REVIEW

Sleep-related problems of Parkinson’s disease

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Abstract

Objective: to define the epidemiology, characteristics and aetiology of nocturnal symptoms and sleep disorders in patients with Parkinson’s disease (PD) and evaluate the available methods for their diagnosis and management.

Methods: a review of the English-language literature pertaining to sleep disturbances associated with PD, using the Medline database and bibliographies in relevant articles.

Results: sleep-related problems specific to PD may occur early and even predate the diagnosis of the disease but are generally more frequent and more severe in patients with advanced PD. These problems can seriously compromise patients’ quality of life and lead to impaired functioning in daily activities. Scales designed specifically for the assessment of sleep problems in patients with PD have recently been developed. Evidence base for the treatment of sleep disturbances in PD is poor, and only nocturnal akinesia, excessive day-time sleepiness and rapid eye movement behaviour disorder have been partially addressed.

Conclusions: sleep disorders associated with PD are a common and under-recognised problem. The assessment of sleep should be part of the routine evaluation of patients with PD, and large-scale controlled therapeutic trials are necessary.

Keywords: Parkinson’s disease, sleep disorders, dopaminergic therapy, elderly

Introduction

The documentation of sleep-related problems associated with Parkinson’s disease (PD) dates as far back as James Parkinson’s original monograph about the disease: ‘His attendants observed, that of late the trembling would sometimes begin in his sleep, and increase until it awakened him: when he always was in a state of agitation and alarm’ [1]. However, it is only recently that sleep disturbances related to PD have received much diagnostic and therapeutic attention, and there have been a large number of relevant reviews and research publications. A particular reason for maintaining or improving the quality of sleep is the observation that sleep may temporarily improve the motor symptoms of PD [2–4].

Epidemiology and symptoms

As many as 98% of patients with PD may suffer at some time from nocturnal symptoms that can disturb their sleep [2]. A community-based study reported 60% of patients with PD (144 of 239) with sleep problems, compared with 33% of healthy controls (33 of 100) with the same age and sex distribution [3], whereas Karlsen et al. [4] reported that 64% of patients with PD had a sleep disorder, compared with 33% of controls. A recent study in 123 PD patients across all age groups and 96 age-matched controls using a newly validated non-motor questionnaire for PD (NMSQuest) reported that sleep problems such as restless legs syndrome (RLS), excessive day-time sleepiness and rapid eye movement (REM) behaviour disorder (RBD) were highly significantly more common in PD patients compared with those in controls [5].

Sleep disturbances may be grouped into four broad categories: insomnia, motor, urinary and neuropsychiatry problems (Table 1) [6]. In PD, sleep architecture studies show reduced total sleep time and sleep efficiency, sleep arousals and fragmentation, while patients may also have circadian variation of symptoms and can be classified into the ‘morning
better’, ‘morning worse’ and a non-affected group [6, 7]. Excessive day-time somnolence (EDS) may be a cause or effect [8].

### Rapid eye movement behaviour disorder

RBD was first reported by Schenck et al. in 1986 [9, 10]. RBD is a parasomnia that has a population prevalence of 0.5% and characterised by the loss of the normal skeletal muscle atonia during REM sleep. During REM sleep, patients enact their dreams which can be vivid or unpleasant and partners report vocalisations (talking, shouting and vocal threats) and abnormal movements (arm/leg jerks, falling out of bed and violent assaults). Although clinical history may suggest a diagnosis, confirmation can be obtained by a single night of polysomnography with video telemetry—demonstrating increased EMG activity during REM sleep. In a study using polysomnographic recordings and a structured clinical interview, RBD was diagnosed in 11 of 33 consecutive patients with PD. Approximately one-half of the RBD cases would not have been identified by the clinical interview alone [11, 12]. Symptoms of RBD may often predate the diagnosis of PD; Schenk et al. reported that in 11 of 29 men (38%) 50 years or older in whom idiopathic RBD was diagnosed, a parkinsonian disorder was identified after a mean interval of 3.7 ± 1.4 (SD) years following the diagnosis of RBD and 12.7 ± 7.3 years after the onset of RBD [13]. This concept is consistent with the recent hypothesis of Braak and colleagues [14] who suggest that the pre-clinical stages 1 and 2 of PD start at the olfactory and medullary area of the brainstem. Although the pathological basis of RBD is unknown, speculation is that RBD is related to the degeneration of lower brainstem nuclei like the pedunculopontine and subcoeruleal nucleus [15, 16]. A study has suggested an increased risk of developing PD in individuals who have RBD and olfactory disturbance [17].

