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Chapter 1

# Sleep Disorders in Parkinson's Disease

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**Abstract**

Sleep disorders in Parkinson's disease (PD) are common. They can develop due to many factors. PD symptoms like rigidity or tremor, some PD medications, restless legs syndrome, depression, nocturia, and degenerative changes in the brainstem can cause sleep disorders in PD. Sleep disorders in PD may occur during the day or at night. Sleep disorders can occur before or during the disease. Sleep disorders can impair patients' quality of life and worsen their symptoms. For this reason, it is very important to recognize these disorders and treat them appropriately. This chapter discusses the clinical features, diagnosis, comorbidities, management, and pathogenesis of sleep disorders in PD under the literature light. At the same time, it describes the most appropriate treatment considerations.

**Keywords:** Parkinson's disease, sleep disorders, rapid eye movement (REM), sleep behavior disorder, insomnia, daytime sleepiness

## 1. Introduction

Parkinson's disease (PD) is a neurodegenerative disease characterized clinically by bradykinesia, resting tremor, postural instability, and rigidity [1]. Parkinson's disease is not only associated with motor symptoms but also with many non-motor symptoms such as sleep disorders, autonomic disorders, olfactory disorders, and psychiatric symptoms [2]. The spectrum of sleep disorders in PD is broad. In PD, the most common sleep disorders include insomnia [difficulty initiating sleep and its associated restless legs syndrome (RLS), as a reason for the difficulty of falling into sleep, sleep fragmentation, or early awakening], excessive daytime sleepiness (EDS), and rapid eye movement sleep behavior disorder (RBD) [2–4]. While most sleep disorders occur in the advanced stages of the disease, RBD and EDS can be observed in the early phase and even in the premotor phase [5]. A study reported that RBD occurred in the premotor phase of the disease in 38% of 29 patients with PD [5]. On the other

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hand, it has been reported that only one in four patients with PD develops RBD before the disease [6]. Sleep disorders, which affect more than half of the PD patients, can significantly affect the quality of life [7]. It has been reported that the prevalence of sleep disorders in patients with PD is 2–3.5 times higher than in healthy controls [6]. In the pathogenesis of sleep disorders in PD, many etiological factors affecting mainly the sleep-related structures play a role [3, 7]. In addition, in the PD, secondary factors that can negatively affect sleep include pharmacological agents (e.g., selective serotonin reuptake inhibitors-SSRI, serotonin-norepinephrine reuptake inhibitors (SNRI)), nocturnal motor symptoms (e.g., akinesia and dystonia), nocturia, depression, cognitive impairment, and pain [3, 7, 8]. Each of the sleep disorders in PD can be seen individually or more than one sleep disorder can be seen in the same patient at the same time [3]. A recent meta-analytic study found that there was a significant overlap of various sleep-related symptoms in the patients with PD [3]. The study reported that the coexisting prevalence of two out of three sleep-related symptoms (EDS, PD-related sleep problems and RBD) was approximately 20%. The coexistence of all these three symptoms is 12.2% [3].

In this chapter, sleep disorders in patients with PD were classified, and their clinical features, pathophysiology, diagnostic assessment, and management were reviewed. First, a diagnosis of each sleep disorder was given separately, and at the end of the chapter, a general assessment of sleep disorders in the PD was given. In addition, the deep brain stimulation (DBS) in the treatment of sleep disorders in PD was processed at the end of the chapter. This chapter only addresses sleep disorders related to PD.

## 2. Classification of sleep disorders in Parkinson's disease

Sleep disorders in PD may occur during the day or at night. In PD, sleep disorders can be classified into three major categories such as abnormal behaviors and events during or around sleep (e.g., RBD), inability to sleep (e.g., insomnia), and EDS (**Table 1**) [6, 8]. These three categories of sleep disorders can be seen separately or together [6].

| Categories | Sleep disorders |
|---|---|
| Parasomnia | REM parasomnias (e.g., RBD) |
| | NREM parasomnias (e.g., sleepwalking, confusional arousals, and sleep terrors) |
| Inability to sleep/sleeping difficulty | İnsomnia |
| | • Initial insomnia (i.e., difficulties initiating sleep) |
| | • Maintenance insomnia (i.e., sleep fragmentation) |
| | • Terminal insomnia(i.e., early awakening) |
| Sleepiness | EDS |

REM: rapid eye movement; RBD: rapid eye movement sleep behavior disorder; NREM: Non-rapid eye movement; EDS: excessive daytime sleepiness.

