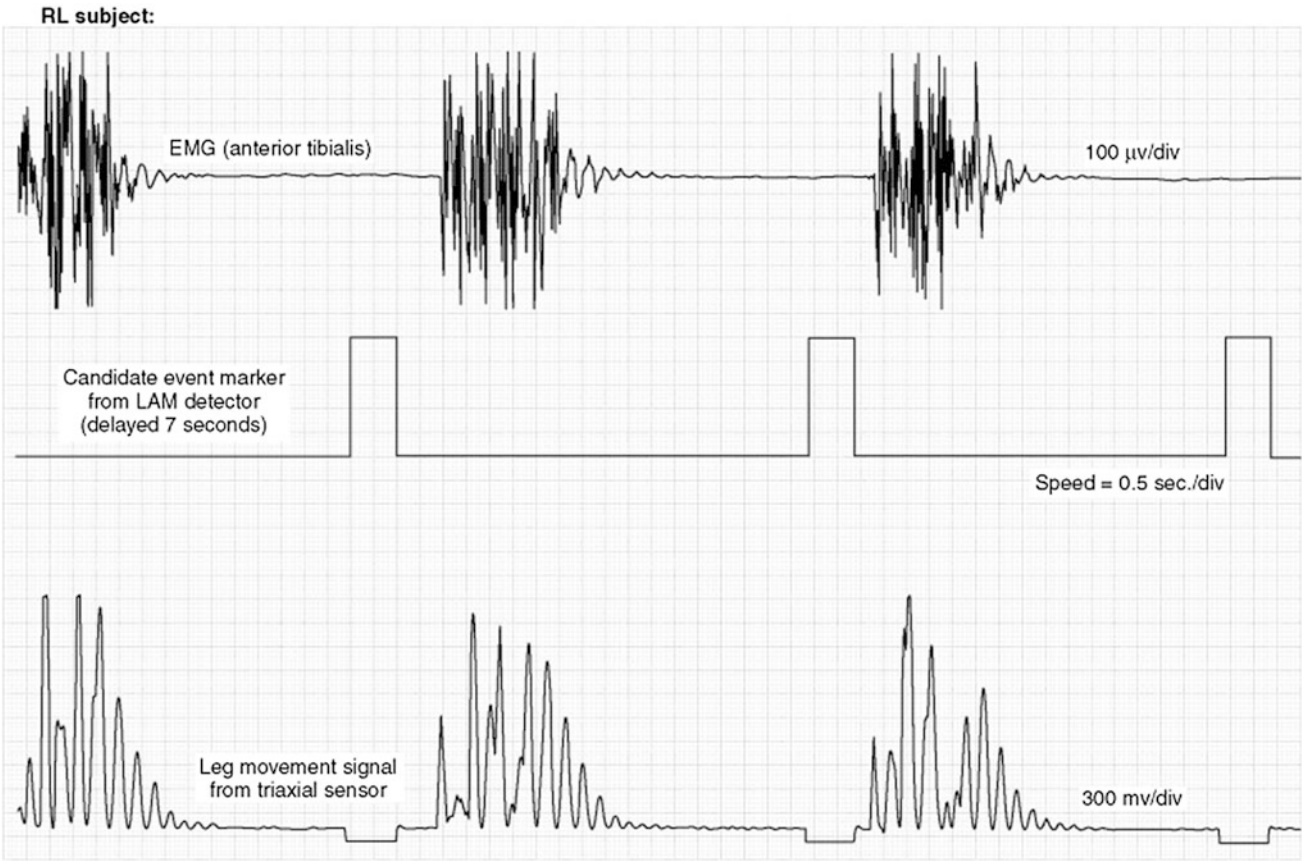

Fig. 39.13 Example of the real-time output of a high-precision activity monitor worn on the ankle (*bottom line*) compared to anterior tibilais EMG activity (*top line*). The *middle line* shows the real-time automatic detection of a significant leg movement made by the activity meter. The decision rules for the real-time leg movement detector create a 7-s delay in the detection

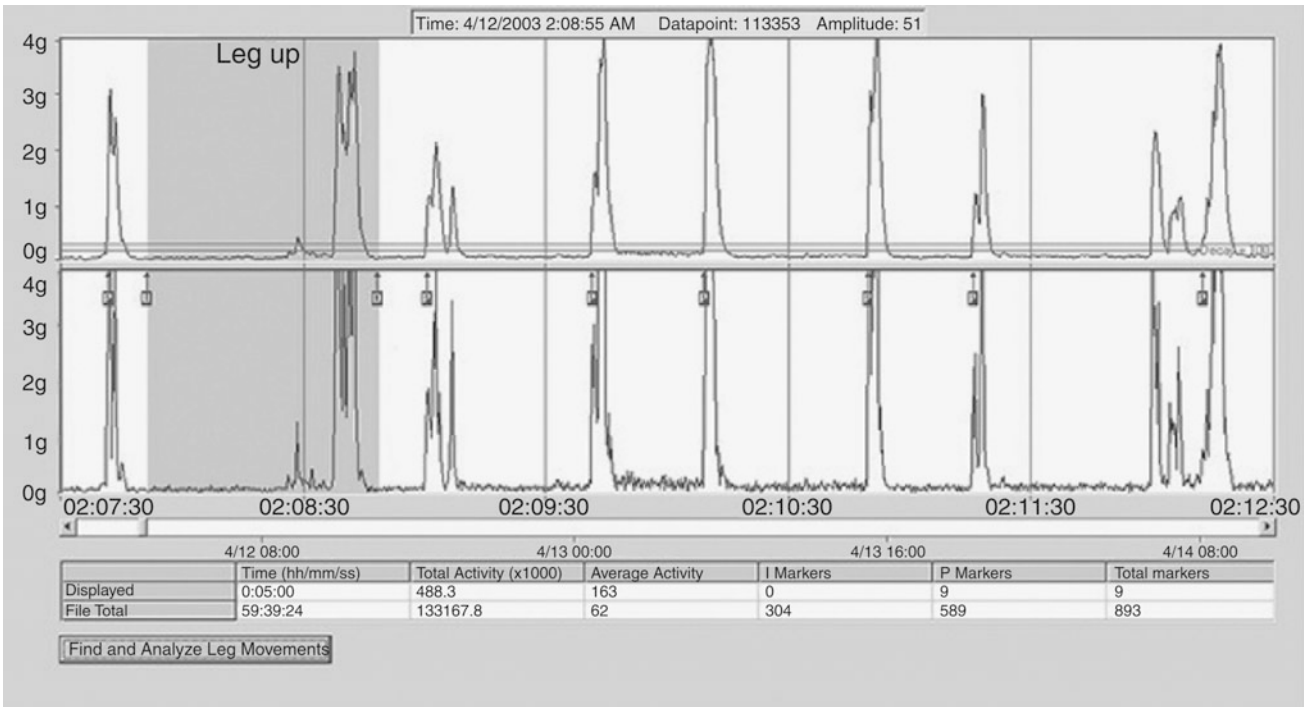

Fig. 39.14 Example of a computer display of stored leg activity and leg position data from a high-precision activity monitor worn on the ankle. The lighter areas on the graph (*white background*) indicate the leg is in a mostly horizontal position

ii. Consumer-oriented sleep technology

In recent years, there has been an explosion of inexpensive, consumer-oriented, readily available technology that is meant to monitor, among other parameters, sleep quality and duration. Entries into this category include standalone wearable devices (e.g., FitBit, Jawbone) as well as smartphone-based software programs ("apps") [450, 451]. While they all essentially use accelerometry-based techniques, as does actigraphy, to score sleep or wake (and in some cases distinguish between "light" and "deep" sleep) based on body movement, in most cases, the exact technology is proprietary, which limits detailed evaluation. "No-contact" bedside devices that detect sleep through radiowaves have also recently become available [452]. While such consumer-oriented sleep technology is very popular, mainly due to its convenience and easy accessibility, there is very little data validating it against established means of evaluating sleep [453]. Therefore, the sleep community remains uncertain as to how to approach this technology and how to interpret the information obtained from such devices and apps that patients bring with them to their clinic evaluations [454]. Recently published studies do suggest that this technology, while showing variable correlation with PSG-based scoring, has a sensitivity and specificity for sleep–wake detection that may be comparable to actigraphy [452, 455–458]. However the data are preliminary as of now. Thus, although the use of consumer-oriented sleep technology is likely to increase in the coming years, until larger studies that evaluate this technology are available, its exact role in clinical sleep medicine and research, if any, remains unclear.

B. Neurophysiological Studies

Polysomnography

Video PSG is the gold standard in diagnosing a variety of sleep disorders, specifically sleep-disordered breathing, abnormal movements in sleep, and nocturnal seizures. PSG techniques are discussed in detail in Chap. 17, and the scoring of sleep stages and respiratory events in sleep is discussed in Chaps. 24 and 25 respectively. Many abnormal movements in sleep as well as parasomnias are induced by arousals, which can be due to factors not obviously associated with the movements themselves, most commonly OSA. Treating OSA will decrease arousals, in turn decreasing the abnormal movements and parasomnias. Thus, even patients with what appear to be typical abnormal movements in sleep (HFT, ALMA, RMD, etc.) should be screened for possible OSA and undergo a PSG if they present with risk factors for sleep-disordered breathing.

When dealing with patients with abnormal movements in sleep, certain modifications to the PSG montage are helpful (see Chap. 18). While the standard PSG with a single EMG lead for the legs does provides a certain degree of information about certain motor disturbances, specifically PLMS, they may not be helpful when dealing with abnormal movements involving the upper extremities, the cranially innervated muscles, or even more proximal or more distal lower extremity muscles. For this reason, a multiple muscle montage that includes extra EMG channels recording from additional cranially innervated muscles (such as the sternocleidomastoideus, masseter and other muscles), upper limb (e.g., biceps, triceps, extensor digitorum communis, flexor digitorum subliminis), and lower limb muscles (e.g., quadriceps, hamstrings, gastrocnemius, and extensor digitorum brevis) and axial muscles (e.g., cervical, thoracic and lumbar paraspinals, rectus abdominis, intercostal muscles) (see Table 18.4) is recommended in those patients who have more complex movements by history. Similarly, an extended seizure montage with extra EEG channels (see Table 18.2), or a hybrid montage using select additional EEG and EMG channels (see Table 18.5) may be of benefit in patients in whom abnormal movements in sleep are suspected to be secondary to nocturnal seizures. Technician observations are invaluable in the documentation and description of events, and where the question is one of RBD, in eliciting dream recall. The sleep specialist can ask for no stronger ally than a vigilant technician who is aware of the clinical question being asked and is able to focus the camera on the area and movement of interest when abnormal movements occur.

Where patients complain of daytime sleepiness or abnormal movements during daytime naps, multiple sleep latency testing (MSLT), with multiple muscle montage if indicated, may be considered (see Chap. 22).

While ambulatory sleep studies (or home sleep tests [HST]) are gaining increasing acceptability and use in the evaluation of OSA, they suffer from significant limitations in the evaluation of abnormal movements in sleep, including a limited number or most often no EEG or EMG channels, no corresponding video recording, and no observer to document unusual behavior. Therefore, at the present time, HST is not recommended in the evaluation of patients with abnormal movements in sleep, such patients need to be evaluated by in-laboratory PSG.

Motor Evoked Responses

To more directly examine the impact of sleep on the motor system itself, motor evoked potentials (MEPs) can be studied. In one study of MEPs evoked by stimulating the motor cortex with a strong magnetic stimulus during sleep, it was noted that the MEPs decreased during NREM sleep [459]. Results during REM sleep have shown a much greater degree of variability in amplitude of evoked responses. Hess et al. [459] found that responses were of normal or increased amplitude, suggesting enhanced cortical excitability during REM sleep. In contrast, Fish et al. [261] found that average amplitude was decreased in 3 normal subjects with prolonged latencies in REM sleep compared to wakefulness

despite variability of response amplitudes indicating maintenance of motor inhibition during REM sleep. In a group of narcoleptic patients, stimulation during cataplexy resulted in apparently normal MEPs [460]. While these results remain to be harmonized, the variability is consistent with the fluctuating balance between inhibitory and excitatory processes in REM. A finding of decreased mean amplitude, however, is more consistent with the general inhibitory balance of REM sleep in normals. When sleep apneas are superimposed on sleep, MEP amplitude may decrease further [461]. The use of MEPs in the evaluation of abnormal movements in sleep is mainly in the realm of research at this point and not of much value in everyday clinical practice.

Other methods used in Special Circumstances

In selected cases, a number of specialized techniques to evaluate for abnormal movements occurring in sleep can be performed. These include EEG–EMG studies with back averaging, reciprocal inhibition, long loop reflex (the "C" reflex), startle reflex, and somatosensory evoked potentials (SEP, e.g., giant SEP in cortical myoclonus). A detailed description of these techniques is beyond the scope of this chapter, but the reader is referred to other sources for further information [462].

C. Neuroimaging Studies

The development of new imaging techniques that permit assessment of activity in the waking brain provides an additional method of studying regional contributions to state-dependent motor activity. Studies of cerebral blood flow and metabolism have largely paralleled those of cellular activity. Techniques, including functional magnetic resonance imaging (fMRI), SPECT, and PET scans including ligand studies, MR spectroscopy, functional or resting connectivity, diffusion tensor imaging (DTI) and tractography (for white matter imaging), voxel-based morphometry (for gray matter imaging), and transcranial sonography have all been employed in research and are discussed in greater detail in Chap. 21.

