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Nocturnal Disturbances in Patients with Parkinson's Disease

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1. Introduction

Sleep disturbances are common problems in patients with Parkinson's disease (PD) caused by various factors including nocturnal motor symptoms, psychiatric symptoms, dementia, medication use and circadian cycle disruptions as well as comorbidity with sleep apnea syndrome (SAS), restless legs syndrome (RLS) and rapid eye movement sleep behavior disorder (RBD) (Table 1). As impaired sleep quality and sleep fragmentation due to nighttime problems are associated with daytime motor dysfunction and have a negative impact on the quality of life of the patient (Gómez-Esteban et al., 2010), an intensive and detailed evaluation of nighttime problems is warranted. Patients often may be unaware of sleep disturbances and even neurologists have been reported to fail to recognize sleep disorders in approximately 40% of PD patients (Shulman et al., 2002). Here, we review sleep disorders in patients with PD, mainly focusing on nighttime problems.

2. Sleep disturbances related to Parkinson's disease itself

Impaired sleep architecture and sleep-wakefulness systems are observed in PD as disease related changes. Insomnia in patients with the early stage of disease or in untreated patients may be associated with disease-related sleep disturbances rather than sleep disturbances caused by other factors including motor dysfunction, medication use, neuropsychiatric symptoms and cognitive dysfunction, though non-motor symptoms can occur in the early phase of the disease. Polysomnography (PSG) recordings yield altered sleep structure that is characterized by a reduction in The percentage of slow wave sleep and a decrease in the amount of REM sleep (Petit et al., 2004) caused by the degeneration of cholinergic neurons in the basal forebrain, noradrenergic neurons in the locus ceruleus and serotonergic neurons in the raphe nucleus (N.J. Diederich & Comella, 2003).

Serotonin, acetylcholine and noradrenalin play a role in maintaining wakefulness, and thus, disturbances lead to excessive daytime sleepiness. In some patients with PD, excessive daytime sleepiness and sudden onset of sleep episodes have been associated with a short sleep latency and sleep onset REM period recorded by the multiple sleep latency test (Arnulf et al., 2002). Similar features are observed in narcolepsy, a sleep disorder characterized by severe daytime sleepiness caused by loss of orexin neurons. Loss of orexinergic neurons in the

posterior portion of the lateral hypothalamus (Fronczek et al., 2007) and the reduction of the A10 dopaminergic group in the ventral tegmental area (Rye, 2004) have also been implicated in impaired wakefulness in PD. Further study is required to examine whether impairment of the orexin system accounts for excessive daytime sleepiness in PD and whether decreased orexin levels reflect disease-related changes or secondary compensatory changes resulting from dopaminergic dysfunctions (Baumann et al., 2008; Compta et al., 2009).

Impairment of sleep architecture
Involvement of the cholinergic, serotonergic and noradrenergic systems reduces REM and slow-wave sleep
Impairment of the arousal system (orexin, serotonin, noradrenalin, acetylcholine and dopamine)
Nocturnal motor symptoms
(wearing-off phenomenon, rigidity, akinesia, tremor, medication-related dyskinesia and dystonia)
Psychiatric symptoms including depression and psychosis
Nightmares and vivid dreams
Hallucinations
Cognitive dysfunction
Nocturia
Pain
Medication use
Sleep apnea syndrome
REM sleep behavior disorder
Restless legs syndrome
Periodic limb movement disorder

Table 1. Multifactorial causes associated with sleep disorders in PD

3. Dopamine and sleep

Dopamine has a role in regulating the sleep-wake cycle (Rye & Jankovic, 2002). Biphasic effects of dopaminergic stimulation on sleep have been reported based on animal studies. High doses of D2 agonists reduce slow-wave sleep and REM sleep and increase wakefulness mediated via postsynaptic receptors, whereas low doses of D2 stimulants increase slow wave sleep and induce sleep mediated via presynaptic receptors (Monti et al., 1988). A D1 receptor agonist suppresses the amount of REM sleep in dose-dependent manner and enhanced wakefulness, while D1 antagonists increase REM sleep (Trampus et al., 1991). The study by Qu et al. examined the mechanism by which modafinil increases wakefulness. They found that the pretreatment of D2 receptor knockout mice with a D1 receptor antagonist completely abolished the arousal effects of modafinil, strongly indicating that dopaminergic D1 and D2 receptors are essential for the wakefulness induced by modafinil (Qu et al., 2008). The involvement of dopamine systems in the mesocorticolimbic and striatal systems in conjunction with dopaminergic therapy further complicates the role of dopamine in PD sleep disturbances.