**Table 1.** Classification of sleep disorders in Parkinson's disease.

## 3. Parasomnias in Parkinson's disease

In PD, parasomnias are quite common, and REM parasomnias are more common than those in NREM [6]. As REM parasomnia in PD, RBD can be seen in near two-thirds of patients [9]. In PD, non-NREM (NREM) parasomnias can include sleepwalking, confusional arousals, and sleep terrors. However, NREM parasomnias are not a frequent cause of sleep disorders in PD [6].

## 4. Rapid eye movement sleep behavior disorder

### 4.1. Clinical features of RBD

Rapid eye movement sleep behavior disorder is a parasomnia characterized by dream-related vocalizations such as screaming, talking, and shouting and/or complex motor movements such as kicking, and punching with episodic loss of atonia during REM sleep [10, 11]. In severe cases, patients may be able to jump out of bed and injure themselves [6]. It has been reported that the prevalence of RBD in PD patients varies from 20 to 72% [9]. However, the most recent meta-analysis revealed that the overall prevalence of RBD symptoms in PD was 23.6% compared to 3.4% in control [12]. In PD, the frequency of RBD in the stages of the disease is reported differently in studies. Although, in PD, RBD is a sleep disorder that can be seen before the disease, it can also occur at the same time or after the disease in the majority of patients [6]. It has been reported that RBD is associated with some specific features such as age, gender, motor sub types, cognition, disease duration, disease severity, antiparkinsonian medication, and autonomic dysfunction in PD patients [9]. It has been known that some of the abovementioned features such as cognitive and autonomic dysfunction in PD patients with RBD are more common than those without RBD. In our study, 57.6% of patients with PD had a clinical RBD diagnosis [13]. The frequency of clinical RBD was unrelated to motor subtypes of PD [13]. However, we found a weak correlation between clinical severity (i.e., the unified Parkinson's disease rating scale-UPDRS and Hoehn–Yahr-HY stage scores) of PD and severity of clinical RBD in the non-tremor dominant-NTD subtype but not in the tremor dominant-TD subtype. In our study, RBD symptoms appeared before motor symptoms in approximately one-third of PD patients with RBD [13].

### 4.2. Diagnosis of RBD in PD

The diagnosis of RBD can be based on a questionnaire or clinical manifestations without confirmation by polysomnography (PSG) [2, 13, 14].Therefore, a detailed history of complex motor behaviors and vocalizations during REM sleep is very important for a clinical diagnosis of RBD. However, for the objective diagnosis of RBD, complex motor behaviors during REM sleep and the presence of REM sleep without atonia should be confirmed by PSG [11]. Additionally, this sleep disturbance should not be better explained by another disorder [11]. PSG can detect increased chin muscle tone (i.e., absence of atonia) by the submental EMG or increased phasic muscle activity by the limb EMG during REM sleep [2, 15]. Thus, PSG is not required for the clinical diagnosis of RBD [13, 14]. It has been reported that a total score of 6 or

higher obtained from 'the RBD screening questionnaire (RBDSQ)' used for the clinical diagnosis of RBD may strongly support (sensitivity = 0.842, specificity = 0.962) the diagnosis [16].