Blood flow and metabolism may be greater during REM sleep than in waking but are widely depressed during NREM sleep, especially SWS [463, 464]. Examining differential regional activities in relation to sleep states or features can provide insights into sleep mechanisms. In one study, Hofle et al. [465] correlated activity in different brain regions with power in different EEG frequency domains (e.g., delta, here 1.5–4.0 Hz). The greatest decrement associated with increased delta power (characteristic of SWS) was in the thalamus, consistent with the depressed thalamic activity of sleep. The presence of sleep spindles, most common in stage N2 sleep, is associated with activation of the thalamus, paralimbic areas, and the superior temporal gyrus [466]. Slow (11–13 Hz) and fast (13–15 Hz) spindles show this common activation, plus distinctive activations of the superior frontal gyrus (slow spindles) compared to sensorimotor cortical areas (fast spindles), medial frontal areas, and hippocampus. During REM sleep, in contrast to NREM sleep, there is activation of the brain stem core and thalamus as well as limbic areas of the brain and primary and secondary sensory areas [467–469], including visual cortices [470]. Hong et al. [471] examined the association between REMs and blood flow and found associations both with the midline attentional system active in REM sleep and areas involved in generating waking saccadic eye movements and subserving visual attention. Higher cortical areas, including prefrontal cortex and multimodal sensory and associative cortex, remain suppressed during all sleep stages [472]. REM sleep can be divided into those baseline periods without REMs and the periods with REMs, during which sensory receptivity is decreased [473]. During actual rapid eye movements, fMRI studies have shown additional activation in posterior thalamus and occipital visual cortex [474] or within a thalamocortical network including limbic and parahippocampal areas. Additional studies have shown that the basal ganglia are suppressed in SWS, but very strongly activated in REM sleep [463]. The significance of these basal ganglia changes for the motor system and for movement disorders in sleep remains unclear but is of great potential interest. These results in imaging studies suggest an evolving of sleep states in terms of the involved brain structures, including the motor system.

Imaging studies can also begin to assess potential deficits due to altered sleep conditions, such as sleep deprivation [475], which can cause depression of frontal lobe activity that is only partially restored after a compensatory sleep.

Principles of Treatment of Sleep Disorders Related to Abnormal Movements

The first and foremost step is to determine if sleep dysfunction is related to these abnormal movements at night, or if these are due to an associated common primary sleep disorder (e.g., OSA which has a prevalence in the population of about 14 % in men and 6 % in women between 30 and 70 years old; or a persistent insomnia disorder which may affect the quality of life in about 10 % of the population), or a comorbid psychiatric illness (e.g., anxiety, depression).

The basic treatment can be divided into two categories:

1. Treatment of the abnormal movements at night possibly responsible for sleep dysfunction using standard treatment for these movements. If these movement disorders are causing sleep dysfunction, optimal treatment of these involuntary movements should improve patient's sleep dysfunction. Pharmacologic treatment of these jerks and shakes has been addressed briefly in the text (see above).

Most of these abnormal movements do not require a specific treatment as these are mostly benign and will disappear in time but sometimes may persist into adulthood. However, treatment may be required if the movements are violent, injurious, or potentially violent. Pharmacotherapy usually includes benzodiazepines, selective serotonin reuptake inhibitors (SSRIs), or other antidepressants or anxiolytics for short-term relief. Non-pharmacological treatment may consist of psychotherapy, reassurance, and education of the patient and the family, progressive relaxation, and good sleep hygiene (sleep health) practice (e.g., regularize sleep–wake schedule, avoid alcohol, coffee consumption, and smoking near bed-time.). Also, attention should be paid to environmental safety measures, such as removing harmful sharp objects from bedroom, placing a mattress or other soft surface next to the bed, locking doors, and windows to prevent the patient from injuring himself/herself.

2. If sleep dysfunction is due to a primary sleep disorder, this should be treated using the standard method (e.g., CPAP for OSA and cognitive behavioral therapy (CBT) for insomnia with or without hypnotics used intermittently). Any comorbid psychiatric illness should be treated using generally accepted measures (e.g., SSRIs or other antidepressants and anxiolytics for depression and anxiety). Patients should always follow some common sense sleep hygiene measures. In a subset of patients with sleep onset or maintenance insomnia and circadian disruption associated with abnormal movements, especially when caused by neurodegenerative disease (e.g., Alzheimer's disease and Parkinson's disease) appropriately timed bright light therapy has been found to be useful. A word of caution is in order. Pharmacotherapy should be initiated at low doses, particularly in the elderly and those with neurodegenerative diseases, to minimize side effects. Finally, patients should be advised to avoid prolonged use of sedative-hypnotics and reduce or eliminate medications that may contribute to sleep dysfunction or OSA.

Box 39.2 lists these general principles of treatment.

Box 39.2: Principles of Treatment of Sleep Dysfunction Related to Abnormal Nocturnal Movements

- First determine if sleep dysfunction is related to abnormal nocturnal movements or a primary sleep disorder or a comorbid psychiatric-illness
- Treat primary movement disorder if it is causing sleep dysfunction
- Treat associated primary sleep disorder
- Treat comorbid psychiatric illness
- Initiate good sleep hygiene measures including regular sleep–wake dysfunction
- For pharmacotherapy try a non-benzodiazepine receptor agonist or a melatonin receptor agonist for short-term hypnotic use
- Start with a small dose and gradually increase the dose to minimize side effects in the elderly or those with neurodegerative disease
- Reduce or eliminate medications that may contribute to sleep disturbance or sleep apnea
- Attend to environmental safety precautions to avoid injury to patients
- Use appropriately timed bright light exposure in a subset of patients with insomnia and circadian rhythm disruption.

Summary and Conclusion

This chapter discussed an important aspect of human motor control (and dyscontrol) that has been largely neglected for a long time because it sits in the borderland of two important disciplines in medicine—those specializing in movement disorders and those specializing in sleep medicine. An understanding of motor control mechanisms is important for both fields. A breakdown in the delicate balance of motor control due to an affection of the afferent, central, or efferent structures can cause a dysfunction of voluntary movements or appearance of abnormal movements causing both positive and negative symptoms. Sleep modulates motor phenomena with progressive decline of motor activity due to increasing dominance of central inhibitory drive; concomitantly, the excitatory mechanism breaks through the inhibitory phase causing the appearance of motor events (some are physiological, but others are clearly pathological) Movement disorder specialists deal with diurnal involuntary movements, whereas sleep specialists encounter abnormal motor activities during sleep that may disturb sleep and result in impaired daytime functioning. The question often arises as to whether these are diurnal movements persisting during sleep, or abnormal movements triggered by sleep or intruding into sleep. This dilemma is highlighted by the fact that there are considerable similarities and overlaps between nocturnal and diurnal movements, and sleep may be disturbed by both diurnal and nocturnal motor events. There is a growing realization that both diurnal and nocturnal motor events may result from a common neurobiological alteration in the molecular mechanisms of motor control and sleep wakefulness. In this chapter, we briefly outlined motor control of human voluntary movements in wakefulness and sleep as well as suggested some pathophysiological mechanisms for abnormal jerks and shakes at night. We also provided a brief description of these conditions based on a method of

classification for easy comprehension. Finally, we summarized principles of treatment of sleep dysfunction associated with these abnormal nocturnal motor events.

References

1. Kandel ER, Schwartz JH, Jessell TM, Siegelbaum SA, Hudspeth AJ (eds) (2013) Principles of neural science, 5th edn. McGraw-Hill, New York
2. Brookhart JM, Mountcastle VB, Brooks VB et al (1981) Handbook of physiology section 1. The nervous system, volume 2. Motor control, part 2. American Physiological Society, Bethesda, MD
3. Desmedt JE (ed) (1983) Motor control mechanisms in health and disease. Raven Press, New York
4. American Academy of Sleep Medicine (2014) International classification of sleep disorders, 3rd edn. American Academy of Sleep Medicine, Darien, IL
5. Brooks R, Gamaldo CE, Harding SM, Lloyd RM, Marcus CL, Vaughn BV (2015) For the American academy of sleep medicine. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications, version 2.2. American Academy of Sleep Medicine, Darien, Illinois
6. Fahn S, Jankovic J, Hallet M (eds) (2011) Principles and practice of movement disorders, 2nd edn. Elsevier Saunders, Philadelphia
7. Donaldson I, Marsden CD, Schenider S, Bhatia KP (eds) (2012) Marsden's book of movement disorders. Oxford University Press, New York
8. Kandel ER et al (eds) (2005) Principles of neural science, ed. 4. McGraw Hill, New York
9. Aserinsky E, Kleitman N (1953) regularly occurring periods of eye motility and concomitant phenomenon during sleep. Science 118:273
10. Jouvet M, Michel F (1959) [Electromyographic correlations of sleep in the chronic decorticate & mesencephalic cat]. [Article in French]. C R Seances Soc Biol Fil 153(3):422–425
11. Berger RJ (1961) Tonus of extrinsic laryngeal muscles during sleep and dreaming. Science 134:840
12. Pompiano O (1979) Mechanisms of sensorimotor integrations during sleep. In: Stellar E, Sprague JM (eds) Progress in psychobiology and physiological psychology, Vol 8. Academic Press, New York, pp 3–179
13. Chase MH, Morales FR, Boxer Boxer PA et al (1986) Effect of stimulation of the nucleus retigularis gigantocellularis on the membrane potentials of cat lumbar motoneurons during sleep and wakefulness. Brain Res 386:237–244
14. Morrison AR (1979) Brainstem regulation of behavior in sleep and wakefulness. In: Sprague JM, Epstein AW (eds) Progress in psychobiology and physiological psychology, vol 8. Academic Press, New York, pp 91–131
15. Seigel JM (2004) Hypocretin (orexin): role in normal behavior and neuropathology. Ann Rev Psychol 55:125–148
16. Chase MH, Fung SJ, Yamuny J, Xi M (2013) The control of motoneurons during sleep. In: Chokroverty S, Allen RP, Walters AS, Montagna P (eds) Sleep and movement disorders, 2nd edn. Oxford, New York
17. McGinty D, Szymusiak R (2011) Neural control of sleep in mammals. In: Kryger MH, Roth T, Dement D (eds) Principles and practices of sleep medicine, 5th edn. Elsevier-Saunders, St. Louis, MO
18. Evarts EV (1964) Temporal patterns of discharge of pyramidal tract neurons during sleep and waking in the monkey. J Neurophysiol 27:152–171
19. Steriade M, Hobson JA (1976) Neuronal activity during the sleep-waking cycle. Progr Neurobiol 6:155–376
20. Harris CD (2005) Neurophysiology of sleep and wakefulness. Respir Care Clin N Am 11:567–586
21. McCarley RW (2004) Mechanisms and models of REM sleep control. Arch Ital Biol 142:429–467
22. Rye DB (1997) Contributions of the pedunculopontine region to normal and altered REM sleep. Sleep 20:757–788
23. Thakkar MM, Strecker RE, McCarley RW (1998) Behavioral state control through differential serotonergic inhibition in the mesopontine cholinergic nuclei: a simultaneous unit recording and microdialysis study. J Neurosci 18:5490–5497
24. Imon H, Ito K, Dauphin L, McCarley RW (1996) Electrical stimulation of the cholinergic laterodorsal tegmental nucleus elicits scopolamine-sensitive excitatory postsynaptic potentials in medial pontine reticular formation neurons. Neuroscience 74:393–401
25. Kodama T, Lai YY, Siegel JM (1998) Enhanced glutamate release during REM sleep in the rostromedial medulla as measured by in vivo microdialysis. Brain Res 780:178–181
26. Hagan JJ, Leslie RA, Patel S et al (1999) Orexin A activates locus coeruleus cell firing and increases arousal in the rat. Proc Natl Acad Sci U S A 96:10911–10916
27. Hodes R, Dement WC (1964) Depression of electrically induced reflexes ("H-Reflexes") in man during low voltage EEG "sleep". Electroencephalogr Clin Neurophysiol 117:617–629
28. Pompeiano O (1967) The neurophysiological mechanisms of the postural and motor events during desynchronized sleep. In: Kety SS, Evarts EV, Williams HL (eds) Sleep and altered states of consciousness. Williams and Wilkins, Baltimore, pp 351–423
29. Horner RL, Innes JA, Morrell MJ, Shea SA, Guz A (1994) The effect of sleep on reflex genioglossus muscle activation by stimuli of negative airway pressure in humans. J Physiol (London) 476:141–151
30. Shea SA, Edwards JK, White DP (1999) Effect of wake-sleep transitions and rapid eye movement sleep on pharyngeal muscle response to negative pressure in humans. J Physiol (London) 520 (3):897–908.113
31. Eckert DJ, McEvoy RD, George KE, Thomson KJ, Catcheside PG (2007) Genioglossus reflex inhibition to upper-airway negative-pressure stimuli during wakefulness and sleep in healthy males. J Physiol 581:1193–1205
32. Kimura J, Harada O (1972) Excitability of the orbicularis oculi reflex in all night sleep: its suppression in non-rapid eye movement and recovery in rapid eye movement sleep. Electroencephalogr Clin Neurophysiol 33:369–377
33. Reding GR, Fernandez C (1968) Effects of vestibular stimulation during sleep. Electroencephalogr Clin Neurophysiol 24:75–79
34. Hoshina Y, Sakuma Y (1991) Changes in photically evoked blink reflex during sleep and wakefulness. Jpn J Ophthalmol 35:182–187
35. Kasper J, Diefenhardt A, Mackert A, Thoden U (1992) The vestibulo-ocular response during transient arousal shifts in man. Acta Otolaryngol (Stockh) 112:1–6
36. Morrison AR, Sanford LD, Ball WA, Mann GL, Ross RJ (1995) Stimulus-elicited behavior in rapid eye movement sleep without atonia. Behav Neurosci 109:972–979
37. Lim AS, Lozano AM, Moro E et al (2007) Characterization of REM-sleep associated ponto-geniculo-occipital waves in the human pons. Sleep 30:823–827