### Excessive day-time sleepiness and sudden onset of sleep

Excessive day-time sleepiness (EDS), a common complaint of patients with PD [6–8], affects approximately 15.5% of these patients compared with only 1% of healthy age-matched controls [3]. A combination of the disease process, the effect of poor nocturnal sleep and anti-parkinsonian or other drugs may be causative (Table 2). EDS manifests in many ways, and while some patients may feel sleepy and slowly drift off to sleep, others may have rapid-onset sleep without any preceding drowsiness resembling narcolepsy [18, 19]. Excessive day-time sleepiness can occur early in PD [20], may predate the diagnosis [21] and, left untreated, can result in poor attention and memory and predisposition to accidents [22, 23], and needs to be differentiated from fatigue. ‘Sleep attacks’ related to the dopamine agonists pramipexole and ropinirole have been controversially reported to lead to road traffic accidents [24], but recent reviews suggest that ‘sleep attacks’ are not drug specific but rather a class effect of all dopamine agonists used to treat PD as well as dopaminergic agents such as levodopa [22–26]. Furthermore, the terminology of ‘sleep attack’ is discouraged, the proper term used being ‘sudden onset of sleep’.

### Restless legs, periodic limb movements and sleep-disordered breathing

Both drug-naïve and drug-treated PD patients may develop a syndrome of nocturnal restlessness resembling RLS and

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**Table 1. Causes of night-time sleep disruption and day-time sleepiness in Parkinson’s disease** [adapted from 6]

<table>
<thead>
<tr>
<th>Disease related</th>
<th>Insomnia</th>
<th></th>
<th>Motor function related</th>
<th>Akinesia (difficulty turning)</th>
<th>Restless legs</th>
<th>Periodic limb movements of sleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urinary difficulties</td>
<td>Nocturia</td>
<td></td>
<td></td>
<td></td>
<td>Nocturia with secondary postural hypotension</td>
<td></td>
</tr>
<tr>
<td>Neuropsychiatric/parasomnias</td>
<td>Depression</td>
<td>Vivid dreams</td>
<td>Altered dream content</td>
<td>Nightmares</td>
<td>Night terrors</td>
<td>Sleep talking</td>
</tr>
<tr>
<td>Treatment related motor</td>
<td>Nocturnal off-period-related tremor</td>
<td>Dystonia</td>
<td>Dyskinesias</td>
<td>Off-period-related pain/paraesthesia/muscle cramps</td>
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<tr>
<td>Urinary</td>
<td>Off-period-related incontinence of urine</td>
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<tr>
<td>Neuropsychiatric</td>
<td>Hallucinations</td>
<td>Vivid dreaming</td>
<td>Off-period-related panic attacks</td>
<td>REM behaviour disorder</td>
<td>Akathisia</td>
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<tr>
<td>Sleep-altering medications</td>
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</tbody>
</table>

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**Table 2. Possible causes of excessive day-time sleepiness in Parkinson’s disease** [8]

<table>
<thead>
<tr>
<th>Disease related</th>
<th>Advancing disease</th>
<th>Nocturnal sleep disruption</th>
<th>Parasomnias</th>
<th>Depression</th>
<th>Drug therapy related</th>
<th>Dopaminergic therapy in susceptible patients</th>
<th>Anxiolytics</th>
<th>Antihistamines</th>
<th>Hypnotics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment related motor</td>
<td>Nocturnal off-period-related tremor</td>
<td>Dystonia</td>
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<tr>
<td>Urinary</td>
<td>Off-period-related incontinence of urine</td>
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<td>Sleep-altering medications</td>
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</tbody>
</table>
periodic leg movements (PLM) during sleep, whereas RLS has been reported to occur in PD at a rate twice the normal prevalence of RLS in general population [23, 27, 28].

Sleepy PD patients may also have day-time somnolence because of sleep-disordered breathing, and formal polysomnography will identify sleep apnoea in a considerable number of such patients [29]. Obstructive sleep apnoea may occur in up to 50% of patients with PD with resultant day-time sleepiness and tiredness. Sleep apnoea may co-exist with RLS or PLM or RBD [19, 20]. This is important to diagnose as these patients need specific and targeted treatment.

Other issues

In early, mild PD, a delay in sleep latency may be the only significant finding compared with that in controls, whereas sleep disturbances such as EDS occur most often with more advanced disease [7, 8, 20, 30]. In advanced disease, nocturnal symptoms such as wearing-off, early-morning akathisia, dystonia, freezing and tremor become more troublesome. Nocturia and ‘off’-period-related urinary incontinence complicate sleep pattern in advanced disease.

