Review Article

Sleep-Related Disorders in Neurology and Psychiatry

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Summary

Background: Sleep-related disorders are a group of illnesses with marked effects on patients' quality of life and functional ability. Their diagnosis and treatment is a matter of common interest to multiple medical disciplines.

Methods: This review is based on relevant publications retrieved by a selective search in PubMed (Medline) and on the guidelines of the German Society for Sleep Medicine, the German Neurological Society, and the German Association for Psychiatry, Psychotherapy and Psychosomatics.

Results: A pragmatic classification of sleep disorders by their three chief complaints—insomnia, daytime somnolence, and sleep-associated motor phenomena—enables tentative diagnoses that are often highly accurate. Some of these disorders can be treated by primary care physicians, while others call for referral to a neurologist or psychiatrist with special experience in sleep medicine. For patients suffering from insomnia as a primary sleep disorder, rather than a symptom of another disease, meta-analyses have shown the efficacy of cognitive behavioral therapy, with high average effect sizes. These patients, like those suffering from secondary sleep disorders, can also benefit from drug treatment for a limited time. Studies have shown marked improvement of sleep latency and sleep duration from short-term treatment with benzodiazepines and Z-drugs (non-benzodiazepine agonists such as zolpidem and zopiclone), but not without a risk of tolerance and dependence. For sleep disorders with the other two main manifestations, specific drug therapy has been found to be beneficial.

Conclusion: Sleep disorders in neurology and psychiatry are a heterogeneous group of disorders with diverse manifestations. Their proper diagnosis and treatment can help prevent secondary diseases and the worsening of concomitant conditions. Care structures for the treatment of sleep disorders should be further developed.

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Sleep is essential for a person's health and wellbeing. Disturbed sleep reduces the quality of life and restfulness of sleep, is a risk factor for secondary diseases and may be caused by other medical conditions. Sleep is a dynamic and complex behavioral process. Sleep disturbances may occur in this complexity. The International Classification of Sleep Disorders pragmatically groups disorders into six major categories (*Table 1*) (1). Patients reporting sleeping problems, typically do not follow the structure of the classification, but describe the following 3 cardinal symptoms:

- The inability to fall asleep or sleep through the night
- Excessive daytime sleepiness; or
- Sleep-related movement phenomena.

The diversity of sleep-related disorders is reflected in the variety of specialties involved in the care of these patients—ranging from respiratory medicine to otorhinolaryngology to dentistry. The aim of this review is to describe the sleep-related disorders directly linked to neurology and psychiatry and present these according to their chief complaints (*Table 1*).

Methods

This review includes original articles, reviews, and meta-analyses. It is based on pertinent publications retrieved by a selective search in PubMed (Medline), while also taking secondary literature into account. The guidelines of the German Society of Sleep Medicine (DGSM, Deutsche Gesellschaft für Schlafmedizin), the German Society of Neurology (DGN, Deutsche Gesellschaft für Neurologie) and the German Association for Psychiatry, Psychotherapy and Psychosomatics (DGPPN, Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde) were also included in this review. The levels of evidence were determined following the recommendations of the Association of the Scientific Medical Societies in Germany (AWMF).

Cardinal symptom: Disorders of initiating and maintaining sleep

Disorders of initiating and maintaining sleep are collectively referred to as insomnias (*Box 1*). They represent the typical cardinal symptom of "poor sleep". Transient (acute, short-term) insomnia has a 1-year prevalence of up to 30%, but does not necessarily require treatment due to its short duration. If it persists for more than 4 weeks, is of high intensity or associated with other signs and symptoms, a comprehensive work-up is indicated (2). Insomnia may be a symptom of an underlying disease or a distinct entity.