38. Soja PJ, Oka JI, Fragoso M (1993) Synaptic transmission through cat lumbar ascending sensory pathways is suppressed during active sleep. J Neurophysiol 70:1708–1712
39. Cairns BE, Fragoso MC, Soja PJ (1996) Active-sleep-related suppression of feline trigeminal sensory neurons: evidence implicating presynaptic inhibition via a process of primary afferent depolarization. J Neurophysiol 75:1152–1162
40. Cirignotta F, Montagna P, Lugaresi E (1983) Reversal of motor excitation to motor inhibition induced by sleep in man. In: Chase M, Weitzman ED (eds) Sleep disorders: basic and clinical research. Spectrum Publications, New York, pp 129–135
41. Kohlmeier KA, Lopez-Rodriguez F, Morales FR, Chase MH (1998) Effects of excitation of sensory pathways on the membrane potential of cat masseter motoneurons before and during cholinergically induced motor atonia. Neuroscience 86:557–569
42. Kleitman N (1971) Sleep and wakefulness, 2nd ed. University of Chicago Press, Chicago, 1963
43. Fujiki A, Shimizu A, Yamada Y, Yamamoto J, Kaneko Z (1971) The Babinski reflex during sleep and wakefulness. Electroencephalogr Clin Neurophysiol 31:610–613
44. Chase MH, Chandler SH, Nakamura Y (1980) Intracellular determination of membrane potential of trigeminal motoneurons during sleep and wakefulness. J Neurophysiol 44(2):349–358
45. Montagna P, Liguori R, Zucconi M et al (1988) Physiological hypnic myoclonus. Electroencephalogr Clin Neurophysiol 70:172–176.58, 59
46. Dagnino N, Loeb C, Massazza G, Sacco G (1988) Hypnic physiological myoclonus in man: an EEG-EMG study in normals and neurological patients. Eur Neurol (1969) 2:47–58
47. Broughton R, Tolentino MA, Krelina M (1985) Excessive fragmentary myoclonus in NREM sleep: a report of 38 cases. Electroencephalogr Clin Neurophysiol 61:121–133
48. Gardner R Jr, Grossman WI (1975) Normal motor patterns in sleep in man. In: Weitzman E (ed) Advances in sleep research, vol 2. Spectrum, New York, pp 67–107
49. Wilde-Frenz J, Schulz H (1983) Rate and distribution of body movements during sleep in humans. Percept Mot Skills 56:275–283
50. Shimohira M, Shiiki T, Sugimoto J et al (1998) Video analysis of gross body movements during sleep. Psychiatr Clin Neurosci 52:176–177
51. Hakamada S, Watanabe K, Hara K, Miyazaki S (1981) Development of the motor behavior during sleep in newborn infants. Brain Dev 3:345–350
52. Jouvet M, Mounier D (1960) Effets des lésions de la formation reticulairepontiquesur le sommeil du chat. C R Soc Biol 154:2301–2305
53. Hendricks JC, Morrison AR, Mann GL (1982) Different behaviors during paradoxical sleep without atonia depend on pontine lesion site. Brain Res 239:81–105.66, 67
54. Iranzo A, Santamaria J, Rye DB et al (2005) Characteristics of idiopathic REM sleep behavior disorder and that associated with MSA and PD. Neurology 65:247–252
55. McCarley RW (1989) The biology of dreaming sleep. In: Kryger MH, Roth T, Dement WC (eds) Principles and practice of sleep medicine. W. B. Saunders, Philadelphia, pp 173–183
56. Yamuy J, Mancillas JR, Morales FR, Chase MH (1993) C-fos expression in the pons and medulla of the cat during carbachol-induced active sleep. J Neurosci 13:2703–2718
57. Yamuy J, Fung SJ, Xi M, Morales FR, Chase MH (1999) Hypoglossal motoneurons are postsynaptically inhibited during carbachol-induced rapid eye movement sleep. Neuroscience 94:11–15
58. Chase MH, Morales FR (1990) The atonia and myoclonia of active (REM) sleep. Annu Rev Psychol 41:557–584
59. Chase MH (1980) lhe motor functions of the reticular formation are multifaceted and state.determined. In: Hobson JM, Brazier MAB (eds) Reticular formation revisited. Raven Press, New York, p 449
60. Minors DS, Waterhouse JM (1986) Circadian rhythms and their mechanisms. Experientia 42:1–13
61. Honma S, Honma K (1999) Light-induced uncoupling of multioscillatory circadian system in a diurnal rodent, Asian chipmunk. Am J Physiol 276:R1390–R1396
62. Ikeda M, Sagara M, Inoue S (2000) Continuous exposure to dim illumination uncouples temporal patterns of sleep, body temperature, locomotion and drinking behavior in the rat. Neurosci Lett 279:185–189
63. Nakahata Y, Grimaldi B, Sahar S, Hirayama J, Sassone-Corsi P (2007) Signaling to the circadian clock: plasticity by chromatin remodeling. Curr Opin Cell Biol 19:230–237
64. Partch CL, Shields KF, Thompson CL, Selby CP, Sancar A (2006) Posttranslational regulation of the mammalian circadian clock by cryptochrome and protein phosphatase 5. Proc Natl Acad Sci U S A 103:10467–10472
65. Kohsaka A, Bass J (2007) A sense of time: how molecular clocks organize metabolism. Trends Endocrinol Metab 18:4–11
66. Ko CH, Takahashi JS (2006) Molecular components of the mammalian circadian clock. Hum Mol Genet 15 Spec no 2:R271–277
67. Sakamoto K, Nagase T, Fukui H et al (1998) Multitissue circadian expression of rat period homolog (rPer2) mRNA is governed by the mammalian circadian clock, the suprachiasmatic nucleus in the brain. J Biol Chem 273:27039–27042
68. Saper CB, Lu J, Chou TC, Gooley J (2005) The hypothalamic integrator for circadian rhythms. Trends Neurosci 28:152–157
69. Zeitzer JM, Buckmaster CL, Lyons DM, Mignot E (2004) Locomotor-dependent and -independent components to hypocretin-1 (orexin A) regulation in sleep-wake consolidating monkeys. J Physiol 557:1045–1053
70. Selbach O, Haas HL (2006) Hypocretins: the timing of sleep and waking. ChronobiolInt 23:63–70
71. Blagrove M, Owens DS, MacDonald I, Sytnik N, Tucker P, Folkard S (1998) Time of day effects in, and the relationship between, sleep quality and movement. J Sleep Res 7:233–239
72. Curzi-Dascalova L, Kauffmann F, Gaultier C, Caldas de Amorim RH (1999) Heart rate modifications related to spontaneous body movements in sleeping premature and full-term newborns. Pediatr Res 45:515–518
73. Gardner R Jr, Grossman WI (1975) Normal motor patterns in sleep in man. In: Weitzman E (ed) Advances in sleep research, vol 2. Spectrum, New York, pp 67–107
74. Vecchierini-Blineau MF, Nogues B, Louvet S (1989) [Evolution of gross body movements during sleep in healthy infants aged from 1 to 4 months]. Neurophysiol Clin 19:231–239
75. Kohyama J (1996) A quantitative assessment of the maturation of phasic motor inhibition during REM sleep. J Neurol Sci 143:150–155
76. Laberge L, Tremblay RE, Vitaro F, Montplaisir J (2000) Development of parasomnias from childhood to early adolescence. Pediatrics 106:67–74
77. Remulla A, Guilleminault C (2004) Somnambulism (sleepwalking). Expert Opin Pharmacother 5:2069–2074
78. Manni R, Terzaghi M (2005) Rhythmic movements during sleep: a physiological and pathological profile. Neurol Sci 26(3):s181–s185
79. DeKoninck J, Lorrain D, Gagnon P (1992) Sleep positions and position shifts in five age groups: an ontogenetic picture. Sleep 15:143–149

80. Ohnaka T, Tochihara Y, Kanda K (1995) Body movements of the elderly during sleep and thermal conditions in bedrooms in summer. Appl Human Sci 14:89–93
81. Parrino L, Boselli M, Spaggiari MC, Smerieri A, Terzano MG (1998) Cyclic alternating pattern (CAP) in normal sleep: polysomnographic parameters in different age groups. Electroencephalogr Clin Neurophysiol 107:439–450
82. Critchley M (1955) The pre-dormitum. Rev Neurol (Paris) 93:101–106
83. Santamaria J, Chiappa KH (1987) The EEG of drowsiness in normal adults. J Clin Neurophysiol 4:327–382
84. Montagna P, Provini F, Plazzi G, Liguori R, Lugaresi E (1997) Propriospinal myoclonus upon relaxation and drowsiness: a cause of severe insomnia. Mov Disord 12:66–72
85. Fish DR, Sawyers D, Allen PJ et al (1991) The effect of sleep on the dyskinetic movements of Parkinson's disease, Gilles de la Tourette syndrome, Huntington's disease, and torsion dystonia. Arch Neurol 48:210–214
86. Llinas RR, Steriade M (2006) Bursting of thalamic neurons and states of vigilance. J Neurophysiol 3297–3308
87. Horner RL, Sanford LD, Pack AI, Morrison AR (1997) Activation of a distinct arousal state immediately after spontaneous arousal from sleep. Brain Res 778:127–134
88. Schacter DL (1976) The hypnagogic state: a clinical review of the literature. Psychol Bull 83:452–481
89. Braun AR, Balkin TJ, Wesenten NJ, Carson RE, Varga N, Baldwin P et al (1997) Regional cerebral blood flow throughout the sleep-wake cycle. An H2(15)O PET study. Brain 120:1173–1197
90. Vetrugno R, Montagna P (2011) Sleep-to-wake transition movement disorders. Sleep Med 12:S11–S16
91. Chokroverty S (1980) Phasic tongue movements in human rapid eye-movement sleep. Neurology 30(6):665–668
92. Mahowald MW, Schenck CH (1991) Status dissociatus-a perspective on states of being. Sleep 14:69–79
93. Pollmacher T, Schulz H (1993) Periodic leg movements (PLM): their relationship to sleep stages. Sleep 16:572–577
94. Lugaresi E, Cirignotta F, Coccagna G, Montagna P (1986) Nocturnal myoclonus and restless legs syndrome. In: Fahn S, Marsden CD, Van Woert M (eds) Myoclonus (Adv Neurology 43). Raven Press, New York, pp 295–307
95. Lapierre O, Montplaisir J (1992) Polysomnographic features of REM sleep behavior disorder: development of a scoring method. Neurology 42:1371–1374
96. Dauvilliers Y, Rompre S, Gagnon JF, Vendette M, Petit D, Montplaisir J (2007) REM sleep characteristics in narcolepsy and REM sleep behavior disorder. Sleep 30:844–849.41, 42
97. Schenck CH, Milner DM, Hurwitz TD, Bundlie SR, Mahowald MW (1989) A polysomnographic and clinical report on sleep-related injury in 100 adult patients. Am J Psychiatr 146:1166–1173
98. Bhat S, Patel D, Rosen D, Chokroverty S (2012) A case of a confusional arousal arising from REM sleep. Sleep Med 13 (3):317–318
99. Bhat S, Chokroverty S, Kabak B, Yang QR, Rosen D (2012) Dream-enacting behavior in non-rapid eye movement sleep. Sleep Med 13(4):445–446
100. Parrino L, Boselli M, Spaggiari MC, Smerieri A, Terzano MG (1998) Cyclic alternating pattern (CAP) in normal sleep: polysomnographic parameters in different age groups. Electroencephalogr Clin Neurophysiol 107:439–450
101. Terzano MG, Mancia D, Salati MR, Costani G, Decembrino A, Parrino L (1985) The cyclic alternating pattern as a physiological component of normal NREM sleep. Sleep 8:137–145
102. Terzano MG, Parrino L, Sherieri A et al (2001) Atlas, rules, and recording techniques for the scoring of cyclic alternating pattern (CAP) in human sleep. Sleep Med 2:537–555
103. De Carli F, Nobili L, Beelke M et al (2004) Quantitative analysis of sleep EEG microstructure in the time-frequency domain. Brain Res Bull 63:399–405
104. Parrino L, Boselli M, Buccino GP, Spaggiari MC, Di Giovanni G, Terzano MG (1996) The cyclic alternating pattern plays a gate-control on periodic limb movements during non-rapid eye movement sleep. J Clin Neurophysiol 13:314–323
105. Macaluso GM, Guerra P, Di Giovanni G, Boselli M, Parrino L, Terzano MG (1998) Sleep bruxism is a disorder related to periodic arousals during sleep. J Dent Res 77:565–573
106. Guilleminault C, Lee JH, Chan A, Lopes MC, Huang YS, da Rosa A (2005) Non-REM-sleep instability in recurrent sleep-walking in pre-pubertal children. Sleep Med 6:515–521
107. Guilleminault C, Kirisoglu C, da Rosa AC, Lopes C, Chan A (2006) Sleepwalking, a disorder of NREM sleep instability. Sleep Med 7:163–170
108. Cosentino FI, Iero I, Lanuzza B, Tripodi M, Ferri R (2006) The neurophysiology of the alternating leg muscle activation (ALMA) during sleep: study of one patient before and after treatment with pramipexole. Sleep Med 7:63–71
109. Terzano MG, Monge-Strauss MF, Mikol F, Spaggiari MC, Parrino L (1997) Cyclic alternating pattern as a provocative factor in nocturnal paroxysmal dystonia. Epilepsia 38:1015–1025
110. Bruni O, Ferri R, Miano S et al (2005) Sleep cyclic alternating pattern in normal preschool-aged children. Sleep 28:220–230
111. Bruni O, Ferri R, Miano S et al (2002) Sleep cyclic alternating pattern in normal school-age children. Clin Neurophysiol 113:1806–1814
112. Lopes MC, Rosa A, Roizenblatt S et al (2005) Cyclic alternating pattern in peripubertal children. Sleep 28:215–219
113. Parrino L, Ferri R, Bruni O, Terzano MG (2013) Cyclic alternating pattern in sleep: measurement and clinical significance. In: Chokroverty S, Allen RP, Walters AS, Montagna P (eds) Sleep and movement disorders, 2nd edn. Oxford, New York
114. Chokoverty S, Thomas R (eds) (2012) Atlas of sleep medicine, 2nd edn. Elsevier/Saunders, Philadelphia
115. Silvestri RC (2013) Persistence of daytime movement disorders during sleep. In: Chokroverty S Allen RP, Walters AS, Motagna P (eds) Sleep and movements disorders, 2nd edn. Oxford, New York, pp 535–545
116. Hening WA, Walters AS, Chokroverty S (1990) Movement disorders and sleep. In: Chokroverty S (ed) Movement disorders: PMA Publishing, USA, pp 127–157
117. Poppi M, Pazzaglia P (1967) Abnormal movements persisting during sleep (fasciculations, facial spasm, spinal automatic movements). Electroencephalogr Clin Neurophysiol 23:189
118. Chokroverty S, Barron KD (1969) Palatal myoclonus and rhythmic ocular movements; a polygraphic study. Neurology 19:975–982
119. Hoehn MM, Cherington M (1977) Spinal myoclonus. Neurology 27:942–946
120. Montagna P, Imbriaco A, Zucconi M, Liguori R, Cirignotta F, Lugaresi E (1986) Hemifacial spasm in sleep. Neurology 36:270–273
121. Tan NC, Chan LL, Tan EK (2002) Hemifacial spasm and involuntary facial movements. QJM 95:493–500
122. Montagna P, Liguori R, Zucconi M, Lugaresi A, Cirignotta F, Lugaresi E (1987) Fasciculations during wakefulness and sleep. Acta Neurol Scand 76:152–154
123. Parkinson J (1817) An essay on the shaking palsy. Whittingham and Rowland, London