4. Nocturnal motor problems

Nocturnal disturbances have been reported in up to 98% of patients with PD (Lees et al., 1988). Disturbances include rigidity, tremor, dystonia, akinesia, nightmares, hallucinations, muscle cramps and nocturia. These symptoms result in frequent nocturnal awakenings that contribute to sleep maintenance insomnia, a common form of insomnia in PD (Chaudhuri et al., 2002; Factor et al., 1990; Lees et al., 1988; Suzuki et al., 2007; Tandberg et al., 1998). Sleep onset insomnia can be seen in PD, but it does not seem to account for the majority of insomnia in PD when compared with age-matched controls. In a community-based sleep study, sleep onset insomnia, sleep maintenance insomnia and early awakening were observed in 31.8%, 38.9% and 23.4% of PD patients compared with 22%, 12% and 11% of healthy controls, respectively (Tandberg et al., 1998). The frequency of sleep onset insomnia was not significantly different between the groups. Identification of the nature of nocturnal motor symptoms and the appropriate treatment (e.g., an increase or reduction in the amount of dopaminergic drugs) can improve nocturnal disturbances. A further tool is necessary for assessing nighttime disabilities related to PD. Although PSG is considered to be the gold standard in the assessment of sleep disorders because it provides information about the patient's actual sleep status, including sleep efficiency, sleep latency and sleep structure and can detect SAS, RBD or RLS, several questionnaires have been developed to address insomnia or daytime sleepiness in the general population (the Pittsburgh Sleep Quality Index, or the Epworth sleepiness scale, ESS) (Buysse et al., 1989; Johns, 1991).

4.1 Parkinson's disease sleep scale

Chaudhuri et al. developed the Parkinson's disease sleep scale (PDSS) (Chaudhuri et al., 2002), a visual analogue scale that assesses 15 PD-related nocturnal symptoms of nocturnal disability in PD. This scale is now regarded as a recommended, reliable scale (Högl et al., 2010). The scale includes the following: overall quality of night's sleep (item 1); sleep onset and maintenance insomnia (items 2 and 3); nocturnal restlessness (items 4 and 5); nocturnal psychosis (items 6 and 7); nocturia (items 8 and 9); nocturnal motor symptoms (items 10-13); sleep refreshment (item 14); and daytime dozing (item 15). It has been validated and used extensively in a number of countries with high reliability (Abe et al., 2005; Margis et al., 2009; Martinez-Martin et al., 2004; Suzuki et al., 2007; Wang et al., 2008). Their study found that patients with advanced disease had more severe nocturnal disabilities when compared to patients with early or moderate disease. Our multicenter study also revealed more severe nocturnal disturbances measured by PDSS in patients with advanced PD [Hoehn & Yahr (H&Y), stage IV] when compared to those with early and moderate PD (H&Y, stages I -III). The characteristics of sleep disturbances in PD were distinguishable from that in the control subjects (Figure 1A and B). Sleep disturbances were associated with disease duration, depressive symptoms and complications with dopaminergic treatment (dyskinesia and wearing off) (Suzuki et al., 2007). However, it has been shown that although nocturnal symptoms assessed by PDSS, such as nocturia, nighttime cramp, dystonia and tremor, were more severe in advanced PD patients, they could also be observed in untreated or early stage PD patients when compared with control subjects (Dhawan et al., 2006). This suggests that nocturnal disturbances can develop in the early stages of PD, even when the patients are untreated and exhibit only mild motor symptoms. Thus, nocturnal problems can be treated with dopaminergic treatments.