Insomnia as a primary disorder

Disorders of initiating and maintaining sleep, which have a negative impact on performance or daytime wellbeing and which cannot be explained by other underlying medical issues, are referred to as nonorganic insomnia, a common condition, affecting 6% of the population in Western industrialized countries (3). Nonorganic insomnia takes a chronic course, with more than 70% of persons with insomnia still meeting the diagnostic criteria after one year (e1). Women are one and a half times as likely to be affected as men and the condition is more prevalent among older people. Insomnia results in reduced quality of life (e2) and limitations in performance (e3). In addition, longitudinal studies have shown that insomnia is a risk factor for cardiovascular disease (risk ratio [RR]: 1.3–1.5), diabetes (RR: 1.5–1.8), depression (odds ratio [OR]: 2.1), and suicidality (RR: 1.9–3.0) (e4–e7). It is likely that insomnia is also a risk factor for dementia (e8), anxiety disorders (e9), and alcohol dependence (e10). Hence, sleep disorders and health are closely related in a bidirectional fashion. Insomnia is associated with a significant increase in consumption of health services, along with higher levels of absence from work and reduced work performance (4)

Epidemiological studies have found that sleep disorders are increasing in prevalence (e11). The guidelines recommend psychotherapy specifically designed for sleep problems, so-called cognitive behavioral therapy for insomnia (CBT-I, core modules in *Table 2*), for which, on average, large effect sizes have been found (5–6; e11), as demonstrated in meta-analyses with large effect sizes (improvement of the measured values by 0.5 to 1 standard deviation) and level Ia evidence (e12). Studies have been conducted to determine how many patients actually receive treatment; according to expert estimates, it is only a minority of those affected (5, 7). By contrast, sleeping pills are not recommended as the primary treatment option for insomnia (6, 7). Medications can be used for short-term support; in this case, they are similar to those used to treat symptomatic insomnia (*Table 3*).

BOX 1

5 tips for good sleep

- The bedroom should be a quiet space reserved for sleeping.
- Regular habits of going to bed and falling asleep improve sleep.
- Keeping a regular sleep schedule improves sleep.
- Alcohol is not a suitable sleeping aid.
- Relaxation exercises help to switch to sleep.

BOX 2

Secondary causes of disorders of initiating and maintaining sleep*

- Psychiatric disorders (e.g. depression, anxiety disorders, alcohol dependence)
- Disorders of the central nervous system (e.g. neurodegenerative, inflammatory, tumor)
- Disorders of the peripheral nervous system (e.g. polyneuropathies)
- Restless legs syndrome
- Sleep-related breathing disorders (e.g. obstructive sleep apnea syndrome)
- Cardiac disease (e.g. heart failure)
- Endocrine disorders (e.g. hyperthyroidism)
- External factors (e.g. noise, light, shift work)

*also refer to (7)

Secondary insomnias

Insomnia may be caused by other medical conditions (*Box 2*). With more than 50% of disorders of initiating and maintaining sleep being caused by psychiatric illnesses (including addiction), psychiatric examination plays a key role in the assessment of insomnia (7). Similarly, diseases of the central and peripheral nervous system, such as restless legs syndrome (RLS), are among the most common causes of insomnia; thus, neurological evaluation is conducive to diagnosing important underlying problems. In patients with abnormal breathing during sleep, the chief complaint of excessive daytime tiredness is very prominent; therefore, the often present disorder of initiating and maintaining sleep should be explicitly addressed during history taking (10).

Treatment should be directed at the cause. While basic treatment can be provided by general practitioners, more complex constellations require the involvement of a specialized physician or sleep specialist. Pharmacological intervention should be specific, e.g. a sedating antidepressant should be used to treat patients with depression-related sleep disorder. Symptomatic treatment with traditional sleeping pills and other GABA (γ-aminobutyric acid)ergic substances (Z-drugs such as zolpidem and zopiclone) should typically be short term (up to 4 weeks) (5, e13)

TABLE 1

Classification of sleep disorders according to ICSD-3 with typical examples and symptoms*