124. Karlsen KH, Larsen JP, Tandberg E, Maeland JG (1999) Influence of clinical and demographic variables on quality of life in patients with Parkinson's disease [see comments]. J Neurol Neurosurg Psychiatr 66:431–435
125. Kumar S, Bhatia M, Behari M (2002) Sleep disorders in Parkinson's disease. Mov Disord 17:775–781
126. Pushpanathan ME1, Loftus AM2, Thomas MG3, Gasson N2, Bucks RS4 (2015) The relationship between sleep and cognition in Parkinson's disease: a meta-analysis. Sleep Med Rev 26:21–32
127. Yong MH1, Fook-Chong S, Pavanni R, Lim LL, Tan EK (2011) Case control polysomnographic studies of sleep disorders in Parkinson's disease. PLoS ONE 6(7):e22511
128. Martinez-Ramirez D1, De Jesus S1, Walz R2, Cervantes-Arriaga A3, Peng-Chen Z1, Okun MS4, Alatriste-Booth V5, Rodríguez--Violante M3 (2015) A polysomnographic study of Parkinson's disease sleep architecture. Parkinsons Dis 2015:570375
129. Ferreira T, Prabhakar S, Kharbanda PS (2014) Sleep disturbances in drug naïve Parkinson's disease (PD) patients and effect of levodopa on sleep. Ann Indian Acad Neurol 17(4):416–419
130. Nishida N1, Murakami T, Kadoh K, Tohge R, Yamanegi M, Saiki H, Ueda K, Matsumoto S, Ishikawa M, Takahashi JA, Toda H (2011) Subthalamic nucleus deep brain stimulation restores normal rapid eye movement sleep in Parkinson's disease. Mov Disord 26(13):2418–2422
131. Breen DP, Vuono R, Nawarathna U, Fisher K, Shneerson JM, Reddy AB, Barker RA (2014) Sleep and circadian rhythm regulation in early Parkinson disease. JAMA Neurol 71(5):589–595
132. Bolitho SJ, Naismith SL, Rajaratnam SM, Grunstein RR, Hodges JR, Terpening Z, Rogers N, Lewis SJ (2014) Disturbances in melatonin secretion and circadian sleep-wake regulation in Parkinson disease. Sleep Med 15(3):342–347
133. Chaudhuri KR, Pal S, DiMarco A et al (2002) The Parkinson's disease sleep scale: a new instrument for assessing sleep and nocturnal disability in Parkinson's disease. J Neurol Neurosurg Psychiatr 73:629–635
134. Marinus J, Visser M, van Hilten JJ, Lammers GJ, Stiggelbout AM (2003) Assessment of sleep and sleepiness in Parkinson disease. Sleep 26:1049–1054
135. Scaravilli T, Gasparoli E, Rinaldi F, Polesello G, Bracco F (2003) Health-related quality of life and sleep disorders in Parkinson's disease. Neurol Sci 24:209–210
136. Pacchetti C, Manni R, Zangaglia R et al (2004) A questionnaire on sleep and mental disorders in Parkinson's disease (QSMDPD): development and application of a new screening tool. Funct Neurol 19:83–99
137. Tse W, Liu Y, Barthlen GM et al (2005) Clinical usefulness of the Parkinson's disease sleep scale. Parkinsonism Relat Disord 11:317–321
138. Askenasy JJ, Yahr MD (1990) Parkinsonian tremor loses its alternating aspects during Non-REM sleep and is inhibited by REM sleep. J Neurol Neursurg Psychiatr 53:749–753
139. Currie LJ, Bennett JP Jr, Harrison MB, Trugman JM, Wooten GF (1997) Clinical correlates of sleep benefit in Parkinson's disease. Neurology 48:1115–1117
140. Merello M, Hughes A, Colosimo C, Hoffman M, Starkstein S, Leiguarda R (1997) Sleep benefit in Parkinson's disease [see comments]. Mov Disord 12:506–508
141. Hogl BE, Gomez-Arevalo G, Garcia S et al (1998) A clinical, pharmacologic, and polysomnographic study of sleep benefit in Parkinson's disease. Neurology 50:1332–1339
142. Poceta JS, Parsons L, Engelland S, Kripke DF (2009) Circadian rhythm of CSF monoamines and hypocretin-1 in restless legs syndrome and Parkinson's disease. Sleep Med 10(1):129–133
143. Yamamura Y, Hattori N, Matsumine H, Kuzuhara S, Mizuno Y (2000) Autosomal recessive early-onset parkinsonism with diurnal fluctuation: clinicopathologic characteristics and molecular genetic identification. Brain Dev 22(Suppl 1):S87–S91
144. Valente EM, Brancati F, Ferraris A et al (2002) PARK6-linked parkinsonism occurs in several European families. Ann Neurol 51:14–18
145. Rye DB (2004) The two faces of Eve: dopamine's modulation of wakefulness and sleep. Neurology 63:S2–S7
146. Braak H, Del Tredici K, Bratzke H, Hamm-Clement J, Sandmann-Keil D, Rub U (2002) Staging of the intracerebral inclusion body pathology associated with idiopathic Parkinson's disease (preclinical and clinical stages). J Neurol 249(Suppl 3): III/1–5
147. Braak H, Ghebremedhin E, Rub U, Bratzke H, Del Tredici K (2004) Stages in the development of Parkinson's disease-related pathology. Cell Tissue Res 318:121–134
148. Boeve BF, Silber MH, Saper CB et al (2007) Pathophysiology of REM sleep behaviour disorder and relevance to neurodegenerative disease. Brain 130(11):2770–2788
149. Stiasny-Kolster K, Doerr Y, Moller JC et al (2005) Combination of 'idiopathic' REM sleep behaviour disorder and olfactory dysfunction as possible indicator for alpha-synucleinopathy demonstrated by dopamine transporter FP-CIT-SPECT. Brain 128:126–137
150. Gagnon JF, Postuma RB, Mazza S, Doyon J, Montplaisir J (2006) Rapid-eye-movement sleep behaviour disorder and neurodegenerative diseases. Lancet Neurol 5:424–432
151. Postuma RB, Lang AE, Massicotte-Marquez J, Montplaisir J (2006) Potential early markers of Parkinson disease in idiopathic REM sleep behavior disorder. Neurology 66:845–851
152. Mazza S, Soucy JP, Gravel P et al (2006) Assessing whole brain perfusion changes in patients with REM sleep behavior disorder. Neurology 67:1618–1622
153. Miyamoto T, Miyamoto M, Inoue Y, Usui Y, Suzuki K, Hirata K (2006) Reduced cardiac 123I-MIBG scintigraphy in idiopathic REM sleep behavior disorder. Neurology 67:2236–2238
154. Kumru H, Santamaria J, Tolosa E, Iranzo A (2007) Relation between subtype of Parkinson's disease and REM sleep behavior disorder. Sleep Med 8:779–783
155. Tuin I, Voss U, Kessler K et al (2008) Sleep quality in a family with hereditary parkinsonism (PARK6). Sleep Med 9(6):684–688
156. Benbir G, Ozekmekci S, Cinar M, Beskardes F, Apaydin H, Erginoz E (2006) Features associated with the development of hallucinations in Parkinson's disease. Acta Neurol Scand 114:239–243
157. Onofrj M, Bonanni L, Albani G, Mauro A, Bulla D, Thomas A (2006) Visual hallucinations in Parkinson's disease: clues to separate origins. J Neurol Sci 248:143–150
158. Vendette M, Gagnon JF, Decary A et al (2007) REM sleep behavior disorder predicts cognitive impairment in Parkinson disease without dementia. Neurology 69:1843–1849
159. Frauscher B, Gschliesser V, Brandauer E et al (2007) Video analysis of motor events in REM sleep behavior disorder. Mov Disord 22:1464–1470
160. De Cock VC, Vidailhet M, Leu S et al (2007) Restoration of normal motor control in Parkinson's disease during REM sleep. Brain 130:450–456
161. Ondo WG, Vuong KD, Jankovic J (2002) Exploring the relationship between Parkinson disease and restless legs syndrome. Arch Neurol 59:421–424
162. Garcia-Borreguero D, Odin P, Serrano C (2003) Restless legs syndrome and PD: a review of the evidence for a possible association. Neurology 61(S49–55):275

163. Krishnan PR, Bhatia M, Behari M (2003) Restless legs syndrome in Parkinson's disease: a case-controlled study. Mov Disord 18:181–185
164. Adel S, Djarmati A, Kabakci K et al (2006) Co-occurrence of restless legs syndrome and Parkin mutations in two, families. Move Disord 21(2):258–263
165. Poewe W, Hogl B (2004) Akathisia, restless legs and periodic limb movements in sleep in Parkinson's disease. Neurology 63: S12–S16
166. Rye DB (2004) Parkinson's disease and RLS: the dopaminergic bridge. Sleep Med 5:317–328
167. Walters AS, LeBrocq C, Passi V et al (2003) A preliminary look at the percentage of patients with restless legs syndrome who also have parkinson disease, essential tremor or tourette syndrome in a single practice. J Sleep Res 12:343–345
168. Allen RP, Earley CJ (1996) Augmentation of the restless legs syndrome with carbidopa/levodopa. Sleep 19:205–213
169. Kedia S, Moro E, Tagliati M, Lang AE, Kumar R (2004) Emergence of restless legs syndrome during subthalamic stimulation for Parkinson disease. Neurology 63:2410–2412
170. Wetter TC, Collado-Seidel V, Pollmacher T, Yassouridis A, Trenkwalder C (2000) Sleep and periodic leg movement patterns in drug-free patients with Parkinson's disease and multiple system atrophy. Sleep 23:361–367
171. Happe S, Pirker W, Klosch G, Sauter C, Zeitlhofer J (2003) Periodic leg movements in patients with Parkinson's disease are associated with reduced striatal dopamine transporter binding. J Neurol 250:83–86
172. Wetter TC, Brunner H, Hogl B, Yassouridis A, Trenkwalder C, Friess E (2001) Increased alpha activity in REM sleep in de novo patients with Parkinson's disease. Mov Disord 16:928–933
173. Tandberg E, Larsen JP, Karlsen K (1999) Excessive daytime sleepiness and sleep benefit in Parkinson's disease: a community-based study. Mov Disord 14:922–927
174. Verbaan D, van Rooden SM, Visser M, Marinus J, van Hilten JJ (2008) Nighttime sleep problems and daytime sleepiness in Parkinson's disease. Mov Disord 23(1):35–41
175. Tan EK, Lum SY, Fook-Chong SM et al (2002) Evaluation of somnolence in Parkinson's disease: comparison with age- and sex-matched controls. Neurology 58:465–468
176. Brodsky MA, Godbold J, Roth T, Olanow CW (2003) Sleepiness in Parkinson's disease: a controlled study. Mov Disord 18:668–672
177. Frucht S, Rogers JD, Greene PE, Gordon MF, Fahn S (1999) Falling asleep at the wheel: motor vehicle mishaps in persons taking pramipexole and ropinirole [see comments]. Neurology 52:1908–1910
178. Manni R, Pacchetti C, Terzaghi M, Sartori I, Mancini F, Nappi G (2002) Hallucinations and sleep-wake cycle in PD: a 24-hour continuous polysomnographic study. Neurology 59:1979–1981
179. Meindorfner C, Korner Y, Moller JC, Stiasny-Kolster K, Oertel WH, Kruger HP (2005) Driving in Parkinson's disease: mobility, accidents, and sudden onset of sleep at the wheel. Mov Disord 20:832–842
180. Rissling I, Korner Y, Geller F, Stiasny-Kolster K, Oertel WH, Moller JC (2005) Preprohypocretin polymorphisms in Parkinson disease patients reporting "sleep attacks". Sleep 28:871–875
181. Rissling I, Geller F, Bandmann O et al (2004) Dopamine receptor gene polymorphisms in Parkinson's disease patients reporting "sleep attacks". Mov Disord 19:1279–1284
182. Rye DB, Johnston LH, Watts RL, Bliwise DL (1999) Juvenile Parkinson's disease with REM sleep behavior disorder, sleepiness, and daytime REM onset. Neurology 53:1868–1870
183. Rye DB, Bliwise DL, Dihenia B, Gurecki P (2000) FAST TRACK: daytime sleepiness in Parkinson's disease. J Sleep Res 9:63–69
184. Thannickal TC, Lai YY, Siegel JM (2007) Hypocretin (orexin) cell loss in Parkinson's disease. Brain 130:1586–1595
185. Baumann C, Ferini-Strambi L, Waldvogel D, Werth E, Bassetti CL (2005) Parkinsonism with excessive daytime sleepiness a narcolepsy-like disorder? J Neurol 252:139–145
186. Happe S, Pirker W, Sauter C, Klosch G, Zeitlhofer J (2001) Successful treatment of excessive daytime sleepiness in Parkinson's disease with modafinil. J Neurol 248:632–634
187. Hogl B, Saletu M, Brandauer E et al (2002) Modafinil for the treatment of daytime sleepiness in Parkinson's disease: a double-blind, randomized, crossover, placebo-controlled polygraphic trial. Sleep 25:905–909
188. Rye DB (2006) Excessive daytime sleepiness and unintended sleep in Parkinson's disease. Curr Neurol Neurosci Rep 6:169–176
189. Ondo WG, Fayle R, Atassi F, Jankovic J (2005) Modafinil for daytime somnolence in Parkinson's disease: double blind, placebo controlled parallel trial. J Neurol Neurosurg Psychiatr 76:1636–1639
190. Béland SG, Postuma R, Latreille V, Bertrand JA, Panisset M, Chouinard S, Wolfson C, Gagnon JF (2015) Observational study of the relation between Parkinson's disease and sleep apnea. J Parkinsons Dis 5(4):805–811
191. Corbin DO, Williams AC (1987) Stridor during dystonic phases of Parkinson's disease [letter]. J Neurol Neurosurg Psychiatr 50:821–822
192. Vincken WG, Gauthier SG, Dollfuss RE, Hanson RE et al (1984) Involvement of upper airway muscles in extrapyramidal disorders. New Eng J Med 311:438–442
193. Efthimiou J, Ellis SJ, Hardie RJ, Stern GM (1986) Sleep apnea in idiopathic and postencephalitic Parkinsonism. In: Yahr MD, Bergmann KJ (eds) Parkinson's disease (Advances in neurology 45). Raven Press, New York, pp 275–276
194. Braga-Neto P, da Silva FP, Jr., Sueli Monte F, de Bruin PF, de Bruin VM (2004) Snoring and excessive daytime sleepiness in Parkinson's disease. J Neurol Sci 217:41–45
195. Apps MCP, Sheaff PC, Ingram DA, Kennard C, Empey DW (1985) Respiration and sleep in Parkinson's disease. J Neurol Neurosurg Psychiatr 48:1240–1245
196. Ferini-Strambi L, Franceschi M, Pinto P, Zucconi M, Smirne S (1992) Respiration and heart rate variability during sleep in untreated Parkinson patients. Gerontology 38:92–98
197. Maria B, Sophia S, Michalis M et al (2003) Sleep breathing disorders in patients with idiopathic Parkinson's disease. Respir Med 97:1151–1157
198. Cochen De Cock V, Benard-Serre N2 Driss V, Granier M, Charif M, Carlander B, Desplan M, Croisier Langenier M, Cugy D, Bayard S (2015) Supine sleep and obstructive sleep apnea syndrome in Parkinson's disease. Sleep Med 16(12):1497–1501
199. Valko PO, Hauser S, Sommerauer M, Werth E, Baumann CR (2014) Observations on sleep-disordered breathing in idiopathic Parkinson's disease. PLoS ONE 9(6):e100828
200. Gjerstad MD, Wentzel-Larsen T, Aarsland D, Larsen JP (2007) Insomnia in Parkinson's disease: frequency and progression over time. J Neurol Neurosurg Psychiatr 78:476–479
201. Karlsen KH, Larsen JP, Tandberg E, Maeland JG (1999) Influence of clinical and demographic variables on quality of life in patients with Parkinson's disease [see comments]. J Neurol Neurosurg Psychiatr 66:431–435