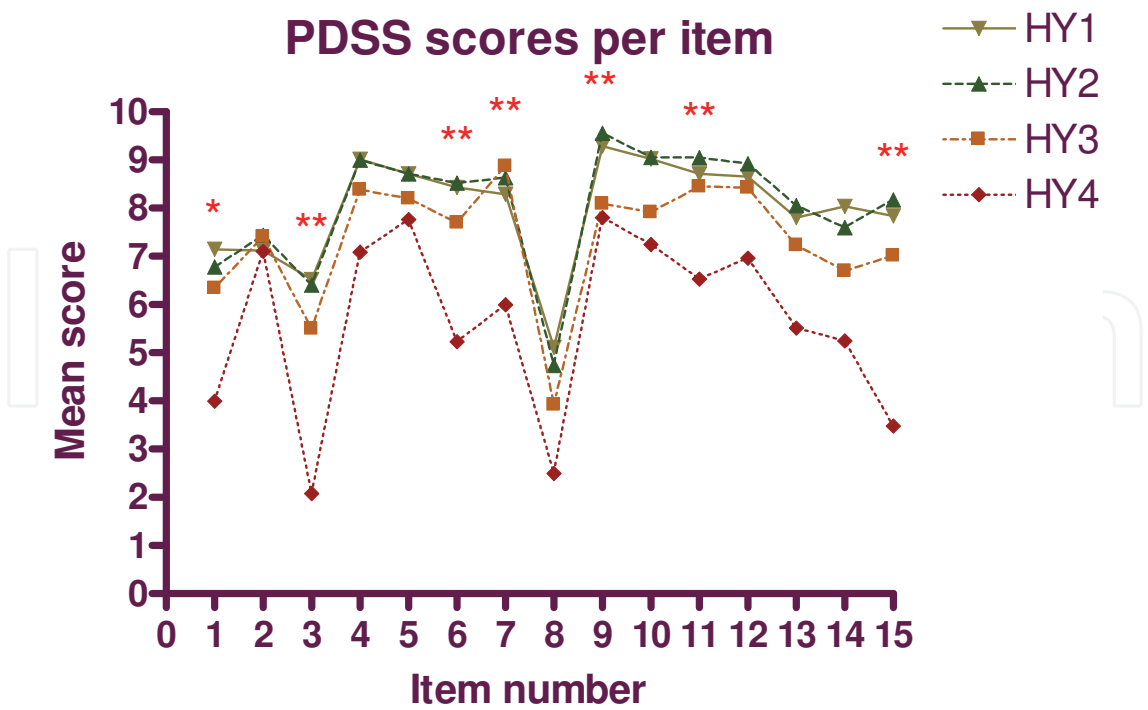


Fig. 1A. Profiles of the mean PDSS scores of each item according to the stage of the disease as defined by H&Y. There were highly significant differences between H&Y Stage 4 and H&Y Stages 1-3 for item 3 (sleep maintenance insomnia), item 6 (distressing dreams at night), item 11 (painful muscle cramp) and item 15 (falling asleep unexpectedly).



Fig. 1B. Profiles of mean PDSS scores for each item in PD and control patients. The most severe ratings in both groups were found for sleep maintenance insomnia (item 3) and nocturia (item 8). With the exception of item 2 (sleep onset insomnia), item 11 (painful muscle cramp) and item 14 (tiredness and sleepiness after waking in the morning), PDSS scores of patients with PD were significantly lower when compared to healthy subjects.

4.2 Parkinson's disease sleep scale-2

Importantly, the PDSS does not screen for sleep apnea syndrome (SAS). Recently, a modified version of PDSS, PDSS-2, has been published and is shown to have excellent validity and reliability (Trenkwalder et al., 2011b). The item regarding unexpected daytime sleepiness was removed because it can be caused by numerous factors in PD, and a new item to screen for SAS was added. Three aspects of sleep problems can be obtained by factor analysis: sleep-specific disturbance, such as sleep onset and the maintenance insomnia, unrestored sleep in the morning, getting up to pass urine and the overall quality of sleep; PD-specific nocturnal motor symptoms at night, such as akinesia, early morning dystonia, tremor during waking periods at night, periodic limb movements, restless behavior and motor symptoms probably due to RBD; and PD-specific nocturnal non-motor symptoms, such as hallucinations, confused states, pain, difficulty breathing with snoring and immobility. A recent study assessing the effect of rotigotine, a non-ergot dopamine agonist with 24-hour transdermal delivery, on early morning motor function and sleep have shown that rotigotine administration improved motor abilities as assessed by the Unified Parkinson Disease Rating Scale (UPDRS) motor score and sleep problems as assessed by PDSS-2 (Trenkwalder et al., 2011a). In clinical practice, the use of both ESS and PDSS-2 would be useful for assessing daytime sleepiness and nighttime problems in PD.

5. Motor symptoms at night

Importantly, disabling motor symptoms, such as akinesia, resting tremor and rigidity, occur not only during the daytime but also during the nighttime. Patients in the advanced stages of the disease are likely to have motor dysfunction throughout the day, but some patients, especially those in the early stages of the disease, may predominantly have nighttime motor problems (Dhawan et al., 2006). This is supported by the results of several studies showing a weak or nonexistent correlation between sleep disturbances and daytime motor symptoms (UPDRS motor score) (Chaudhuri & Martinez-Martin, 2004; Tandberg et al., 1998) and no correlation between nocturnal motor symptoms obtained by PDSS-2 and UPDRS motor score (Trenkwalder et al., 2011b). Kumar et al., however, found a patient's UPDRS motor score to be a significant determinant of sleep disturbances (Kumar et al., 2002).