### 4.3. Pathophysiology of RBD in PD

REM sleep is regulated by the brain stem, hypothalamus, thalamus, substantia nigra, basal forebrain, and frontal cortex [17]. The brain stem structures involved in REM sleep include the pedunculopontine nucleus (PPN), retro-rubral nucleus, subcoeruleus/sublateral dorsal nucleus, and medullary magnocellular reticular formation (MRF) [17]. These brain stem structures provide REM atonia by inhibiting the spinal motor neurons through direct and indirect pathways (the reticular formation as an intermediate station inhibiting the spinal motor neurons) [4, 18, 19]. Thus, these two inhibitory pathways play a role in skeletal muscle atonia during REM sleep [4, 18, 19]. The PPN and the retro-rubral nucleus also act as a phasic generator circuitry [18]. It is well known that the PPN/laterodorsal tegmental nuclei (LDN) have both cholinergic activity and non-cholinergic (e.g., GABAergic) activity. So the PPN/LDN also contains glutamatergic and GABAergic neurons [20]. On the other hand, the cholinergic neurons in the PPN/LDN innervate the pontine reticular formation (PRF), MRF, and thalamus [19, 20]. Thus, descending projections of the PPN stimulate the inhibitory interneurons via the reticulospinal neurons and inhibit directly the motor neurons in the spinal cord and modulate the activations of the mesencephalic locomotor region (**Figure 1**) [4, 19, 21, 22]. It has been reported that inhibition of GABA activity in the PPN, an important part of locomotion, results in explosive motor behavior [23]. In addition, the ascending projections to the thalamus from the PPN modulate the *sleep–wake cycle.* It has been reported that RBD emerges as a result of the involvement of the atonia system and locomotor regions [4, 24]. Experimental studies suggest that the locomotor regions are activated during the REM sleep and suppress locomotor activity [24]. Thus, neuronal dysfunction in RBD is mainly in the PPN/LDN and the sublaterodorsal nucleus (SLD)/pre-coeruleus (REM-on areas) directly and indirectly inhibiting the spinal motor neurons (**Figure 1**) [2, 19, 20, 23]. Finally, the PPN/LTD produces both skeletal muscle atonia (together with SLD) and decreased locomotion during REM sleep [4, 19]. As a result, by the degeneration of these neuronal structures involved in the control of REM atonia in RBD in PD, the functions of medullary MRF which is an intermediate station are also significantly affected [4, 17]. In addition, it is clear that the degeneration of the brain stem areas that depress the locomotion during REM sleep also causes the complex motor movements (increasing in locomotion) of the RBD. As a result, loss of function of these brainstem structures regulating REM sleep causes the clinic of RBD to occur (**Figure 1**) [4, 17, 20].

It has been reported that in the first phase of the Braak staging, Lewy body pathology begins at the dorsal motor nucleus of the medulla oblongata. In the second stage, pathology progresses upwards and affects the magnocellular reticular nucleus, sublateral dorsal nucleus, and olfactory structures. The PPN is degenerated by Lewy body pathology in the third phase of the Braak staging [17]. Thus, RBD in PD is caused by Lewy body pathology involving the brain stem structures that play a role in the regulation of REM sleep. It has been reported that there are "REM-on" and "REM-off" zones in the brain stem of the rats [25]. On the other hand, the relationship between hypocretin and REM sleep remains a controversial issue [26, 27].