ICSD-3 major category	Exemplary diagnosis	Typical symptoms
Insomnias	Chronic insomnia	Disorder of initiating and maintaining sleep
Sleep-related breathing disorders	Obstructive sleep apnea syndrome (OSAS)	Excessive daytime sleepiness
Central disorders of hypersomnolence	Narcolepsy	Excessive daytime sleepiness, cataplexy (with narcolepsy)
Parasomnias	Somnambulism	Nighttime movements, getting up
Sleep-related movement disorders	Restless legs syndrome	Urge to move legs, disorder of initiating sleep
Circadian rhythm sleep disorders	Shift work, jetlag	Disorders of initiating and maintaining sleep, early awakening, excessive daytime sleepiness, indigestion

* ICSD-3, International Classification of Sleep Disorders (1). The new ICD-11 classification (scheduled to be effective from 1 January 2022) will feature a separate chapter dedicated to sleep disorders (chapter 7 "sleep-wake disorders") to highlight the clinical relevance of sleep disorders. The classification of disorders will be partially regrouped, the pragmatic strategy of a symptom-oriented approach will be emphasized.

TABLE 2

Core modules of cognitive behavioral therapy for insomnia (CBT-I)

Module	Description
Psychoeducation	Information about "sleep hygiene rules" and basic information about sleep and sleep disorders
Relaxation techniques	Methods of physical and mental relaxation (e.g. progressive muscle relaxation; guided visualization)
Bedtime restriction	Temporary significant restriction of the amount of time spent in bed during the night to the average amount of sleep with subsequent adjustment of the amount of time spent in bed in the weekly rhythm. To this end, the average sleep efficiency (sleeping time/bed time) is calculated for one week; in case of high values (e.g. >90%), the bedtime for the following week is extended by e.g. 30 min, while in case of low values (e.g. <80%) the bedtime for the following week is shortened by e.g. 30 min
Stimulus-control therapy	Reassociation of the sleeping environment with the behavior "sleep" by asking the patient not to engage in any activities other than sleep in bed and to get out of bed if unable to fall asleep in 15–30 minutes.
Cognitive techniques	Psychological methods to reduce worrying or to challenge and change dysfunctional sleep- and insomnia-related cognitions (e.g. the dysfunctional cognitions "The sleep before midnight is the healthiest sleep", "everyone needs 8 hours of sleep" or "If I don't get enough sleep, I will not be able to function tomorrow")