Nocturnal motor symptoms can result in frequent awakenings at night, which sometimes can contribute to daytime sleepiness. In our previous study, however, PD patients with excessive daytime sleepiness ($ESS \geq 10$) had similar PDSS scores, except for falling asleep unexpectedly (item 15), when compared to those without excessive daytime sleepiness ($ESS < 10$), suggesting that excessive daytime sleepiness is more related to disease related changes and dopaminergic medication use than nocturnal disturbances (Suzuki et al., 2008). When wearing off-related motor symptoms or the worsening of motor symptoms during the night are significant problems for a patient, providing continuous dopaminergic stimulation via a long-acting dopamine agonist at nighttime (Pahwa et al., 2007; Poewe et al., 2007), deep brain stimulation (Arnulf et al., 2000) or an overnight subcutaneous infusion of apomorphine (Reuter et al., 1999) has been reported to be beneficial. For hallucinations, psychosis or medication-related dyskinesia at night, however, reductions in the dose of dopaminergic agents and/or the addition of atypical antipsychotics may help. Amantadine or selegiline can cause frequent nocturnal awakenings, and reducing the dose or changing the time of the administration of these drugs to the morning may reduce nocturnal awakening.

6. Nocturia

Urinary bladder related symptoms, such as frequency, urgency and urge incontinence, are common in PD and can cause frequent nocturnal awakenings. Although nocturia is associated with the normal aging process, 80% of PD patients have had two or more episodes of nocturia per night that were caused by overflow incontinence and a spastic bladder (Lees et al., 1988). These symptoms are attributable to diffuse autonomic dysfunction in PD. Lewy bodies can be found in autonomic regulatory regions, including the hypothalamus, sympathetic (intermediolateral nucleus of the thoracic cord and sympathetic ganglia), and parasympathetic nervous systems (dorsal, vagal, and sacral parasympathetic nuclei) (Micieli et al., 2003). Furthermore, the emergence of lesions in the dorsal vagus nucleus and in other autonomic brainstem centers has been found before the manifestation of motor symptoms related to pathological changes in the substantia nigra (Braak et al., 2003).

Dopaminergic mechanisms also play a role in normal bladder control and overactive bladder. In animal studies, the stimulation of D1 receptors inhibits the micturition reflex, while the stimulation of D2 receptors facilitates the micturition reflex. Therefore, D2 depletion of dopaminergic neurons induces overactive bladder and D1 receptor agonists produce a dose dependent inhibition of the micturition reflex (Winge & Fowler, 2006). In PD models, the beneficial effect of concurrent activation of D1/D2 receptors rather than selective stimulation of D2 receptors has been reported (Yoshimura et al., 1998). Kuno et al. reported that switching from bromocriptine to pergolide improved nocturia, thereby improving sleep status in patients with PD (Kuno et al., 2004). Anticholinergic drugs, such as oxybutinin and tolterodine, are commonly used for detrusor hyperreflexia. The beneficial effect of subthalamic deep brain stimulation on detrusor hyperreflexia has been reported (Seif et al., 2004). When nocturia is related to wearing off symptoms, changing medications to a long-acting dopamine agonist before bedtime can be beneficial. A urologic examination is recommended to rule out underlying urologic diseases.

7. Pain

Pain has been reported in approximately 60% of PD patients (Barone et al., 2009) and is associated with sleep disorders and depressive symptoms (Goetz et al., 1987; Starkstein et al., 1991), in addition to tremor, rigidity, akinesia, dystonia and akathisia. A recent review classified pain into the following categories: musculoskeletal pain, radicular or neuropathic pain, dystonia-related pain, akathitic discomfort and primary central parkinsonian pain (Ford, 2010). Pain is thought to be mediated through medial and lateral pain pathways. However, the pathophysiology of pain perception is not yet well understood. The basal ganglia appear to have an important role for the relay of nociceptive information within the striatum and limbic system (Ford, 2010), and dopamine has been implicated in endogenous pain modulation systems (Potvin et al., 2009). Nocturnal pain is related to nocturnal awakening but not to all sleep disorders. Primary central parkinsonian, akathitic and dystonia-related pain may respond to dopaminergic treatment, and painful symptoms can worsen during wearing off periods. Thus, the appropriate evaluation of pain-related symptoms and managing wearing off-related symptoms during nighttime can improve pain-related sleep disturbances.