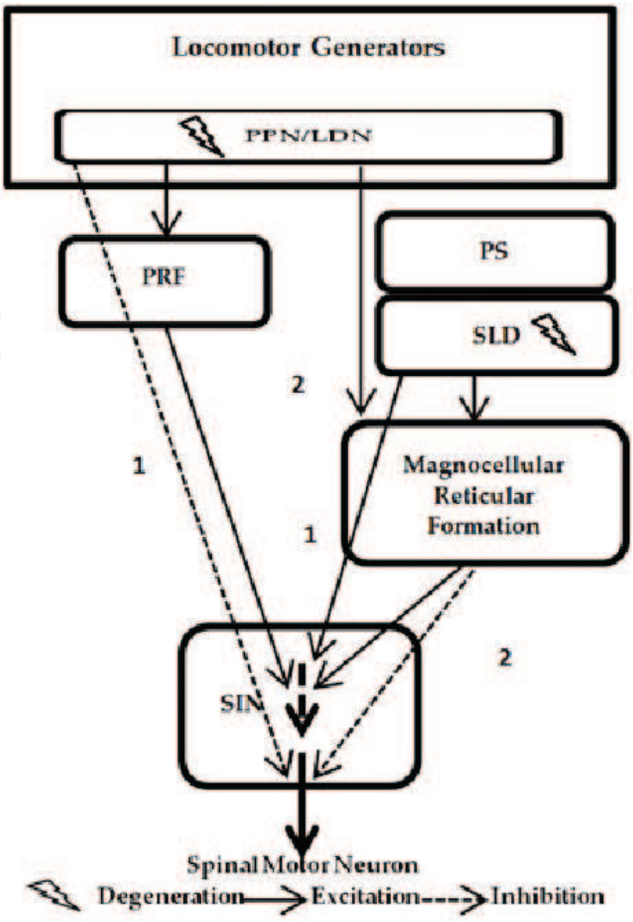


**Figure 1.** Pathophysiology of rapid eye movement (REM) sleep behavior disorder in PD. PD: Parkinson's disease; PPN/LDN: pedunculopontine nucleus/laterodorsal tegmental nucleus; PS: pre-coeruleus; SLD: sublaterodorsal nucleus; PRF: pontine reticular formation; MRF: medullary magnocellular reticular formation; SIN: spinal interneuron. 1. Direct route; 2. indirect route inhibiting the spinal motor neurons via the reticular formation. In REM sleep, muscle atonia occurs following the activation of the medullary magnocellular and the pontine reticular formations inhibiting the spinal motor neurons [4, 19]. There are descending connections from the PPN to the pontine and medullary reticular formations, and the spinal cord. There are also descending connections from SLD to the MRF and the spinal motor neurons. Thus, it may be considered that inhibition of muscle tone arises both from activating the retikülospinal neurons in both the PRF and the MRF of the cholinergic neurons in the PPN and from activating the retikülospinal neurons in the MFR of the neurons in the SLD [4, 19].

A review article reported that hypocretin can stabilize the REM-on and REM-off pontine areas in the brain and can also participate in spinal motor neuron inhibition [25]. A study suggested that decreased hypocretin levels were associated with RBD due to loss of stabilization in the REM regulation of muscle atonia [26].

### 4.4. Treatment of RBD in PD

Currently, the two most commonly used drugs in the treatment of RBD are melatonin and clonazepam. Melatonin is the second choice in the treatment of RBD and is usually an alternative option in patients with sleep apnea or mental impairment. It is recommended to take melatonin between 3 and 12 mg doses before bedtime [17]. The mechanism of action of melatonin

in RBD is still unclear. However, melatonin may resolve RBD-related complaints by decreasing muscle tone during REM sleep [28, 29]. Melatonin has many side effects such as daytime sleepiness, morning headache, and mental deterioration and is usually associated with high doses [17]. Clonazepam is widely used in RBD and doses between 0.25 and 1.0 mg taken before bedtime are sufficient for treating the RBD symptoms [17]. Like melatonin, the mechanisms of action of clonazepam in RBD are not fully clear. However, it has been believed that clonazepam modulates dreaming/complex motor behaviors at supratentorial levels [17]. Clonazepam may worsen symptoms of sleep apnea and mental disorder [30]. It has been reported that the most important side effects of clonazepam are sedation, imbalance, and sexual dysfunction [17]. If these two treatments are not adequately answered or there is a contraindication, rivastigmine, donepezil, pramipexole, and paroxetine may be tried [8]. One study showed that rivastimine significantly reduced the frequency of RBD episodes at the end of the third week in 12 PD patients with classical treatment-resistant RBD [31]. The authors suggest that this effect is related to the peripheral cholinergic action of rivastigmine [31]. In a recent review, it has been reported that there are limited evidences indicating that drugs such as zopiclone, desipramine, clozapine, carbamazepine, and sodium oxybate may be effective in RBD [8].

## 5. Insomnia

### 5.1. Clinical features of insomnia

Insomnia is defined as difficulties initiating sleep (initial insomnia), sleep maintenance problem (i.e., frequent awakenings/sleep fragmentation) or early awakening [2, 6]. In studies, it has been reported that the frequency of insomnia in patients with PD varies from 27 to 80% [32–35]. It has been reported that the most common types of insomnia in PD patients are sleep fragmentation (81%), and early awakenings (terminal insomnia; 40%) [8]. It has been reported that insomnia may occur alone or accompany comorbid mental or systemic illnesses, and it is associated with disease duration and female gender [6]. Sleep fragmentation is defined as a deterioration of sleep integrity (i.e., waking up several times during the night), and it leads to a lighter sleep or wakefulness [2]. In studies, it has been reported that sleep fragmentation is the most common sleep disorder (74–88%) in patients with PD [36, 37].