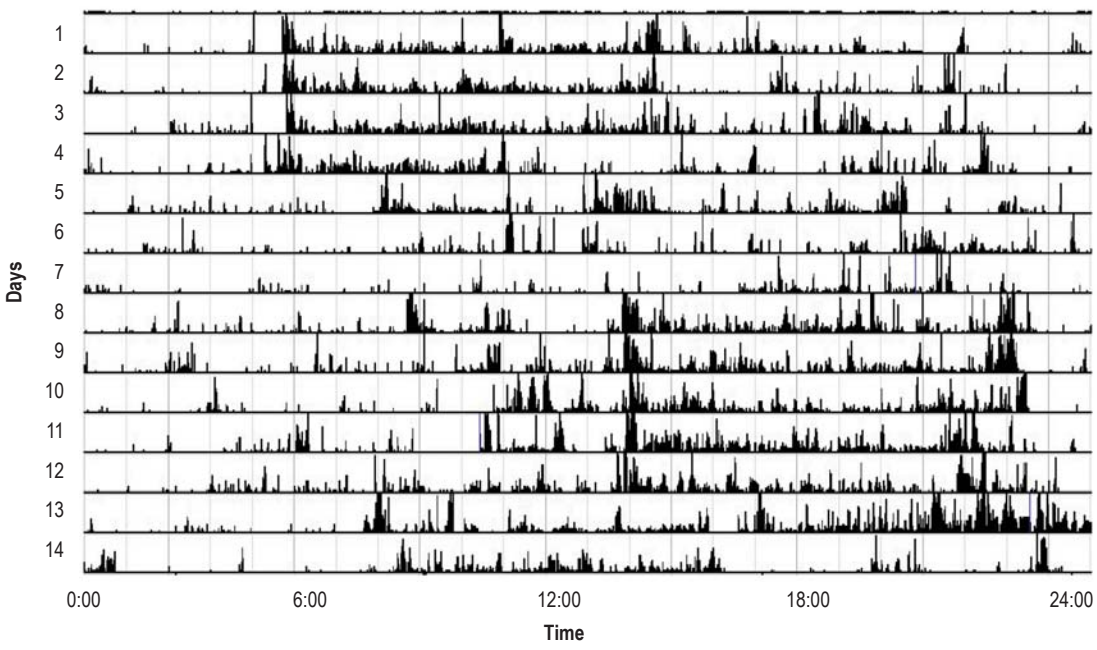
TABLE 3

Symptomatic drug therapy of insomnias*

Substance (and dose)	Effect depending on the study population	Notes
Benzodiazepines and Z-drugs	Zopiclone: Sleep latency − 12 min Sleep duration + 28 min (LoE Ia; e17) (9)	Approved for the treatment of primary insomnia; typically, it is not used longer than 4 weeks. Warning: development of tolerance and dependence
Melatonin	Sleep latency − 5 min Sleep duration n.s. (LoE Ia; e18)	Approved in prolonged-release dosage form for the treatment of insomnia in patients over 55 years of age
Mirtazapine (3.75–15 mg)	Sleep latency − 2 min Sleep duration + 9 min (LoE IIb; e19–e20)	Primarily for symptomatic sleep disorder associated with depression, not approved for the treatment of primary insomnia ("off-label" use)
Doxepin (1–50 mg)	Sleep latency − 3 min Sleep duration + 24 min (LoE Ib; e21–e22)	Primarily for symptomatic sleep disorder associated with depression; in some cases, very low doses (drops) highly effective; not approved for the treatment of primary insomnia ("off-label" use)
Quetiapine (25–75 mg)	Sleep latency − 2 min Sleep duration + 14 min (LoE IIb; e20)	Primarily for symptomatic sleep disorder associated with depression and psychotic disorders; not approved for the treatment of primary insomnia ("off-label" use)
Trimipramine (50–100 mg)	Sleep efficiency + 7% Sleep duration + 18 min (LoE IIb; e23)	Often used with good clinical response; improves sleep efficiency, but not overall sleep time.
Melperone/Pipamperone	No controlled trials (LoE V)	Older butyrophenones, used primarily in gerontopsychiatry („off label" use)

*For details and other eligible substances see (5, 7, 8).
LoE, level of evidence; n.s., non-significant

FIGURE 1



Actimetry of a shift worker over a 2-week period. Four days of morning shift are followed by three days off work and then five days of late shift, identified by the significantly higher level of activity (height of the black bars) on the way to work at the beginning and end of the working day. The sleep is disturbed by frequent awakenings, no consolidated circadian activity–rest rhythm can be identified.

(Table 3). The behavioral treatment strategies for non-organic insomnia described above have been proven beneficial for symptomatic sleep disorders as well, if the condition causing insomnia cannot be completely eliminated. This is supported by evidence from, for example, meta-analyses on the use of CBT-I to treat insomnia in patients with posttraumatic stress disorder (e14), cancer (e15), or chronic pain (e16); here, again, moderate to large effect sizes were achieved.