8. Hallucinations and psychosis

Hallucinations and psychosis affect 30 to 45% of PD patients treated with levodopa for a long period (Goetz, 1999). Among a wide spectrum of hallucinations, visual hallucinations are commonly seen. Sleep disturbances, daily doses of levodopa, older age, depression and cognitive impairment have been shown to increase the risk for hallucinations in PD patients (Goetz, 2010; Nausieda et al., 1982). A single photon emission computed tomography imaging study showed that PD patients with visual hallucinations had perfusion reductions in the bilateral inferior parietal lobule, inferior temporal gyrus, precuneus gyrus and occipital cortex (Matsui et al., 2006). A ten-year longitudinal study of sleep disorders and hallucinations in PD showed that visual hallucinations were associated with concurrent nightmares, vivid dreams and severe sleep fragmentation. At baseline, no sleep abnormalities at study entry predicted future development of hallucinations in PD patients not currently experiencing hallucinations (Goetz et al., 2010). When reductions in dopaminergic treatments are ineffective, administration of antipsychotics should be considered.

9. Depressive symptoms and nocturnal disturbances

A close link between depression and sleep disorders has been reported in PD (Borek et al., 2006; Happe et al., 2001). Both have a negative impact on the quality of life in PD patients (Gómez-Esteban et al., 2010; Rahman et al., 2008). In a recent systematic review, the prevalence of depression in PD patients varies, ranging from 2.7% to 89% (Reijnders et al., 2008). However, the exact details of nocturnal symptoms that contribute to depression in PD are not well studied. In our multi-center study, depressive symptoms (Zung Self-Rating Depression Scale, SDS score ≥ 40) were present in 64.9% of PD patients, and SDS scores were strongly correlated with PDSS scores (Figure 2A) (Suzuki et al., 2009). Using a regression model, PDSS scores and UPDRS Part I (mental state) were significant determinants of depressive symptoms. However, depressed PD patients showed greater disease severity and more severe motor dysfunction than non-depressed PD patients. Similarly, Chaudhuri and Martinez-Martin reported a significant correlation between PDSS score and depressive symptoms (Chaudhuri & Martinez-Martin, 2004). Compared to patients without depressive symptoms and controls, patients with depressive symptoms had significantly impaired scores in almost all PDSS items except item 2 (difficulty in initiating sleep) and item 11 (painful muscle clamp) (Figure 2B). Surprisingly, there were no significant differences between controls and non-depressed patients in PDSS sub-items, suggesting that depressive symptoms play a pivotal role in developing nocturnal disturbances. Upon detailed evaluation of nocturnal symptoms, early morning tremor and nocturnal dystonia were closely associated with depressive symptoms. This result is in line with the finding that depressive symptoms were exacerbated during periods of time in which patients experienced nocturnal wearing off-related (hypodopaminergic state) motor symptoms (Cummings, 1992). While depression can trigger motor fluctuations, such as the wearing off phenomenon (Lieberman, 2006). Raising awareness of depressive symptoms and the application of appropriate management techniques may improve both depression and sleep disorders in PD patients.