202. Van den Kerchove M, Jacquy J, Gonce M, De Deyn PP (1993) Sustained-release levodopa in parkinsonian patients with nocturnal disabilities. Acta Neurol Belg 93:32–39
203. Priano L, Albani G, Brioschi A et al (2003) Nocturnal anomalous movement reduction and sleep microstructure analysis in parkinsonian patients during 1-night transdermal apomorphine treatment. Neurol Sci 24:207–208
204. Iranzo A, Valldeoriola F, Santamaria J, Tolosa E, Rumia J (2002) Sleep symptoms and polysomnographic architecture in advanced Parkinson's disease after chronic bilateral subthalamic stimulation. J Neurol Neurosurg Psychiatr 72:661–664
205. Antonini A, Landi A, Mariani C, DeNotaris R, Pezzoli G (2004) Deep brain stimulation and its effect on sleep in Parkinson's disease. Sleep Med 5:211–214
206. Gross RA, Spehlmann R, Daniels JC (1978) Sleep disturbances in progressive supranuclear palsy. Electroencephalogr Clin Neurophysiol 45:16–25
207. Laffont F, Autret A, Minz M et al (1979) Étude polygraphique du sommeil dans 9 cas de maladie de Steele-Richardson. Rev Neurol 135:127–142
208. Massetani R, Arena R, Bonuccelli U, Salerno P, Muratorio A (1982) Sleep in progressive supranuclear palsy. Riv Patol Nerv Ment 103:215–224
209. Laffont F, Leger JM, Penicaud A (1988) Sleep abnormalities and evoked potentials (VEP-BAER-SEP) in progressive supranuclear palsy. Neurophysiol Clin 18:255–269
210. Aldrich MS, Foster NL, White RF, Bluemlein L, Prokopowicz G (1989) Sleep abnormalities in progressive supranuclear palsy. Ann Neurol 25:577–581
211. De Bruin VS, Machado C, Howard RS, Hirsch NP, Lees AJ (1996) Nocturnal and respiratory disturbances in Steele-Richardson-Olszewski syndrome (progressive supranuclear palsy). Postgrad Med J 72:293–296
212. Montplaisir J, Petit D, Decary A et al (1997) Sleep and quantitative EEG in patients with progressive supranuclear palsy. Neurology 49:999–1003
213. Arnulf I, Merino-Andreu M, Bloch F et al (2005) REM sleep behavior disorder and REM sleep without atonia in patients with progressive supranuclear palsy. Sleep 28:349–354
214. Pareja JA, Caminero AB, Masa JF, Dobato JL (1996) A first case of progressive supranuclear palsy and pre-clinical REM sleep behavior disorder presenting as inhibition of speech during wakefulness and somniloquy with phasic muscle twitching during REM sleep. Neurologia 11:304–306
215. Nomura T, Inoue Y, Takigawa H, Nakashima K (2012) Comparison of REM sleep behaviour disorder variables between patients with progressive supranuclear palsy and those with Parkinson's disease. Parkinsonism Relat Disord 18(4):394–396
216. Yasui K, Inoue Y, Kanbayashi T, Nomura T, Kusumi M, Nakashima K (2006) CSF orexin levels of Parkinson's disease, dementia with Lewy bodies, progressive supranuclear palsy and corticobasal degeneration. J Neurol Sci 250:120–123
217. Wenning GK, Tison F, Ben Shlomo Y, Daniel SE, Quinn NP (1997) Multiple system atrophy: a review of 203 pathologically proven cases. Mov Disord 12:133–147
218. Boeve BF, Silber MH, Ferman TJ, Lucas JA, Parisi JE (2001) Association of REM sleep behavior disorder and neurodegenerative disease may reflect an underlying synucleinopathy. Mov Disord 16:622–630
219. Ghorayeb I, Yekhlef F, Chrysostome V, Balestre E, Bioulac B, Tison F (2002) Sleep disorders and their determinants in multiple system atrophy. J Neurol Neurosurg Psychiatr 72:798–800
220. Lauterbach EC (2004) The neuropsychiatry of Parkinson's disease and related disorders. Psychiatr Clin North Am 27:801–825
221. Vetrugno R, Provini F, Cortelli P et al (2004) Sleep disorders in multiple system atrophy: a correlative video-polysomnographic study. Sleep Med 5:21–30
222. Seppi K, Hogl B, Diem A, Peralta C, Wenning GK, Poewe W (2006) Levodopa-induced sleepiness in the Parkinson variant of multiple system atrophy. Mov Disord 21:1281–1283
223. Pierangeli G, Provini F, Maltoni P et al (2001) Nocturnal body core temperature falls in Parkinson's disease but not in multiple-system atrophy. Mov Disord 16:226–232
224. Plazzi G, Corsini R, Provini F et al (1997) REM sleep behavior disorders in multiple system atrophy. Neurology 48:1094–1097
225. Plazzi G1, Cortelli P, Montagna P, De Monte A, Corsini R, Contin M, Provini F, Pierangeli G, Lugaresi E (1998) REM sleep behaviour disorder differentiates pure autonomic failure from multiple system atrophy with autonomic failure. J Neurol Neurosurg Psychiatr 64(5):683–685
226. Bannister R, Gibson W, Michaels L, Oppenheimer DR (1981) Laryngeal abductor paralysis in multiple system atrophy. Brain 104:351–368
227. Vetrugno R, Liguori R, Cortelli P et al (2007) Sleep-related stridor due to dystonic vocal cord motion and neurogenic tachypnea/tachycardia in multiple system atrophy. Mov Disord 22:673–678
228. Kakitsuba N, Sadaoka T, Kanai R, Fujiwara Y, Takahashi H (1997) Peculiar snoring in patients with multiple system atrophy: its sound source, acoustic characteristics, and diagnostic significance. Ann Otol Rhinol Laryngol 106:380–384
229. Kurisaki H (1999) Prognosis of multiple system atrophy—survival time with or without tracheostomy. Rinsho Shinkeigaku 39:503–507
230. Sadaoka T, Kakitsuba N, Fujiwara Y, Kanai R, Takahashi H (1996) Sleep-related breathing disorders in patients with multiple system atrophy and vocal fold palsy. Sleep 19:479–484
231. Hughes RG, Gibbin KP, Lowe J (1998) Vocal fold abductor paralysis as a solitary and fatal manifestation of multiple system atrophy. J Laryngol Otol 112:177–178
232. Isozaki E, Naito A, Horiguchi S, Kawamura R, Hayashida T, Tanabe H (1996) Early diagnosis and stage classification of vocal cord abductor paralysis in patients with multiple system atrophy. J Neurol Neurosurg Psychiatr 60:399–402
233. Miyamoto M, Miyamoto T, Katayama S, Hirata K (1998) Effective nasal CPAP therapy for heavy snoring and paradoxical respiration during sleep in a case of multiple system atrophy. Rinsho Shinkeigaku 38:1059–1063
234. Garcia-Sanchez A, Fernandez-Navarro I, Garcia-Rio F (2016) Central apneas and REM sleep behavior disorder as an initial presentation of multiple system atrophy. J Clin Sleep Med 12 (2):267–270
235. Lazar AS, Panin F, Goodman AO, Lazic SE, Lazar ZI, Mason SL, Rogers L, Murgatroyd PR, Watson LP, Singh P, Borowsky B, Shneerson JM, Barker RA (2015) Sleep deficits but no metabolic deficits in premanifest Huntington's disease. Ann Neurol 78 (4):630–648
236. Neutel D, Tchikviladzé M2, Charles P3, Leu-Semenescu S4, Roze E5, Durr A6, Arnulf I7 (2015) Nocturnal agitation in Huntington disease is caused by arousal-related abnormal movements rather than by rapid eye movement sleep behavior disorder. Sleep Med 16(6):754–759
237. Wiegand M, Moller AA, Lauer CJ et al (1991) Nocturnal sleep in Huntington's disease. J Neurol 238:203
238. Morton AJ, Wood NI, Hastings MH et al (2005) Disintegrtion of the sleep-wake cycle and circadian timing in Huntington's disease. J Neurosci 25:157–163
239. Hansotia P, Wall R, Berendes J (1985) Sleep disturbances and severity of Huntington's disease. Neurology 35:1672