### 5.2. Diagnosis of insomnia in PD

In the diagnosis of insomnia in PD, the clinical history including the stages (defined above) of insomnia and its associated factors are essential. For example, the factors associated with initial insomnia should be learned from the clinical history because the identification of factors associated with insomnia is necessary for the treatment plan. **Table 2** shows the factors associated with insomnia [2, 6]. For example, for the diagnosis of RLS, as a reason for the difficulty of falling into sleep, clinical assessment (sleep history) is sufficient. Thus, patients should be asked for the features in the definition mentioned below for the diagnosis of RLS [6]. In contrast to idiopathic RLS, family history of RLS is less frequent in PD [6]. Polysomnography

and actigraphy can be used to detect the objective findings of the insomnia [15]. It has been reported that insomnia's PSG findings may be an increase in the number of brief EEG arousals—or arousal index, number of stage shifts to stage 1 or wake, wake time after sleep onset (WASO), and percentage of stage 1 sleep [2]. The actigraphic findings of insomnia include the presence of irregularity in sleep onset and increased number of awakening times during the night [15]. One review has been reported that studies comparing PSG to actigraphy in insomnia show that PSG and actigraphy have no significant difference in showing the measurements of WASO, total sleep time (TST), and sleep efficacy [38].

### 5.3. Pathophysiology of insomnia in PD

In the pathogenesis of insomnia in PD, damage of the brain regions associated with sleep has an essential role [6]. In addition to PD pathophysiology, motor symptoms of PD, medications, mood disorders, pain, physical disability (lack of exercise), and poor sleep hygiene are other factors contributing to the pathogenesis of insomnia in PD [6, 8]. Thus, the etiology of insomnia in PD is multifactorial, and it can include intrinsic sleep disorders such as altered dream phenomena, RBD, restless leg syndrome (RLS), and periodic leg movements in sleep-PLMS), PD symptoms such as nocturnal akinesia and rigidity, pain, nocturia, and psychiatric comorbidities such as anxiety, and medications (**Table 2**) [6, 8].

The restless legs syndrome, which is a cause of insomnia (by making sleeping difficult), is characterized by an urge to move the legs typically accompanied by tingling, paresthesia, or unpleasant sensations in the legs, which is worsened during periods of inactivity and improved by voluntary movement [2, 6]. In RLS, symptoms are often worse in the evening or at night [2, 6]. It has been reported that the prevelance of RLS in PD varies from 0 to 50% [6]. It has been reported that there has a role of central dopaminergic depletion in the pathophysiology

| Factors | Initial insomnia | Maintenance insomnia |
|---|---|---|
| Psychiatric comorbidities | Depression and anxiety | Depression and anxiety |
| Intrinsic sleep disorders | RLS | RBD |
| Medications | Selegiline, amantadine, caffeine, SSRI | Excessive dopaminergic therapy |
| Sleep-related movement disorders | RLS, painful leg cramps | Periodic leg movements |
| Pain | Back pain | Dystonia-related pain |
| PD symptoms | Annoying tremor | Nocturnal akinesia/difficulty turning right and left in bed |
| Others | Non-motor fluctuations, systemic illnesses | Nocturia, systemic illnesses |

PD: Parkinson's disease; RBD: rapid eye movement sleep behavior disorder; SSRI: selective serotonin reuptake inhibitors; RLS: restless legs syndrome.

**Table 2.** Factors associated with insomnia in PD.

of both RLS and PD [2]. On the other hand, it has been reported that the most common causes of wakings during the night are nocturia and difficulty turning right and left in bed [6]. Studies have shown that the frequency of sleep fragmentation in PD is related to the clinical severity of the disease, as evidenced by the UPDRS and Hoehn and Yahr (HY) scales [39, 40].