Circadian rhythm disorders

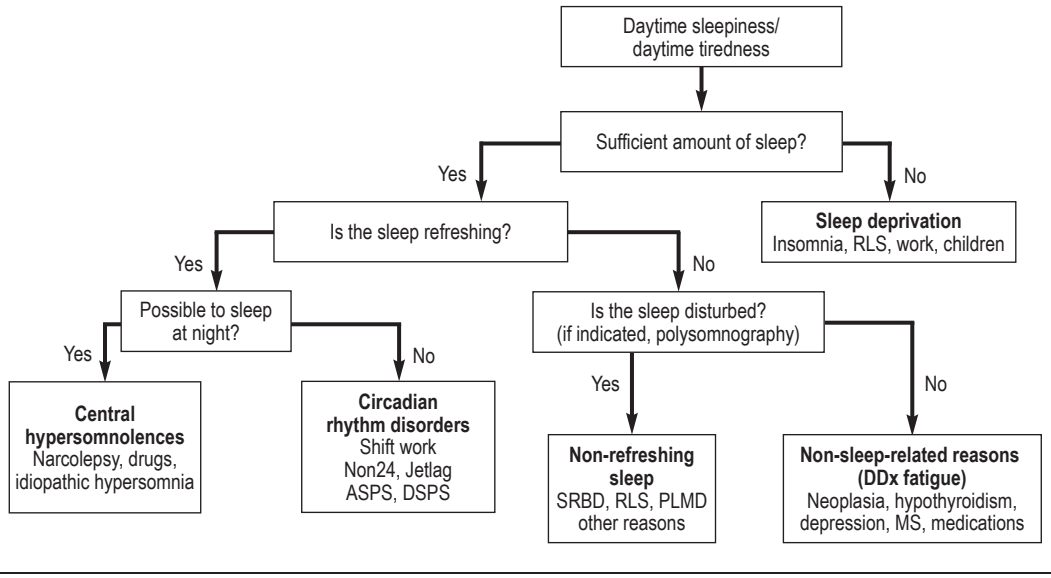
A distinct cause of insomnia are disturbances of the internal ("body") clock. Circadian rhythm abnormalities are characterized by deviation of the internal body rhythm (e.g. sleep, digestion) from the external time of the day, e.g. being awake at night or sleeping during the day. A broad spectrum of related disorders illustrates the effect of the internal clock, influencing the activity of every system of the body throughout the day. Shift work (in Germany 10.8% night work, 13.5% rotating shift work, and 35.3% evening work, *Figure 1*) (e24) and jetlag (traveling to different time zones) are among the most common reasons for disturbances of the internal clock. They can have a massive negative impact on sleep (e25, e26).

The lack of daily circadian adaption (typically, the rhythm is slightly longer than 24 hours) results in a constantly shifting, non-synchronous periodicity compared to the day–night rhythm (e27). Frequently, blind people are affected, because light as a timer does not get through to their internal clock. In periods of significant divergence between internal and external time, sleep disorders (the internal clock triggers activity at nighttime) and daytime tiredness (due to sleep deprivation and the internal clock demanding rest) can occur. These disorders are diagnosed based on the medical history, actimetry findings and sleep diary records (e28). Actimetry shows the shift of the rhythm compared to the day–night rhythm. Treatment is based on behavioral interventions and melatoninergic drugs which restore normal rhythm in 40–57% of cases (level Ib evidence; e29, e30). The melatonin receptor agonist tasimelteon has recently been approved for non-24-hour sleep–wake disorder in blind individuals (e31, e32).

Chief complaint: excessive daytime sleepiness

Sleepiness and sudden sleep attacks during the daytime have a negative impact on performance and may be indicative of abnormal sleep regulation or disturbed sleep at night. Sleepiness can be measured using the Epworth Sleepiness Scale (ESS) (e33) and be objectively determined after a night in the sleep laboratory using the Multiple Sleep Latency Test (MSLT) (*Figure 2*). Especially in patients with comorbidities such as cancer or multiple sclerosis, it can be difficult to distinguish it from daytime tiredness and/or fatigue (reduced performance and feeling of exhaustion) (11).

FIGURE 2



Diagnostic flowchart for daytime sleepiness/daytime tiredness. The diagnoses are only examples, comorbid causes may be present. ASPS/DSPS, advanced/delayed sleep phase syndrome; DDx, differential diagnosis; MS, multiple sclerosis; Non24, non–24-hour sleep–wake disorder; PLMD, periodic leg movement disorder; RLS, restless legs syndrome; SRBD, sleep-related breathing disorders

Central disorders of hypersomnolence

Narcolepsy and idiopathic hypersomnia are disorders typically associated with excessive daytime tiredness (tiredness without falling asleep in monotonous situations) and fall into the category of "central disorders of hypersomnolence". The primary symptom is always excessive daytime sleepiness (uncontrollable episodes of falling asleep during the daytime) and/or prolonged sleep not explained by other sleep disorders or other medical conditions. Another central symptom, which is also used to distinguish between two types of narcolepsy, is cataplexy (type I narcolepsy with cataplexy; type 2 narcolepsy without cataplexy). Facultative symptoms include hypnagogic/hypnopompic hallucinations, sleep paralysis, automatic behaviors, and fragmented sleep at night (12).