240. Emser W, Brenner M, Stober T, Schimrigk K (1988) Changes in nocturnal sleep in Huntington's and Parkinson's disease. J Neurol 235:177
241. Hansotia P, Wall R, Berendes J (1985) Sleep disturbances and severity of Huntington's disease. Neurology 35:1672
242. Wiegand M, Moller AA, Schreiber W et al (1991) Brain morphology and sleep EEG in patients with Huntington's disease. Eur Arch Psychiatry Clin Neurosci 240:148
243. Piano C, Losurdo A, Della Marca G, Solito M, Calandra-Buonaura G, Provini F, Bentivoglio AR, Cortelli P (2015) Polysomnographic findings and clinical correlates in huntington disease: a cross-sectional cohort study. Sleep 38 (9):1489–1495
244. Bollen EL, Den Heijer JC, Ponsioen C et al (1988) Respiration during sleep in Huntington's chorea. J Neurol Sci 84:63
245. Broughton R, Tassinari CA, Gastaut JR et al (1967) A polygraphic study of abnormal movements during different stages of sleep. Can Med Assoc J 97:24
246. Yamamoto T, Hirose G, Shimazaki K, Takado S, Kosoegana H, Saeki H (1982) Movement disorders of familial neuroacanthocytosis syndrome. Arch Neurol 39:298–301
247. Danek A, Jung HH, Metone MA et al (2005) Neuroacanthocytosis: new developments in a neglected group of dementing disorders. J Neurol Sci 2290–2230:171–186
248. Danek A, RubioJP Rampoldi L et al (2001) McLeod Neuroacankocytosis: genotype and phenotype. Ann Neurol 50:755–764
249. Silvestri R, De Domenico P, Di Rosa AE, Bramanti P, Serra S, Di Perri R (1990) The effect of nocturnal physiological sleep on various movement disorders. Mov Disord 5(8–14):421
250. Silvestri R, Raffaele M, De Domenico P et al (1995) Sleep features in Tourette's syndrome, neuroacanthocytosis and Huntington's chorea. Neurophysiol Clin 25:66–77
251. Hori A, Kazukawa S, Nakamura I, Endo M (1985) Electroencephalographic findings in neuroacanthocytosis. Electroencephalogr Clin Neurophysiol 61:342–348
252. Hernandez Vara J, Fernandez Cortijo J, Purroy Garcia F, Miquel Rodriguez F (2005) [Restless legs syndrome and neuroacanthocytosis]. Med Clin (Barc) 124:717–718
253. Fahn S (1990) Recent concepts in the diagnosis and treatment of dystonias. In: Chokroverty S (ed) Movement disorders. PMA, Costa Mesa, CA, p 237
254. Ozelius LJ, Hewett JW, Page CE et al (1997) The early-onset torsion dystonia gene (DYT1) encodes an ATP-binding protein. Nat Genet 17:40
255. Zhu L, Wrabl JO, Hayashi AP et al (2008) The torsin family AAA + protein OOC-5 contains a critical disulfide adjacent to Sensor-II that couples redox state to nucleotide binding. Mol Biol Cell 19:3599
256. Clarimon J, Asgeirsson H, Singleton A et al (2005) Torsin A haplotype predisposes to idiopathic dystonia. Ann Neurol 57:765–767
257. Rostasy K, Augood SJ, Hewett JW et al (2004) Torsin A protein and neuropathology in early onset generalized dystonia with GAG deletion. Neurobiol Dis 12:11–24
258. Breakfield XO, Kamm C, Hanson PI (2001) Torsin A: movement at many levels. Neuron 31:9–12
259. Bressman SB, de Leon D, Raymond D et al (1997) Secondary dystonia and the DYTI gene. Neurology 48:1571
260. Jankel WR, Allen RP, Niedermeyer E, Kalsher MJ (1983) Polysomnographic findings in dystonia musculorum deformans. Sleep 6:281
261. Fish DR, Sawyers D, Smith SJM et al (1991) Motor inhibition from the brainstem is normal in torsion dystonia during REM sleep. J Neurol Neurosurg Psychiatr 54:140–144
262. Jankel WR, Niedermeyer E, Graf M, Kalsher MJ (1984) Case report: polysomnographic effects of thalamotomy for torsion dystonia. Neurosurgery 14:495
263. Wagle Shukla A, Brown R, Heese K, Jones J, Rodriguez RL, Malaty IM, Okun MS, Kluger BM (2016) High rates of fatigue and sleep disturbances in dystonia. Int J Neurosci 126(10):928–935
264. Jankel WR, Allen RP, Niedermeyer E, Kalsher MJ (1983) Polysomnographic findings in dystonia musculorum deformans. Sleep 6:281
265. Fish DR, Allen PJ, Sawyers D, Marsden CD (1990) Sleep spindles in torsion dystonia. Arch Neurol 47:216
266. Segawa M, Hosaka A, Miyagawa F et al (1976) Hereditary progressive dystonia with marked diurnal fluctuations. Adv Neurol 14:215
267. Segawa M, Nomura Y (1991) Hereditary progressive dystonia with marked diurnal fluctuations. In: Nagatsu T, Narabayashi H, Yoshida M (eds) Parkinson's disease. From clinical aspects to molecular basis. Springer, New York, pp 167
268. Ichinose H, Ohye T, Takahashi E et al (1994) Hereditary progressive dystonia with marked diurnal fluctuation caused by mutations in the GTP cyclohydrolase I gene (see comments). Nat Genet 8:236
269. Bandmann O, Nygaard TG, Surtees R et al (1996) Dopa-responsive dystonia in British patients: new mutations of the GTP-cyclohydrolase I gene and evidence for genetic heterogeneity. Hum Mol Genet 5:403
270. Imaiso Y, Taniwaki T, Yamada T et al (1998) A novel mutation of the GTP-cyclohydrolase I gene in a patient with hereditary progressive dystonia/dopa-responsive dystonia. Neurology 50:517
271. Knappskog PM, Flatmark T, Mallet J et al (1995) Recessively inherited L-DOPA-responsive dystonia caused by a point mutation (Q381K) in the tyrosine hydroxylase gene. Hum Mol Genet 4:1209
272. Jarman PR, Bandmann O, Marsden CD, Wood NW (1997) GTP cyclohydrolase I mutations in patients with dystonia responsive to anticholinergic drugs. J Neurol Neurosurg Psychiatr 63:304
273. Segawa M, Nomura Y, Tanaka S et al (1988) Hereditary progressive dystonia with marked diurnal fluctuations—consideration on its pathophysiology based on the characteristics of clinical and polysomnographical findings. In: Fahn S, Marsden CD, Calne DB (eds) Dystonia 2, advanced neurology 50. Raven, New York, p 367
274. de Yebenes JG, Moskowitz C, Fahn S, Saint-Hilaire MH (1988) Long-term treatment with levodopa in a family with autosomal dominant torsion dystonia. In: Fahn S, Marsden CD, Calne DB (eds) Dystonia 2. Raven, New York, p 101
275. Segawa M, Nomura Y, Yamashita S et al (1990) Long-term effects of L-dopa on hereditary progressive dystonia with marked diurnal fluctuation. In: Berardelli A, Benecke R, Manfredi M, Marsden CD (eds) Motor disturbances II. Academic, New York, p 305
276. Nygaard TG, Takahashi H, Heiman GA et al (1992) Long-term treatment response and fluorodopa positron emission tomographic scanning of parkinsonism in a family with dopa-responsive dystonia. Ann Neurol 32:603
277. Sawle GV, Leenders KL, Brooks DJ et al (1991) Dopa-responsive dystonia: [18F] dopa positron emission tomography. Ann Neurol 30:24
278. Gordon N (2008) Segawa's disease: dopa-responsive dystonia. Int J Clin Pract 62:943–946
279. Mazurek MF, Rosebush PI (1996) Circadian pattern of acute, neuroleptic-induced dystonic reactions. Am J Psychiatr 153:708
280. Davila R, Zumarraga M, Andia I, Friedhoff AJ (1989) Persistence of cyclicity of the plasma dopamine metabolite, homovanillic

acid, in neuroleptic treated schizophrenic patients. Life Sci 44:1117
281. Lugaresi E, Cirignotta F (1981) Hyponogenic paroxysmal dystonia: epileptic seizure or a new syndrome? Sleep 4:129
282. Zucconi M, Oldani A, Ferini-Strambi L, Bizzozero D, Smirne S (1997) Nocturnal paroxysmal arousals with motor behaviors during sleep: frontal lobe epilepsy or parasomnia? J Clin Neurophysiol 14:513–522
283. Pedley TA, Guilleminault C (1977) Episodic nocturnal wanderings reponsive to anticonvulsant drug therapy. Ann Neurol 2:30–35
284. Plazzi G, Tinuper P, Montagna P, Provini F, Lugaresi E (1995) Epileptic nocturnal wanderings. Sleep 18:749–756
285. Huang YZ, Chu NS (1998) Episodic nocturnal wandering and complex visual hallucination. A case with long-term follow-up. Seizure 7:67–71
286. Tinuper P, Cerullo A, Cirignotta F, Cortelli P, Lugaresi E, Montagna P (1990) Nocturnal paroxysmal dystonia with short-lasting attacks: three cases with evidence for an epileptic frontal lobe origin of seizures. Epilepsia 31:549–556
287. Meierkord H, Fish DR, Smith SJ, Scott CA, Shorvon SD, Marsden CD (1992) Is nocturnal paroxysmal dystonia a form of frontal lobe epilepsy? Mov Disord 7:38–42
288. Lugaresi E, Montagna P, Sforza E (1991) Nocturnal paroxysmal dystonia. In: Terzano MG, Halasz P, Declerck AC (eds) Phasic events and dynamic organization of sleep. Raven Press, New York City, pp 1–5
289. Montagna P, Cirignotta F, Giovanardi Rossi P, Lugaresi E (1992) Dystonic attacks related to sleep and exercise. Eur Neurol 32:185–189
290. van Sweden B, Kemp B, van Dijk JG, Kamphuisen HA (1990) Ambulatory monitoring in sleep apnoea presenting with nocturnal episodic phenomena. Int J Psychophysiol 10:181–184
291. Lysenko L, Bhat S, Patel D, Salim S, Chokroverty S (2012) Complex sleep behavior in a patient with obstructive sleep apnea and nocturnal hypoglycemia: a diagnostic dilemma. Sleep Med 13 (10):1321–1323
292. Biary N, Singh B, Bahou Y, al Deeb SM, Sharif H (1994) Posttraumatic paroxysmal nocturnal hemidystonia. Mov Disord 9:98–99
293. Fahn S, Marsden CD, Van Woert M (1986) Myoclonus. Raven, New York, p 730
294. Lugaresi E, Coccagna G, Mantovani M et al (1970) The evolution of different types of myoclonus during sleep. A polygraphic study. Eur Neurol 4:321
295. Hoehn MM, Cherington M (1977) Spinal myoclonus. Neurology 27:942
296. Bauleo S, De Mitri P, Coccagna G (1996) Evolution of segmental myoclonus during sleep: polygraphic study of two cases. Ital J Neurol Sci 17:227
297. Lugaresi E, Cirignotta F, Montagna P, Coccagna G (1983) Myoclonus and related phenomena during sleep. In: Chase M, Weitzman ED (eds) Sleep disorders: basic and clinical research. Spectrum, New York, p 123
298. Lapresle J (1986) Palatal myoclonus. In: Fahn S, Marsden CD, Van Woert MH (eds) Myoclonus. Lippincott-Raven, New York, p 265
299. Chokroverty S (2012) Unusual movements disorders. In: Chokroverty S, Allen RP, Walters AS, Motagna P (eds) Sleep and movements disorders, 2nd edn. Oxford, New York, pp 710–713
300. Chokroverty S, Barron KD (1969) Palatal myoclonus and rhythmic ocular movements: a polygraphic study. Neurology 19:975
301. Tahmoush AJ, Brooks JE, Keltner JL (1972) Palatal myoclonus associated with abnormal ocular and extremity movements: a polygraphic study. Arch Neurol 27:431
302. Deuschl G, Toro C, Valls-Sole J et al (1994) Symptomatic and essential palatal tremor. 1. Clinical, physiological and MRI analysis. Brain 117:775
303. Postert T, Amoiridis G, Pohlau D et al (1997) Episodic undulating hyperkinesias of the tongue associated with brainstem ischemia. Mov Disord 12:619
304. Kayed K, Sjaastad O, Magnussen I, Marvik R (1983) Palatal myoclonus during sleep. Sleep 6:130–136
305. Yokota T, Atsumi Y, Uchiyama M, Fukukawa T, Tsukagoshi H (1990) Electroencephalographic activity related to palatal myoclonus in REM sleep. J Neurol 237:290–294
306. Jacobs L, Newman RP, Bozian D (1981) Disappearing palatal myoclonus. Neurology 31:748
307. Sakurai N, Koike Y, Kaneoke Y et al (1993) Sleep apnea and palatal myoclonus in a patient with neuro-Behçet syndrome. Intern Med 32:336
308. Lysenko L, Hanna PA, Chokroverty S (2011) Sleep disruption from movement disorders. In: Barkoukis T, Matheson J, Ferber R, Doghramji K (eds) Movement disorders affecting sleep. Elsevier, Philadelphia
309. Jankovic J (1987) The neurology of tics. In: Marsden CD, Fahn S (eds) Movement disorders 2. Butterworth, Boston, p 383
310. Jankovic J (1997) Tourette syndrome. Phenomenology and classification of tics. Neurol Clin 15:267
311. Van Woert MH (1990) Gilles de la tourette syndrome. In: Chokroverty S (ed) Movement disorders. PMA, Costa Mesa, CA, p 309
312. Nee LE, Caine ED, Polinsky RJ et al (1980) Gilles de la Tourette syndrome: clinical and family study of 50 cases. Ann Neurol 7:41
313. Glaze DG, Frost JD Jr, Jankovic J (1983) Sleep in Gilles de la Tourette's syndrome: disorder of arousal. Neurology 33(5):586–592
314. Drake ME Jr, Hietter SA, Bogner JE, Andrews JM (1992) Cassette EEG sleep recordings in Gilles de la Tourette syndrome. Clin Electroencephalogr 23:142
315. Kosstanecka-Endress T, Banaschewski T, Kinkelbur J et al (2003) Disturbed sleep in children with Tourette syndrome: a polysomnographic study. J Psychosom Res 55(1):23–29
316. Cohrs S, Rasch T, Atmeyer S et al (2001) Decreased sleep quality and increased sleep related movements in patients with Tourette's syndrome. J Neurol Neuroosurg Psychiatry 70(2):192–197
317. Hashimoto T, Endo S, Fukuda K et al (1981) Increased body movements during sleep in Gilles de la Tourette syndrome. Brain Dev 3:31
318. Jankovic J, Glaze DG, Frost JD Jr (1984) Effect of tetrabenazine on tics and sleep of Gilles de la Tourette's syndrome. Neurology 34:688
319. Montagna P, Imbriaco A, Zucconi M, Liguori R, Cirignotta F, Lugaresi E (1986) Hemifacial spasm in sleep. Neurology 36 (2):270–273
320. Guridi J, Obeso JA (2001) The subthalamic nucleus, hemiballismus and Parkinson's disease: reappraisal of a nuerosurgical dogma. Brain 124:5–19
321. Askenasy JJM (1981) Sleep patterns in extrapyramidal disorders. Int J Neurol 15:62–76
322. Puca FM, Minervini MG, Savarese M et al (1984) Evoluzione del sonno in un caso di emiballismo. Bol Soc It Biol Sper 60:981–987
323. Hayashi M, Ishizaki A, Sasaki H, Iwakawa Y (1992) Multimodality evoked potentials in severe athetoid cerebral palsy: correlation with clinical features and all-night polygraphical data. Brain Dev 14:156–160