### 5.4. Treatment of insomnia in PD

The first step in the treatment of insomnia must be to determine the type (i.e., initial, of maintenance, or terminal) of insomnia and the possible factors affecting it such as medications that can cause insomnia [2, 8]. A treatment plan should then be made. For example in initial insomnia, behavioral therapies such as photo therapy, sleep hygiene measures, relaxation, and cognitive therapy may be recommended first and medications such as hypnotics (e.g., Zolpidem, eszopiclone-newer benzodiazepine receptor agonist) or sedating anti-depressants (e.g., mirtazapine and trazodone)may be given if necessary [6, 8, 15, 41]. It has been recommended that hypnotics should be avoided in patients with sleep apnea syndrome [15]. In initial insomnia, melatonin receptor agonists such as ramelteon may also be helpful [8, 15]. Sedating anti-depressants may also be used for maintenance insomnia [8]. However, clonazepam (long-acting sedative) taken at bedtime may be a good option for the treatment of maintenance insomnia (i.e., sleep fragmentation) due to PLMS [42]. If insomnia is due to motor disability of PD, evening dose of controlled-release levodopa to prevent immobility improves insomnia [8]. It has been reported that dopamine agonists may influence the subjective symptoms of insomnia [2]. On the other hand, because of central dopaminergic depletion has a role in the *pathophysiology* of both RLS and PD [2], the dopamine agonists (e.g., pramipexole and ropinirole) used in idiopathic RLS can also be recommended in the treatment of RLS in PD [2, 6]. In addition, since dopamine agonists reduce RLS and PLMS, they may be useful in decreasing sleep fragmentation [43]. Although levodopa is effective in RLS, it is not recommended because it causes side effects such as RLS augmentation and morning rebound [44]. If there is an additional symptom associated with RLS, such as pain, treatment options may be include pregabalin, gabapentin, opiates, and benzodiazepines [45, 46]. In PD, PLMS is less common and its frequency increases in the advanced stages of the disease [47].

Atypical antipsychotics are not recommended for the treatment of insomnia without a psychotic disorder [15].

## 6. Excessive daytime sleepiness

### 6.1. Clinical features of EDS

Excessive daytime sleepiness is a chronic or episodic sleepiness seen throughout the day in PD patients [2]. Anxiety and depression, cognitive dysfunction, changes in sleeping habits, changes in circadian rhythm, the side effects of medications that can produce sleep attacks such as dopamine agonists, and concomitant systemic diseases can cause sleepiness [2, 48]. Also these factors can cause fatigue [2]. Studies have reported that EDS is very common in PD. Verbaan et al. [49] found that compared to controls (10%), 43% of PD patients had

EDS. One study found that EDS was related to age and male gender [50]. Also, other sleep disorders such as PLMS, and sleep fragmentation which cause the deterioration of night sleep quality may be the other causes of EDS [6, 15].

### 6.2. Diagnosis of excessive daytime sleepiness in PD

In patients describing the symptoms of EDS, it is very important to determine the level of sleepiness. The Epworth Sleepiness Scale (ESS) is widely used in the evaluation of EDS. Thus, ESS (score greater than 10) is a useful scale for the subjective assessment of sleepiness in patients with EDS [51].The ESS contains eight items, and each item is rated as maximum three points. A higher score means more sleepiness level. In addition, there are objective tests such as multiple sleep latency test (MSLT) and maintenance of wakefulness test (MWT) for assessment EDS. The MWT is evaluation used as a polysomnographic measurement of EDS. The MSLT is measured after a PSG performed in the night to assess nighttime sleep quality and quantity [52]. One study found that the risk (sensitivity 75%) of traffic accidents increased in PD patients with an ESS score greater than 7 [53].

### 6.3. Pathophysiology of excessive daytime sleepiness in PD

It has been reported that there are three main causes of sleepiness in PD; (1) deterioration of night sleep quality, (2) neurodegeneration of sleep–wake-related brain regions, as a result of disease pathology, and (3) the side effects of antiparkinsonian medications [6, 32]. However, many of the abovementioned causes may be related to EDS. For this reason, it is necessary to consider these causes in the diagnosis and treatment of EDS.