The overall prevalence of narcolepsy is 25–50 per 100 000 population, with an incidence of 0.8/100 000 (e34). The pathogenesis of the two types of narcolepsy is not fully understood. Given the strong HLA association (the HLA marker DQB1*0602 is present in 98% of patients with type 1 narcolepsy, but only in 23% of healthy controls [e35]), autoimmunity is assumed to be involved in the pathogenesis; however, the diagnostic significance of typing is limited to a supporting role, due to the prevalence of the marker in the general population (e35). Pathophysiologically, there is a disturbance of the hypocretin/orexin system (controlling wakefulness) and the histamine system. Reduced hypocretin levels in cerebrospinal fluid (CSF) were found in over 80% of patients with type 1 narcolepsy (e36). CFS hypocretin-1 levels below 110 pg/mL are considered diagnostic of type 1 narcolepsy. This may be a starting point for the development of future biological treatments (13).

The multiple sleep latency test (MSLT) is the key technical investigation. The test consists of five scheduled naps during the daytime in a sleep laboratory setting. Here, daytime sleep latency (threshold: <8 minute) and the occurrence of REM sleep periods are key diagnostic requirements (e37). The test is performed to rule out rare (about 7%), but treatment-relevant symptomatic types of narcolepsy, such as anti-Ma2–associated encephalitis (e38).

In many cases, the various narcolepsy symptom complexes respond well to treatment. *Table 4* summarizes selected medications; the reader is referred to the DGSM guideline for more information (11).

Idiopathic hypersomnia

Idiopathic hypersomnia is an important differential diagnosis of narcolepsy (14). It is characterized by excessive daytime sleepiness without the REM-associated symptoms, such as sleep paralysis or cataplexy. The condition is diagnosed in the presence of clinical symptoms of daytime sleepiness without REM-associated symptoms and a daytime sleep latency of less than 8 minutes in the MSLT (14). While modafinil has proved effective in the treatment of idiopathic hypersomnia (e45), it is not approved for this indication so that reimbursement of costs can be problematic.

Other disorders associated with excessive daytime tiredness

Sleep-related breathing disorders are one of the most important and most common conditions requiring sleep

TABLE 4

Selected medications for the treatment of narcolepsy

Agent	Indication	Posology
Modafinil	EDS (LoE Ia; e39–e40)	200–400 mg/d, max. 600 mg
Methylphenidate (controlled substance prescription required)	EDS (LoE II; e39)	10–60 mg/d
Pitolisant	EDS (LoE Ib; e41) cataplexy (LoE Ib; e41)	4.5–36 mg
Sodium oxybate (controlled substance prescription required)	EDS, cataplexy (reduced by 90%) Improvement of nighttime sleep (LoE for both Ib; e39, e42)	4.5–9 g/d
Clomipramine	Cataplexy (LoE III; e39, e43)	10–150 mg/d
Venlafaxine	Cataplexy (LoE IV; e39, e44)	37.5–300 mg/d not approved

EDS, excessive daytime sleepiness; LoE, level of evidence

TABLE 5

Medications with somnambulism as a potential side effect (17)*

GABAergic substances	Psychotropic drugs	Antipsychotics	Other medications
Zolpidem	*Amitriptyline*	*Olanzapine*	*Propranolol, metoprolol*
Zopiclone	*Paroxetine, fluoxetine*	*Quetiapine*	*Ciprofloxacin*
Zaleplon	*Mirtazapine, reboxetine*	*Chlorprothixene*	
	Bupropion		
	Lithium		

* "Somnambulism" is a well described side effect of the two common Z-drugs (zolpidem and zopiclone); for the other medications (italics), the available information comes from anecdotic reports. Nighttime eating attacks may also be a symptom.

medical care; as distinct entities, these conditions are outside the scope of this review. About 2% to 7% of adults suffer from obstructive sleep apnea (OSAS); prevalence rates have not yet become available for Germany (10).