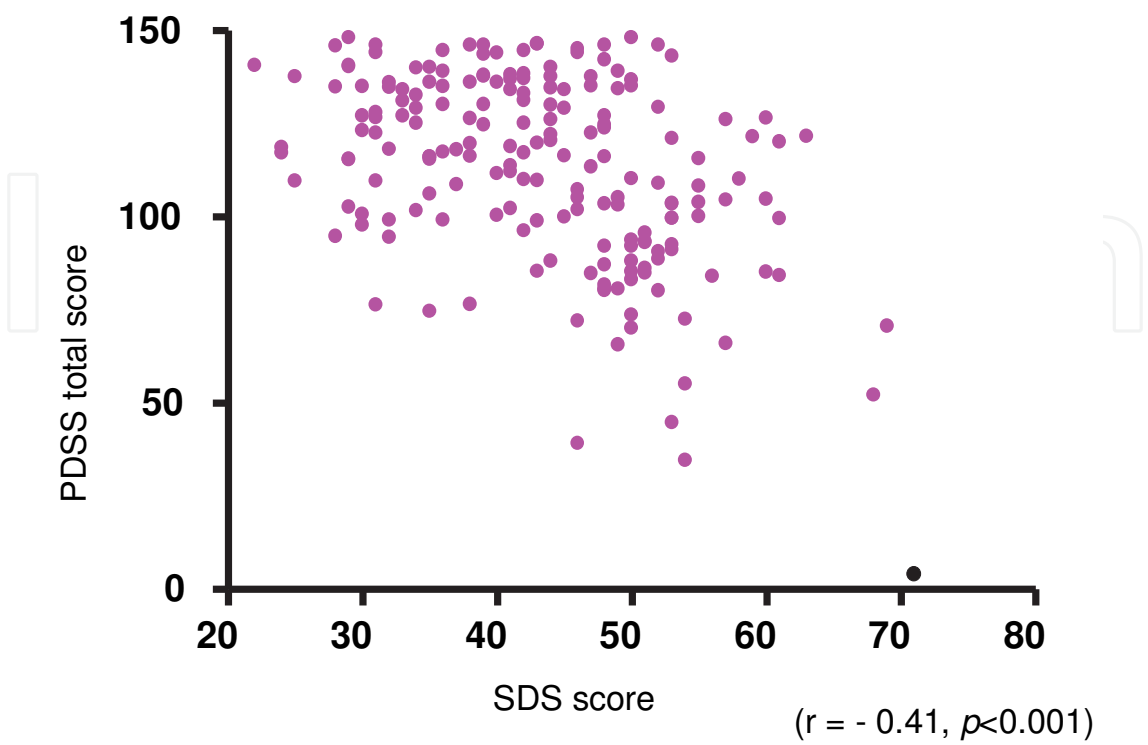


Fig. 2A. Correlation between PDSS total score and SDS score

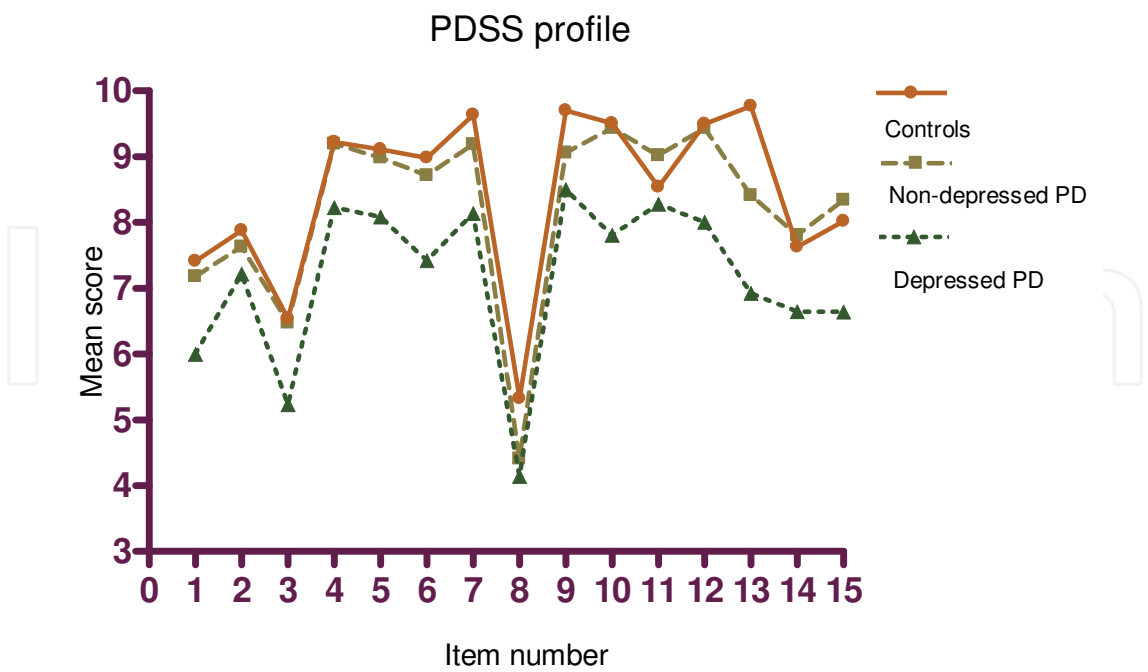


Fig. 2B. Profiles of mean PDSS scores of items in depressed PD (SDS ≥ 40), nondepressed PD (SDS < 40) patients and controls.