324. Byrne E, White O, Cook M (1991) Familial dystonic choreoathetosis with myokymia; a sleep responsive disorder. J Neurol Neurosurg Psychiatr 54:1090–1092
325. Stefanova E, Djarmati A, Momcilovic D et al (2006) Clinical characteristics of paroxysmal nonkinesigenic dyskinesia in Serbian family with Myofibrillogenesis regulator 1 gene mutation. Mov Disord 21:2010–2015
326. Friedman JH (2002) Presumed rapid eye movement behavior disorder in Machado-Joseph disease (spinocerebellar ataxia type 3). Mov Disord 17(6):1350–1353
327. Iranzo A, Munoz E, Santamaria J et al (2003) REM sleep behavior disorder and vocal cord paralysis in Machado-Joseph disease. Mov Disord 18(10):1179–1183
328. Boesch SM, Frauscher B, Brandauer E, Wenning GK, Hőgl B, Poewe W (2006) Disturbance of rapid eye movement sleep in spinocerebellar ataxia type 2. Mov Disord 21(10):1751–1754
329. Tuin I, Voss U, Kang JS et al (2006) Stages of sleep pathology in spinocebellar ataxia type 2 (SCA2). Neurology 67(11):1966–1972
330. Boesch SM, Frauscher B, Brandauer E, Wenning GK, Poewe W, Hőgl B (2006) Restless legs syndrome and motor activity during sleep in spinocerebellar ataxia type 6. Sleep Med 7(6):529–532
331. Howell MJ, Mahowald MW, Gomez CM (2006) Evaluation of sleep and daytime somnolence in spinocerebellar ataxia type 6 (SCA6). Neurology 66(9):1430–1431
332. LisiL De (1932) Su di un fenomeno motoria constante del sonno normale: le mioclonie ipniche fisiologiche. Riv Pat Ment 39:481–496
333. Dagnino N, Loeb C, Massazza G, Sacco G (1969) Hypnic physiological myoclonias in man: an EEG-EMG study in normals and neurological patients. Eur Neurol 2:47–58
334. Montagna P, Liguori R, Zucconi M, Sforza E, Lugaresi A, Cirignotta F et al (1988) Physiological hypnic myoclonus. Electroencephalogr Clin Neurophysiol 70(2):172–176
335. Kunz A, Frauscher B, Brandauer E, Ulmer H, Poewe W, Högl B (2011) Fragmentary myoclonus in sleep revisited: a polysomnographic study in 62 patients. Sleep Med 12(4):410–415
336. Chokroverty S, Bhat S, Gupta D (2013) Intensified hypnic jerks: a polymyographic and polysomnographic analysis. J Clin Neurophysiol 30(4):403–410
337. Gassel MM, Marchiafava PL, Pompeiano O (1964) Phasic changes in muscular activity during desynchronized sleep in unrestrained cats. An analysis of the pattern and organization of myoclonic twitches. Arch Ital Biol 102:449–470
338. Gastaut H (1968) Les myoclonies-Semiologie des myoclonies et nosologie analytique des syndromes myocloniques. Rev Neurol 119:1–30
339. Oswald I (1959) Sudden bodily jerks on falling asleep. Brain 82:92–103
340. Broughton R (1988) Pathological fragmentary myoclonus, intensified sleep starts and hypnagogic foot tremor: three unusual sleep related disorders. In: Koella WP (ed) Sleep 1986. Fischer-Verlag, New York, pp 240–243
341. Mitchell SW (1890) Some disorders of sleep. Int J Med Sci 100–109
342. Gastaut H, Batini C, Broughton R et al (1965) Etude electrocephalographique des phenomenes episodiques non epileptigues au cours du sommeil. In: Fischgold H et al (eds) Le Sommeil du nuit normal et pathologique. Masson & Cie Editeurs, Paris, p 214
343. Gastaut H, Broughton R (1964) A clinical and polygraphic study of episodic phenomena during sleep. Recent Adv Psychiatr 7:197–221
344. Chokroverty S, Bhat S, Thomas R (2014) Uncommon, atypical and often unrecognized psg patterns. In: Chokroverty S, Thomas R (eds) Atlas of sleep medicine, 2nd edn. Elsevier, Philadelphia
345. Wichniak A, Tracik F, Geisler P, Ebersbach G, Morrissey SP, Zulley J (2001) Rhythmic feet movements while falling asleep. Mov Disord 16(6):1164–1170
346. Chervin RD, Consens FB, Kutluay E (2003) Alternating leg muscle activation during sleep and arousals: a new sleep-related motor phenomenon? Mov Disord 18:551–559
347. Cosentino FI, Iero I, Lanuzza B, Tripodi M, Ferri R (2006) The neurophysiology of the alternating leg muscle activation (ALMA) during sleep: Study of one patient before and after treatment with pramipexole. Sleep Med 7:63–71
348. Cruchet R (1912) Six nouveaux cas de rhthmies du sommeil (les rthmies a la caserne). Gaz Hebd Sci Med 33:303–308
349. Crucet R (1928) Les mauvaises habitudes chez les enfants. L'Expansion Scientifique Francais, Paris
350. Putman-Jacobi M (1880) Case of nocturnal rotator spasm. J Nerv Ment Dis 7:390–401
351. Zappert J (1905) Uber nachtliche kopf bewegungen bei kindern (jactatio capitis nocturna). Jahrb Kinderheilkd 62:70–83
352. Kempenaers C, Bouillon E, Mendlewicz J (1994) A rhythmic movement disorder in REM sleep: a case report. Sleep 17:274–279
353. Anderson KN, Smith IE, Shneerson JM (2006) Rhythmic movement disorder (head banging) in an adult during rapid eye movement sleep. Mov Disord 21:866–867
354. Manni R, Terzaghi M, Sartori I, Veggiotti P, Parrino L (2004) Rhythmic movement disorder and cyclic alternating pattern during sleep: a video-polysomnographic study in a 9-year-old boy. Mov Disord 19:1186–1190
355. Bramble D (1995) Two cases of severe head-banging parasomnias in peripubertal males resulting from otitis media in toddlerhood. Child Care Health Dev 21:247–253
356. Bastuji H (1994) Rhythms of falling asleep persisting in adults. Two cases without mental deficiency. Neurophysiol Clin 24:160–166
357. Chisholm T, Morehouse RL (1996) Adult headbanging: sleep studies and treatment. Sleep 19:343–346
358. Alves RS, Aloe F, Silva AB, Tavares SM (1998) Jactatio capitis nocturna with persistence in adulthood. Case report. Arq Neuropsiquiatr 56:655–657
359. Mendez MF, Mirea A (1998) Adult head-banging and stereotypic movement disorders. Mov Disord 13:825–828
360. Lombardi C, Provini F, Vetrugno R, Plazzi G, Lugaresi E, Montagna P (2003) Pelvic movements as rhythmic motor manifestation associated with restless legs syndrome. Mov Disord 18:110–113
361. Stepanova I, Nevsimalova S, Hanusova J (2005) Rhythmic movement disorder in sleep persisting into childhood and adulthood. Sleep 28:851–857
362. Gharagozlou P, Seyffert M, Santos R, Chokroverty S (2009) Rhythmic movement disorder associated with respiratory arousals and improved by CPAP titration in a patient with restless legs syndrome and sleep apnea. Sleep Med 10(4):501–503
363. McGrane IR, Leung JG, St Louis EK, & Boeve BF (2015) Melatonin therapy for REM sleep behavior disorder: A critical review of evidence. Sleep Med, 16(1), 19–26. doi:10.1016/j.sleep.2014.09.011
364. Chokroverty S, Walters A, Zimmerman T, Picone M (1992) Propriospinal myoclonus: a neurophysiologic analysis. Neurology 42:1591–1595
365. Brown P, Rothwell JC, Thompson PD, Marsden CD (1994) Propriospinal myoclonus: evidence for spinal "pattern" generators in humans. Mov Disord 9:571–576
366. Chokroverty S (1995) Propriospinal myoclonus. Clin Neurosci 3:219–222

367. Montagna P, Provini F, Plazzi G, Liguori R, Lugaresi E (1997) Propriospinal myoclonus upon relaxation and drowsiness: a cause of severe insomnia. Mov Disord 12(1):66–72
368. Vetrugno R, Provini F, Meletti S, Plazzi G, Liguori R, Cortelli P et al (2001) Propriospinal myoclonus at the sleep-wake transition: a new type of parasomnia. Sleep 24(7):835–843
369. Tison F, Arne P, Dousset V, Paty J, Henry P (1998) Propriospinal myoclonus induced by relaxation and drowsiness. Rev Neurol (Paris) 154:423–425
370. Vetrugno R, Provini F, Plazzi G, Cortelli P, Montagna P (2005) Propriospinal myoclonus: a motor phenomenon found in restless legs syndrome different from periodic limb movements during sleep. Mov Disord 20:1323–1329
371. Walters AS, Hening WA, Chokroverty S (1988) Frequent occurrence of myoclonus while awake and at rest, body rocking and marching in place in a subpopulation of patients with restless legs syndrome. Acta Neurol Scand 77:418–421
372. Manconi M, Sferrazza B, Iannaccone S, Massimo A, Zucconi M, Ferini-Strambi L (2005) Case of symptomatic propriospinal myoclonus evolving toward acute "myoclonic status". Mov Disord 20:1646–1650
373. Coulter DL, Allen RJ (1982) Benign neonatal sleep myoclonus. Arch Neurol 39:191–192
374. Caraballo R, Yepez I, Cersosimo R, Fejerman N (1998) Benign neonatal sleep myoclonus. Rev Neurol 26:540–544
375. Vaccario ML, Valenti MA, Carullo A, Di Bartolomeo R, Mazza S (2003) Benign neonatal sleep myoclonus: case report and follow-up of four members of an affected family. Clin Electroencephalogr 34:15–17
376. Ramelli GP, Sozzo AB, Vella S, Bianchetti MG (2005) Benign neonatal sleep myoclonus: an under-recognized, non-epileptic condition. Acta Paediatr 94:962–963
377. Resnick TJ, Moshe SL, Perotta L, Chambers HJ (1986) Benign neonatal sleep myoclonus. Relationship to sleep states. Arch Neurol 43:266–268
378. Di Capua M, Fusco L, Ricci S, Vigevano F (1993) Benign neonatal sleep myoclonus: clinical features and video- polygraphic recordings. Mov Disord 8:191–194
379. Alfonso I, Papazian O, Aicardi J, Jeffries HE (1995) A simple maneuver to provoke benign neonatal sleep myoclonus. Pediatrics 96:1161–1163
380. Fukumoto M, Mochizuki N, Takeishi M, Nomura Y, Segawa M (1981) Studies of body movements during night sleep in infancy. Brain Dev 3:37–43
381. Daoust-Roy J, Seshia SS (1992) Benign neonatal sleep myoclonus. A differential diagnosis of neonatal seizures. Am J Dis Child 146:1236–1241
382. Fejerman N (2005) Nonepileptic disorders imitating generalized idiopathic epilepsies. Epilepsia 46(Suppl 9):80–83
383. Turanli G, Senbil N, Altunbasak S, Topcu M (2004) Benign neonatal sleep myoclonus mimicking status epilepticus. J Child Neurol 19:62–63
384. Lavigne GJ, Rompre PH, Poirier G, Huard H, Kato T, Montplaisir JY (2001) Rhythmic masticatory muscle activity during sleep in humans. J Dent Res 80:443–448
385. Kato T, Rompre P, Montplaisir JY, Sessle BJ, Lavigne GJ (2001) Sleep bruxism: an oromotor activity secondary to micro-arousal. J Dent Res 80:1940–1944
386. Huynh N, Kato T, Rompre PH et al (2006) Sleep bruxism is associated to micro-arousals and an increase in cardiac sympathetic activity. J Sleep Res 15:339–346
387. Lobbezoo F, Soucy JP, Montplaisir JY, Lavigne GJ (1996) Striatal D2 receptor binding in sleep bruxism: a controlled study with iodine-123-iodobenzamide and single-photon-emission computed tomography. J Dent Res 75:1804–1810
388. Dube C, Rompre PH, Manzini C, Guitard F, de Grandmont P, Lavigne GJ (2004) Quantitative polygraphic controlled study on efficacy and safety of oral splint devices in tooth-grinding subjects. J Dent Res 83:398–403
389. Kato T, Montplaisir JY, Blanchet PJ, Lund JP, Lavigne GJ (1999) Idiopathic myoclonus in the oromandibular region during sleep: a possible source of confusion in sleep bruxism diagnosis. Mov Disord 14:865–871
390. Vetrugno R, Provini F, Plazzi G et al (2002) Familial nocturnal facio-mandibular myoclonus mimicking sleep bruxism. Neurology 58:644–647
391. Loi D, Provini F, Vetrugno R, D'Angelo R, Zaniboni A, Montagna P (2007) Sleep-related faciomandibular myoclonus: a sleep-related movement disorder different from bruxism. Mov Disord 22:1819–1822
392. Wieselmann G, Permann R, Körner E, Flooh E, Reinhart B, Moser F et al (1986) Distribution of muscle activity during sleep in bruxism. Eur Neurol 25(S2):111–116
393. Reding GR, Rubright WC, Rechtscaffen A, Daniels RS (1964) Sleep pattern of tooth-grinding: its relationship to dreaming. Science 145(3633):725–726
394. Clarke NG, Townsend GC (1984) Distribution of nocturnal bruxing patterns in man. J Oral Rehabil 11(6):529–534
395. Manconi M, Zucconi M, Carrot B, Ferri R, Oldani A, Ferini-Strambi L (2008) Association between bruxism and nocturnal groaning. Mov Disord 15, 23(5):737–739
396. Lobbezoo F, Lavigne GJ, Tanguay R, Montplaisir JY (1997) The effect of catecholamine precursor L-dopa on sleep bruxism: a controlled clinical trial. Mov Disord 12:73–78
397. Kast RE (2005) Tiagabine may reduce bruxism and associated temporomandibular joint pain. Anesth Prog 52:102–104
398. Ivanhoe CB, Lai JM, Francisco GE (1997) Bruxism after brain injury: successful treatment with botulinum toxin-A. Arch Phys Med Rehabil 78:1272–1273
399. Landry ML, Rompre PH, Manzini C, Guitard F, de Grandmont P, Lavigne GJ (2006) Reduction of sleep bruxism using a mandibular advancement device: an experimental controlled study. Int J Prosthodont 19:549–556
400. Harada T, Ichiki R, Tsukiyama Y, Koyano K (2006) The effect of oral splint devices on sleep bruxism: a 6-week observation with an ambulatory electromyographic recording device. J Oral Rehabil 33:482–488
401. van der Zaag J, Lobbezoo F, Wicks DJ, Visscher CM, Hamburger HL, Naeije M (2005) Controlled assessment of the efficacy of occlusal stabilization splints on sleep bruxism. J Orofac Pain 19:151–158
402. Iriarte J, Campo A, Alegre M, Fernández S, Urrestarazu E (2015) Catathrenia: respiratory disorder or parasomnia? Sleep Med 16 (7):827–830
403. Pevernagie DA, Boon PA, Mariman AN, Verhaeghen DB, Pauwels RA (2001) Vocalization during episodes of prolonged expiration: a parasomnia related to REM sleep. Sleep Med 2 (1):19–30
404. Vetrugno R, Provini F, Plazzi G, Vignatelli L, Lugaresi E, Montagna P (2001) Catathrenia (nocturnal groaning): a new type of parasomnia. Neurology 56(5):681–683
405. Vetrugno R, Lugaresi E, Plazzi G, Provini F, D'Angelo R, Montagna P (2007) Catathrenia (nocturnal groaning): an abnormal respiratory pattern during sleep. Eur J Neurol 14(11):1236–1243
406. Ott SR, Hamacher J, Seifert E (2011) Bringing light to the sirens of night: laryngoscopy in catathrenia during sleep. Eur Respir J 37 (5):1288–1289
407. Koo DL, Hong SB, Joo EY (2012) Acoustic characteristic of catathrenia and snoring: different subtypes of catathrenia. Sleep Med 13(7):961–964