Besides excessive daytime sleepiness, OSAS has clinically relevant associations with neurological and psychiatric conditions. The prevalence of OSAS is found significantly increased in psychiatric patients. If left untreated, OSAS can complicate the treatment of depression (e46); on the other hand, excessive daytime tiredness in patients with OSAS is an important differential diagnosis of reduced drive and symptoms of fatigue in patients with depression (e47). Patients with neurological disorders also have relevant comorbidities. Today, OSAS is recognized as an independent risk factor for cardiovascular disease (hazard ratio [HR]: 2.23 for stroke) (e48, e49). It is also a relevant risk factor for the development of atrial fibrillation (HR: 1.55–2.18) (e50) and has a negative impact on survival after stroke (HR: 1.76 for premature mortality) (49). If patients with epilepsy suffer from obstructive sleep apnea, seizure control with medication is significantly more difficult to achieve (e51).

Chief complaint: involuntary sleep-related movements

Involuntary individual movements or movement patterns during sleep are only partially perceived by the patient; in the majority of cases with sleep-related movement disorders, the condition is detected by injuries of the patient or the bedpartner, or by reports of the bed partner. Diagnoses typically associated with motor symptoms are parasomnias (e.g. sleepwalking) and restless legs syndrome. Parasomnias are classified into rapid eye movement (REM) sleep and non–rapid eye movement (NREM) sleep parasomnias. Nocturnal seizures—typically requiring examination in a sleep laboratory or seizure monitoring unit—are the main differential diagnosis of parasomnias (15).

NREM parasomnias

NREM parasomnias, such as sleep (night) terrors (sudden awakening from sleep, frequently associated with crying or screaming) and somnambulism are common (up to 35% and 17%, respectively, depending on age group) (16, e52) and reason to visit a doctor at the time of first manifestation. It can be effectively treated. In this context, protection against self-injury should be ensured (sleepwalkers do not avoid danger with

"somnambulistic confidence") and the sleepers and their families adequately counseled (e53, e54). Commonly, NREM parasomnias start in childhood or adolescence and become less intense or stop in adulthood. Prevalence increases again in the elderly (also drug-induced); such potential drug side effects should be taken into consideration (*Table 5*) (16, 17, e55).

REM sleep behavior disorder

REM-sleep behavior disorder (RBD) is characterized by movements during REM sleep, at times associated with vocalizations (talking, shouting, or screaming). Simultaneously, complex movements may be displayed which are associated with significant risk of injury to self or others. The existing questionnaires on RBD (REM Sleep Behavior Questionnaire, RBDSQ) (18) are not very sensitive, since patients typically miss ("oversleep") their symptoms (e56). Therefore, a third-party medical history and examination in a sleep laboratory are required for a definite diagnosis of RBD. The latter demonstrates the characteristic increase in muscle tone during REM sleep (1). A fact that increases the relevance of RBD is that it is thought to be a precursor to neurodegenerative disease, such as Parkinson's disease or multiple system atrophy (45–81%, depending on the observational period) (19, e57); therefore, it will be of special significance to future treatment studies as a specific early symptom of neurodegeneration (e58). More than 50% of all patients with Parkinson's disease experience RBD, albeit of various severity; treatment should comprise prevention of injuries and pharmacotherapy with clonazepam (0.5–2 mg) or melatonin (2–10 mg).

Restless legs syndrome (RLS)

RLS is one of the most common neurological diseases, but despite its typical symptoms diagnosis is often delayed. With a prevalence of 6% to 9% (female : male 1.5–2 : 1, [e59]), 0.5 to 1% of the general population require pharmacological treatment (e60), especially older and multimorbid patients (e61).

Clinically, RLS is diagnosed based on "four essential criteria" (20):

- Unpleasant sensations (paresthesia, pain, formication) accompanied by an urge to move, usually of the legs
- Typically occurring during periods of rest
- Partially or totally relieved by movement
- Circadian rhythm with worsening in the evening or at night, causing sleep disturbance.