10. REM sleep behavior disorder (RBD)

REM sleep behavior disorder (RBD) is characterized by a loss of muscle atonia during REM sleep, enabling patients to act out dreams, often leading to injuries to themselves or their bed partner (Schenck et al., 1986). RBD is likely to affect older individuals and is predominantly seen in males (Olson et al., 2000). Animal studies show that lesions of the locus coeruleus perialpha in cats and the sublaterodorsal nucleus in rats caused REM sleep without atonia and with complex movements (Sastre & Jouvet, 1979). RBD was initially thought to be an idiopathic disorder; however, a study in 1996 by Schenck demonstrated that 38% of 29 patients with idiopathic RBD developed PD within 3.7 ± 1.4 years (Schenck et al., 1996). RBD is associated with neurodegenerative disorders, particularly with synucleinopathies, such as PD, multiple system atrophy and dementia with Lewy bodies (Olson et al., 2000; Postuma et al., 2009; Stiasny-Kolster et al., 2005). Moreover, nonmotor symptoms of PD, such as impaired visual and olfactory discrimination, cardiac sympathetic denervation and cognitive impairment, that often precede the onset of motor symptoms have been found in idiopathic RBD patients (Gagnon et al., 2006; Miyamoto et al., 2006; Miyamoto et al., 2010; Postuma et al., 2010b; Postuma et al., 2006). In RBD, substantia nigra hyperechogenicity (Iwanami et al., 2010) and decreased regional cerebral blood flow in the parietooccipital and limbic lobes and the cerebellar hemispheres (Hanyu et al., 2011) have been found to correspond with alpha synucleinopathies, including PD. As a possible prodromal phase of neurodegenerative diseases, a diagnosis of RBD is crucial for early intervention. Excessive tonic and phasic EMG activity during REM sleep is increased over time in patients with RBD (Iranzo et al., 2009). Postuma et al. reported that the severity of REM atonia loss during baseline PSG can predict the development of PD (Postuma et al., 2010a).

PD patients with RBD exhibited a nontremor predominant phenotype, increased frequency of falls and poor response to dopaminergic medications (Postuma et al., 2008b). However, the overall disease severity, quantitative motor testing and motor complications did not differ between the PD patients with and without RBD. Additionally, the presence of RBD in PD is associated with orthostatic hypotension and impaired color vision but not olfactory impairment (Postuma et al., 2008a). Interestingly, restored motor control (movements, speech and facial expressions) has been observed in PD and in multiple system atrophy patients with RBD during REM sleep (De Cock et al., 2011; De Cock et al., 2007). The mechanism for the improvement of parkinsonism during RBD was unclear but may be due to enhanced dopamine transmission.

RBD can be triggered by antidepressants. Clonazepam (0.5 to 1.5 mg) at bedtime is the most effective treatment for RBD patients. Melatonin (3-12 mg) at bedtime has been shown to ameliorate RBD (Aurora et al., 2010). Administration of 2.5 g of Yi-Gan San, an herbal medication, three times a day, alone or in conjunction with 0.25 mg clonazepam, has also been reported to be effective in the treatment of RBD (Shinno et al., 2008).

11. Restless legs syndromes (RLS)

Restless legs syndrome (RLS) is a sensorimotor disorder associated with an irresistible urge to move the legs, causing insomnia. Symptoms get worse at rest and become apparent in the evening and at nighttime. Some studies have demonstrated a higher rate of RLS comorbidity in PD when compared to the general population (Gómez-Esteban et al., 2007;

Peralta et al., 2010), while the other studies found no difference (Calzetti et al., 2009; Loo & Tan, 2008). Although the pathophysiology of RLS is unclear, central dopaminergic dysfunction has been implicated based on the estimated impairment of A11 dopaminergic nuclei in the hypothalamus and a favorable response to a dopamine agonist. This structure innervates preganglionic sympathetic neurons and the dorsal horn as well as serotonergic pathways and motor neurons in the spinal cord (Walters & Rye, 2009). Iron deficiency also contributes to impairments in dopamine signaling in the brain. Low iron and ferritin levels in cerebrospinal fluid have been found in patients with RLS (Mizuno et al., 2005).

Caffeine, alcohol and some medications, including antihistamines, dopamine antagonists, tricyclic antidepressants and serotonergic reuptake inhibitors, can exacerbate or cause RLS (Ekbom & Ulfberg, 2009). Iron replacement therapy should be considered when serum ferritin levels are lower than 50 µg/L. Dopamine agonists, pramipexole and ropinirole, at bedtime are effective treatments for RLS.

In PD patients, however, nonmotor symptoms related to nondopaminergic systems (e.g., cognitive impairment, autonomic dysfunction, depression and sleepiness), but not motor symptoms, were found to be associated with RLS (Verbaan et al., 2010). Gómez-Esteban et al. found high prevalence of RLS in PD patients but found no difference in disease severity, UPDRS scores or quality of life between groups with or without RLS (Gómez-Esteban et al., 2007). Peralta et al. found a positive association between motor fluctuation, wearing off phenomenon, and RLS symptoms in PD patients but suggested wearing off-induced restlessness can be an “RLS-mimic” (Peralta et al., 2010).