408. Songu M, Yilmaz H, Yuceturk AV, Gunhan K, Ince A, Bayturan O (2008) Effect of CPAP therapy on catathrenia and OSA: a case report and review of the literature. Sleep Breath 12(4):401–405
409. Iriarte J, Alegre M, Urrestarazu E, Viteri C, Arcocha J, Artieda J (2006) Continuous positive airway pressure as treatment for catathrenia (nocturnal groaning). Neurology 66(4):609–610
410. Xu L, Zhang X (2015) Catathrenia: a new sleep breathing disorder].[Article in Chinese]. Zhonghua Jie He He Hu Xi Za Zhi 38(9):656–658
411. Hao Z, Xu L, Zhang J, Lan X, Gao X, Han F (2015) Anatomical characteristics of catathrenia (nocturnal groaning) in upper airway and orofacial structures. Sleep Breath. (Epub ahead of print)
412. Vetrugno R, Plazzi G, Provini F, Liguori R, Lugaresi E, Montagna P (2002) Excessive fragmentary hypnic myoclonus: clinical and neurophysiological findings. Sleep Med 3(1):73–76
413. Vankova J, Stepanova I, Jech R et al (2003) Sleep disturbances and hypocretin deficiency in Niemann-Pick disease type C. Sleep 26:427–430
414. Vankova J, Stepanova I, Jech R et al (2003) Sleep disturbances and hypocretin deficiency in Niemann-Pick disease type C. Sleep 26:427–430
415. Vetrugno R, Plazzi G, Provini F, Liguori R, Lugaresi E, Montagna P (2002) Excessive fragmentary hypnic myoclonus: clinical and neurophysiological findings. Sleep Med 3:73–76
416. Lins O, Castonguay M, Dunham W, Nevsimalova S, Broughton R (1993) Excessive fragmentary myoclonus: time of night and sleep stage distributions. Can J Neurol Sci 20:142–146
417. Hoque R, McCarty DE, Chesson AL (2013) Jr.Manual quantitative assessment of amplitude and sleep stage distribution of excessive fragmentary myoclonus. J Clin Sleep Med 9(1):39–45
418. Adie W (1926) Idiopathic narcolepsy: a disease sui generis; with remarks on the mechanism of the brain. Brain 49:257–306
419. Wilson S (1928) The narcolepsies. Brain 51:63–77
420. Hishikawa Y, Shimizu T (1995) Physiology of REM sleep, cataplexy, and sleep paralysis. Adv Neurol 67:245–271
421. Dyken ME, Yamada T, Lin-Dyken DC, Seaba P, Yeh M (1996) Diagnosing narcolepsy through the simultaneous clinical and electrophysiologic analysis of cataplexy. Arch Neurol 53:456–460
422. Overeem S, Mignot E (2001) Gert van Dijk J, Lammers GJ. Narcolepsy: clinical features, new pathophysiologic insights, and future perspectives. J Clin Neurophysiol 18:78–105
423. Bell CC, Dixie-Bell DD, Thompson B (1986) Further studies on the prevalence of isolated sleep paralysis in black subjects. J Natl Med Assoc 78:649–659
424. Fukuda K, Miyasita A, Inugami M, Ishihara K (1987) High prevalence of isolated sleep paralysis: kanashibari phenomenon in Japan. Sleep 10:279–286
425. Takeuchi T, Miyasita A, Sasaki Y, Inugami M, Fukuda K (1992) Isolated sleep paralysis elicited by sleep interruption. Sleep 15:217–225
426. Andermann E, Andermann F, Silver K, Levin S, Arnold D (1994) Benign familial nocturnal alternating hemiplegia of childhood. Neurology 44:1812–1814
427. Tassi P, Muzet A (2000) Sleep Inertia. Sleep Med Rev 4:341–353
428. Marzano C, Ferrara M, Moroni F, De Gennaro I (2011) Electroencephalographic sleep inertia of the awakening brain. Neuroscience 176:308–317
429. Roth B, Nevsimalova S, Rechtschaffen A (1972) Hypersomnia with sleep drunkenness. Arch Gen Psychiatr 26:456–462
430. Figorilli M, Puligheddu M, Ferri R (2016) Scoring guidelines (Sleep-related movements). In: Chokroverty S, Ferini-Strambi L (eds) Disorders of sleep. Oxford University Press, Oxford (in press)
431. Colburn T, Smith B, Guarini J, Simmons N (1976) An ambulatory activity monitor with solid state memory. ISA Trans 15:149–154
432. Redmond DP, Hegge FW (1985) Observations on the design and specification of a wrist-worn activity monitor. Behav Res Meth: Instr Comput 17:639–669
433. Marino M, Li Y, Rueschman MN, Winkelman JW, Ellenbogen JM, Solet JM, Dulin H, Berkman LF, Buxton OM (2013) Measuring sleep: accuracy, sensitivity, and specificity of wrist actigraphy compared to polysomnography. Sleep 36(11):1747–1755
434. Bélanger MÈ, Bernier A, Paquet J, Simard V, Carrier J (2013) Validating actigraphy as a measure of sleep for preschool children. J Clin Sleep Med 9(7):701–706
435. Shin M, Swan P, Chow CM (2015) The validity of Actiwatch2 and SenseWear armband compared against polysomnography at different ambient temperature conditions. Sleep Sci 8(1):9–15
436. Hyde M, O'Driscoll DM, Binette S, Galang C, Tan SK, Verginis N, Davey MJ, Horne RS (2007) Validation of actigraphy for determining sleep and wake in children with sleep disordered breathing. J Sleep Res 16(2):213–216
437. Pollak CP, Tryon WW, Nagaraja H, Dzwonczyk R (2001) How accurately does wrist actigraphy identify the states of sleep and wakefulness? Sleep 24(8):957–965
438. Caligiuri MP, Lohr JB, Bracha HS, Jeste DV (1991) Clinical and instrumental assessment of neuroleptic-induced parkinsonism in patients with tardive dyskinesia. Biol Psychiatr 29:139–148
439. Caligiuri MP, Lohr JB, Rotrosen J et al (1997) Reliability of an instrumental assessment of tardive dyskinesia: results from VA cooperative study #394. Psychopharmacology 132:61–66
440. Allen RP, Kaplan PW, Buchholz DW, Earley CJ, Walters JK (1992) Accuracy of a physical activity monitor (PAM) worn on the ankle for assessment of treatment response for periodic limb movements in sleep. Sleep Res 21:329
441. Gorny S, Allen R, Krausman D, Earley C (1998) Accuracy of the PAM-RL system for automated detection of periodic leg movements (Abstract). Sleep 21:S183
442. Sforza E, Zamagni M, Petiav C, Krieger J (1999) Actigraphy and leg movements during sleep: a validation study. J Clin Neurophysiol 16:154–160
443. Sforza E, Johannes M, Claudio B (2005) The PAM-RL ambulatory device for detection of periodic leg movements: a validation study. Sleep Med 6:407–413. 692–695
444. Kemlink D, Pretl M, Sonka K, Nevsimalova S (2008) A comparison of polysomnographic and actigraphic evaluation of periodic limb movements in sleep. Neurol Res 30(3):234–238
445. Allen RP (2007) Improving RLS diagnosis and severity assessment: polysomnography, actigraphy and RLS-sleep log. Sleep Med 8:S13–S18
446. Kohnen R, Allen RP, Benes H et al (2007) Assessment of restless legs syndrome-Methodological approaches for use in practice and clinical trials. Mov Disord 22:S485–S494
447. Kazenwadel J, Pollmacher T, Trenkwalder C et al (1995) New actigraphic assessment method for periodic leg movements (PLM). Sleep 18:689–697
448. Allen RP (1997) Activity monitoring to diagnose and evaluate motor abnormalities of sleep. In: Hening W, Chokroverty S (eds) Topics in movement disorders of sleep (Course syllabus: ASDA annual meeting, San Francisco). American Sleep Disorders Association, Rochester, Minnesota
449. Allen RP, Gorny S, Krausman DT, Cammarata J, Earley CJ (1997) Ambulatory 3-D body position monitor for patients with sleep walking or the restless legs syndrome. Sleep Res 26:639
450. Ko PT, Kientz JA, Choe EK, Kay M, Landis CA, Watson NF (2015) Consumer sleep technologies: a review of the landscape. J Clin Sleep Med 11(12):1455–1461
451. Choi BH, Seo JW, Choi JM, Shin HB, Lee JY, Jeong do U, Park KS (2007) Non-constraining sleep/wake monitoring system using bed actigraphy. Med Biol Eng Comput 45(1):107–114

452. O'Hare E, Flanagan D, Penzel T, Garcia C, Frohberg D, Heneghan C (2015) A comparison of radio-frequency biomotion sensors and actigraphy versus polysomnography for the assessment of sleep in normal subjects. Sleep Breath 19(1):91–98
453. Poyares D, Hirotsu C, Tufik S (2015) Fitness tracker to assess sleep: beyond the market. Sleep 38(9):1351–1352
454. Grifantini K (2014) How's my sleep? Personal sleep trackers are gaining in popularity, but their accuracy is still open to debate. IEEE Pulse 5(5):14–18
455. Bhat S, Ferraris A, Gupta D, Mozafarian M, DeBari VA, Gushway-Henry N, Gowda SP, Polos PG, Rubinstein M, Seidu H, Chokroverty S (2015) Is there a clinical role for smartphone sleep apps? Comparison of sleep cycle detection by a smartphone application to polysomnography. J Clin Sleep Med 11(7):709–715
456. de Zambotti M, Baker FC, Colrain IM (2015) Validation of sleep-tracking technology compared with polysomnography in adolescents. Sleep 38(9):1461–1468
457. de Zambotti M, Claudatos S, Inkelis S, Colrain IM, Baker FC (2015) Evaluation of a consumer fitness-tracking device to assess sleep in adults. Chronobiol Int 32(7):1024–1028
458. Meltzer LJ, Hiruma LS, Avis K, Montgomery-Downs H, Valentin J (2015) Comparison of a commercial accelerometer with polysomnography and actigraphy in children and adolescents. Sleep 38(8):1323–1330
459. Hess CW, Mills KR, Murray NMF, Schriefer TN (1987) Excitability of the human cortex is enhanced during REM sleep. Neurosci Letts 82:47–52
460. Rosler KM, Nirkko AC, Rihs F, Hess CW (1994) Motor-evoked responses to transcranial brain stimulation persist during cataplexy: a case report. Sleep 17:168–171
461. Civardi C, Naldi P, Cantello R (2004) Cortico-motoneurone excitability in patients with obstructive sleep apnoea. J Sleep Res 13:159–163
462. Chokroverty S (1990) An approach to a patient with disorders of voluntary movements. In: Chokroverty S (ed) Movement disorders. PMA Publishing, USA, pp 1–43
463. Maquet P (2000) Functional neuroimaging of normal human sleep by positron emission tomography. J Sleep Res 9:207–231
464. Maquet P (2005) Current status of brain imaging in sleep medicine. Sleep Med Rev 9:155–156
465. Hofle N, Paus T, Reutens D et al (1997) Regional cerebral blood flow changes as a function of delta and spindle activity during slow wave sleep in humans. J Neurosci 17:4800–4808
466. Schabus M, Dang-Vu TT, Albouy G et al (2007) Hemodynamic cerebral correlates of sleep spindles during human non-rapid eye movement sleep. Proc Natl Acad Sci U S A 104:13164–13169
467. Braun AR, Balkin TJ, Wesenten NJ et al (1997) Regional cerebral blood flow throughout the sleep-wake cycle. An H2(15)O PET study. Brain 120:1173–1197
468. Maquet P, Peters J, Aerts J et al (1996) Functional neuroanatomy of human rapid-eye-movement sleep and dreaming. Nature 383:163–166
469. Buchsbaum MS, Hazlett EA, Wu J, Bunney WE (2001) Positron emission tomography with deoxyglucose-f18 imaging of sleep. Neuropsychopharmacology 25:S50–S56
470. Lovblad KO, Thomas R, Jakob PM et al (1999) Silent functional magnetic resonance imaging demonstrates focal activation in rapid eye movement sleep. Neurology 53:2193–2195
471. Hong CC, Gillin JC, Dow BM, Wu J, Buchsbaum MS (1995) Localized and lateralized cerebral glucose metabolism associated with eye movements during REM sleep and wakefulness: a positron emission tomography (PET) study. Sleep 18:570–580
472. Hetta J, Onoe H, Andersson J et al (1995) Cerebral blood flow during sleep—a positron emission tomographic (PET) study of regional changes. Sleep Res 24A:87
473. Wehrle R, Kaufmann C, Wetter TC et al (2007) Functional microstates within human REM sleep: first evidence from fMRI of a thalamocortical network specific for phasic REM periods. Eur J Neurosci 25:863–871
474. Wehrle R, Czisch M, Kaufmann C et al (2005) Rapid eye movement-related brain activation in human sleep: a functional magnetic resonance imaging study. Neuro Report 16:853–857
475. Maquet P (1997) Positron emission tomography studies of sleep and sleep disorders. J Neurol 244:S23–S28