### 6.4. Treatment of excessive daytime sleepiness in PD

The first step in the treatment of EDS should be the correction of underlying conditions [8]. For example, it may be useful to treat the conditions that disturb sleep quality at night or to arrange medications that cause daytime sleep episodes. After that, pharmacological treatment options for EDS should be considered. Nonpharmacological treatment approaches (e.g., good sleep hygiene, bright light therapy) can be performed in the treatment of mild to moderate EDS cases [54]. Modafinil is widely used for the symptomatic treatment of EDS, which appears to stimulate catecholamine production [55]. Common side effects of modafinil are insomnia, headache, dry mouth, dizziness, nausea, nervousness, and depression [56]. A review has reported that sodium oxybate and methylphenidate have inadequate evidence that they are effective in the treatment of EDS in PD [8]. Amantadine and selegiline are reported to have an alerting effect [2]. Thus, amantadine and selegiline may be preferentially used in PD patients with EDS.

## 7. Diagnostic assessment of sleep disorders in PD

The history taken from the patient and its neighbors (e.g., partner) is very important in assessing sleep disorders in PD. The type of sleep disorder should be identified in the history, and information about possible related factors should be obtained from the history. In PD, general

and specific scales can be used to investigate the subtype of sleep disorder and to determine its severity. Objective methods can be used to further investigate the diagnosis of these disorders. Further investigative techniques include sleep recording methods such as actigraphy or PSG. Polysomnographic findings of each sleep disorder have been explained in the relevant section. In addition, information about screening scales used in each sleep disorder has been described in the relevant section.

Actigraphy is an electrophysiological device that measures the movements of the patient during sleep by recording from wrist or ankle for many days. Actigraphy evaluates indirectly the circadian sleep–wake patterns [15]. It is especially used in circadian rhythm disorders or insomnia and prolonged daytime sleepiness [15].

## 8. Deep brain stimulation in the treatment of sleep disorders in PD

Studies investigating the effect of DBS in the treatment of sleep disorders in PD patients showed that DBS improved the sleep scales and quality [57–60]. Baumann-Vogel et al. [58] found that subthalamic nucleus (STN) DBS-enhanced subjective sleep quality, reduced sleepiness measured by the Epworth sleepiness scale, and reduced sleep fragmentation shown by actigraphy recordings. However, the authors observed that subthalamic DBS was not improved REM sleep features [58]. Similarly, Cicolin et al. [59] reported that RBD symptoms did not benefit from STN DBS. On the other hand, Chahine et al. [61] reported that STN DBS improved significantly symptoms of RLS in PD patients. The effect of PPN DBS on sleep disorders in PD has been investigated in several studies [57, 62]. One study showed that PPN DBS improved sleep quality and reduced EDS; however, it caused a reduction in REM latency and a relevant increase in REM sleep [57]. In another study, it has been reported that PPN DBS improved the total duration and rate of REM sleep [62]. As a result, DBS seems to be beneficial in the treatment of sleep disorders in PD because it seems to be useful in improving sleep quality. However, large-scale prospective studies are needed to understand the benefits of DBS in the treatment of sleep disorders in PD.

## 9. Conclusion

Sleep disorders in PD are common. In the pathogenesis of sleep disorders in PD, degeneration of the brain regions associated with sleep has an essential role. Sleep disorders in PD can impair patients' quality of life. For this reason, it is very important to recognize and treat sleep disorders in PD. The history taken from the patient and its neighbors (e.g., partner) is the first step in assessing sleep disorders in PD. Sleep scales and objective assessment methods can be used to further investigate sleep disorders. In addition to the type of the sleep disorder, its related factors (i.e., comorbidities) in PD should be determined from the sleep history of the patient. Symptomatic treatment of sleep disorder and correction of factors associated with it should be the next steps. The age of the patient and accompanying diseases should be considered when choosing medical drugs used for symptomatic treatment of sleep disorders.

Side effects of some medicines may be fatal in patients with comorbidities. For example, clonazepam used RBD may worsen symptoms of sleep apnea and mental disorder [30]. Further studies are needed to improve more specific treatments and better understand the pathophysiology of sleep disorders in PD.

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