Autopsy studies have shown increased substantia nigra iron levels in PD patients (Morris & Edwardson, 1994) and decreased substantia nigra iron levels in RLS patients (Connor et al., 2003). Interestingly, when comparing PD with and without RLS, transcranial sonography findings demonstrated that there were no significant differences in SN echogenicity, which is considered to reflect the amount of tissue iron content, between the two groups, whereas idiopathic RLS patients showed significant substantia nigra hypoechogenicity (Kwon et al., 2010). This suggests that the pathogenesis of RLS in PD and idiopathic RLS may involve different mechanisms.

12. Sleep apnea syndrome (SAS)

Previous studies reported a high incidence (approximately 40-60%) of sleep apnea syndrome (SAS) in PD patients (N. J. Diederich et al., 2005; Maria et al., 2003). Upper airway muscle dysfunction may have a role in the development of obstructive sleep apnea (Vincken et al., 1984). However, recent studies assessing the prevalence of SAS in PD revealed that the apnea-hypopnea index was not significantly different between PD patients and controls, and the rate of obstructive sleep apnea in PD were similar to that seen in the general population (De Cock et al., 2010; Trotti & Bliwise, 2010). These findings indicate that obstructive sleep apnea may be not a relevant issue in PD. Nocturnal stridor caused by vocal cord abductor dysfunction can develop in patients with PD but more frequently occurs in patients with multiple system atrophy (MSA) (Isozaki et al., 1995). It is important to screen for vocal cord abductor dysfunction with a laryngoscopy during sleep when nocturnal stridor occurs. Treatment, such as continuous positive airway pressure therapy or a tracheotomy, is effective. However, these treatments do not always prevent sudden death in patients with MSA, suggesting a mechanism such as central hypoventilation, other than upper airway obstruction, may play a role (Shimohata et al., 2008).

13. Conclusion

Sleep disturbances in PD are complicated by various factors. We reviewed the current literature regarding nighttime problems in PD. Appropriate evaluation and management of nocturnal motor and non-motor symptoms are essential to improve the patient's quality of life. Importantly, several symptoms are responsive to changes in the dose or timing of dopaminergic medications. Substantial research effort has been made to develop effective treatment for motor symptoms, however, treating non-motor symptoms remains a challenging issue.

14. Appendix

The Parkinson's Disease Sleep Scale (Chaudhuri et al., 2002)

1. The overall quality of your night's sleep is:
2. Do you have difficulty falling asleep each night?
3. Do you have difficulty staying asleep?
4. Do you have restlessness of legs or arms at night or in the evening causing disruption of sleep?
5. Do you fidget in bed?
6. Do you suffer from distressing dreams at night?
7. Do you suffer from distressing hallucination at night (seeing or hearing things that you are told do not exist)?
8. Do you get up at night to pass urine?
9. Do you have incontinence of urine because you are unable to move due to "off" symptoms?
10. Do you experience numbness or tingling of your arms or legs which wake you from sleep at night?
11. Do you have painful muscle cramps in your arms or legs whilst sleeping at night?
12. Do you wake early in the morning with painful posturing of arms or legs?
13. On waking do you experience tremor?
14. Do you feel tired and sleepy after waking in the morning?
15. Have you unexpectedly fallen asleep during the day?

Scores for a given individual item range from 0 to 10: 10 represents the best, 0 represents the worst score. For question 1: Awful = 0, Excellent = 10. For question 15: Frequently = 0, Never = 10. For the remainder of the questions: Always = 0, Never = 10.

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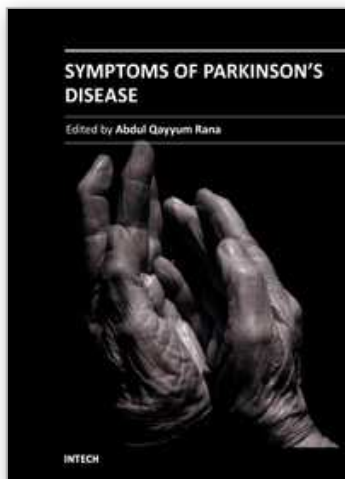
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This book about Parkinson's disease provides a detailed account of various aspects of this complicated neurological condition. Although most of the important motor and non-motor symptoms of Parkinson's disease have been discussed in this book, but in particular a detailed account has been provided about the most disabling symptoms such as dementia, depression, and other psychiatric as well as gastrointestinal symptoms. The mechanisms responsible for the development of these symptoms have also been discussed. Not only the clinicians may benefit from this book but also basic scientists can get enough information from the various chapters which have been written by well known faculty.

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