A new fifth criterion ("The symptoms are not explained by another condition") makes the diagnosis more specific. Supportive criteria include response to dopaminergic medication, positive family history, and detection of periodic limb movement during sleep (PLMS); these criteria are unspecific, but occur in up to 80% of patients and can cause the patient to wake up. Many RLS patients primarily complain of disorders of initiating and maintaining sleep and only report the essential criteria when specifically asked about them.

Key messages

- Healthy and disturbed sleep both influence quality of life.
- Disturbed sleep has a significant impact on other conditions.
- The subjective complaints can be classified into insomnia, increased daytime sleepiness, and abnormal behavior during sleep.
- Treatment should address any underlying condition and not be primarily based on the use of sleeping pills.

The validity of the commonly used classification into "primary" and "secondary" RLS is contestable (e62), because the RLS phenotype manifests as the result of an interaction between genetic factors and comorbidities, such as iron deficiency in women as well as chronic kidney disease, heart disease, diabetes, and Parkinson's disease (21). Medications, such as antipsychotics, antidepressants of the selective serotonin reuptake inhibitor (SSRI) type, and possibly steroids and β-adrenergic agonists (asthma treatment) can trigger symptoms of RLS. Typically, exacerbation of RLS is observed with mirtazapine, which is often used as a sleep-promoting treatment by patients with insomnia (e63).

Polysomnography may be required to rule out other sleep disorders or if the diagnosis cannot be established based on the medical history. Moderate to severe RLS should be treated with medication after stopping treatment with any RLS-aggravating drugs. Iron deficiency should be corrected with iron supplementation (level of evidence [LoE] Ia; e64–e65). RLS is treated with dopamine agonists (pramipexole, ropinirole, or rotigotine, LoE Ia) (22), administered in the respective lowest approved doses; alternatively, gabapentin or pregabalin can be used (effective, but not approved for this indication; LoE Ia) (22, 23). Second-line treatments for severe RLS are low-dose prolonged-release opioids; prolonged-release oxycodone/naloxone is approved as a second-line treatment (level Ib evidence) (22, 24, e66).

The greatest challenge in the treatment of RLS is augmentation, an increase in RLS symptoms after an initially good response to dopaminergic medication. Dopaminergic augmentation is characterized by a worsening of the RLS symptoms (after increasing the dose of dopaminergic treatment) which start to occur earlier in the day and spread to other body parts (arms). Augmentation is treated by rigorously reducing the dose of the dopaminergic medication and starting the patient on a combination therapy with other substances (e66).

Conclusion

Due to their significant negative impact on quality of life, sleep-related disorders in neurology and psychiatry

are highly relevant to patients (25, e2). Their presentation is more complex than the symptom of "poor sleep" reported by a patient; thus, when taking the patient's history, specific questions should be asked to reveal symptoms of sleep-related disorders and associated illnesses, such as depression. Properly diagnosed sleep-related disorders respond well to treatment, but require a differentiated therapeutic strategy. However, in Germany, the current structures for healthcare provision do not cover all patients; depending on the diagnosis, some patients (e.g. with insomnia) may miss out as only few specialized centers for the treatment of patients with sleep-related neurological and psychiatric disorders exist in Germany. Thus, it is critical to establish new treatment structures, complementing the existing offering, in the future.

Conflict of interest statement
Prof. Trenkwalder received consultancy fees from Benevolent, Roche, and Novartis. For the preparation of scientific seminars, she received funds from UCB, Grünenthal, and Otsuka. For a research project that she initiated, she received funds from Mundipharma. For the conduct of clinical studies, she received funds from Vifor Pharma.

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Prof. Young received lecture fees from Adboard, Medice, Vanda, and Sanofi-Genzyme. He received reimbursement of meeting participation fees for congresses as well as travel and accommodation expenses from Medice and Vanda. He received fees for preparing continuing medical education events from Medice and Vanda.

Prof. Pollmächer and Prof. Spiegelhalder declare that no conflict of interests exists.

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► **Supplementary material**

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