Depression is common in PD and affects sleep quality causing insomnia [6, 7]. Selegiline may cause sleep-onset insomnia, probably as a result of its amphetamine metabolite, whereas other drugs, such as amantadine and anti-cholinergics, may also produce an alerting effect. The effect of rasagiline on sleep is unclear. Selective serotonin re-uptake inhibitors (SSRIs) may need to be avoided at bedtime, as they may impair sleep onset [7].

Sleep benefit

Sleep benefit implies improvement in mobility and motor state the morning after drug intake at night [7]. This phenomenon is of variable duration (30 min–3 h) and is frequently seen in PD [31]. The mechanism may be due to (i) the recovery of dopaminergic function and storage during sleep, (ii) a circadian rhythm-related phenomenon or (iii) a pharmacological response to dopaminergic drugs [7, 32]. Post-prandial autonomic change may also precipitate tiredness and sleepiness after meals due to shifting of blood to splanchnic circulation [33].

Key differential diagnosis

Issues around sleep-disordered breathing have already been discussed. EDS may need to be differentiated from fatigue, and also post-prandial hypotension in PD may unmask sleepiness and akinesia [6, 7, 33, 34]. Fatigue may be present in up to 43% of PD patients and is usually associated with sleepiness although tiredness is a key feature. RBD may also occur in multiple system atrophy and Lewy body dementia [9, 10].

Bedside/clinic assessment of sleep dysfunction in PD

Since 2002, a 15-question, validated Parkinson’s Disease Sleep Scale (PDSS) has become available (Figure 1) [35]. Available in five languages (English, German, Italian, Swedish and Spanish), the PDSS is the first formal instrument for quantifying sleep problems in PD and can be easily administered at the bedside and has also undergone formal linguistic validation in Italy, Spain and Japan. The PDSS has robust test–retest reliability and good discriminatory power between patients with PD and healthy controls. More recently, Marinus et al. [36] have described the development of the SCOPA-SLEEP Scale. This short, two-part scale assesses night-time sleep and day-time sleepiness and contains non-disease-specific items. It has been validated and appears to be reliable; however, it is not a visual analogue scale and does not address some problems specific to PD such as nocturnal hallucinations, pain, dystonia, tremor and nocturia. Apart from SCOPA-SLEEP Scale, other scales can be used to assess sleep disorders in patients with PD, but they are not comprehensive or disease specific. The Unified Parkinson’s Disease Rating Scale contains only one sleep-related enquiry: ‘Does the patient have any sleep disturbances, for example, insomnia or hypersomnolence?’ The Epworth Sleepiness Scale (ESS), a self-administered questionnaire, is restricted to assessing EDS in eight situations of daily life [4, 30] and does not quantify the types of sleep disturbances that occur in PD. Furthermore, the interpretation of the ESS suffers from cross-cultural differences and uncertain test–retest reliability. The Pittsburgh Sleep Quality Index, although quantifiable, does not specifically address the sleep disturbances of PD such as restlessness of legs, painful posturing of arms or legs, tremors or fidgeting [6, 7]. Other scales including the Stanford Sleepiness Scale and the Karolinska Sleepiness Scale appear to be too short for a comprehensive assessment of sleep problems.

Pathophysiology

The pathophysiology of sleep disturbance in PD is complex, largely unknown and multifactorial. The degeneration of central sleep regulation centres in the brainstem and thalamocortical pathways is implicated. Sleep disturbance may precede motor symptoms, and this probably reflects the degeneration of areas, such as the raphe nucleus (serotonin) and locus coeruleus (noradrenaline), which constitute those pre-clinical stages 1 and 2 of the pathological staging of PD proposed by Braak [14]. These nuclei appear to play a critical role in thalamocortical arousal and the sleep–wake cycle, and their degeneration leads to the disruption of basic REM and non-REM sleep architecture, manifesting as insomnia, parasomnias and hallucinations [8, 18]. The pedunculopontine nucleus and the retro-rubral nucleus have strong influences on REM atonia and phasic generator circuitry and have been implicated in the pathogenesis of RBD [18]. A flip-flop-switch pattern of regulation of sleep–wake cycle has been proposed by Saper [37], suggesting that the brain can be either ‘off’ (asleep by activating the ventrolateral preoptic area, the sleep promoter) or ‘on’ (in quiet wakefulness with the activation of the tuberomammillary nucleus, the wake-promoting area along with locus coeruleus and the raphe nuclei). The internal rhythm between the two switches is regulated by the suprachiasmatic nucleus. Hypocretin 1 (orexin), a hypothalamic peptide, virtually undetectable in narcolepsy, is now thought to have a complex relationship with the dopaminergic systems in the...
basal ganglia and may function as an external regulator of the flip-flop switch promoting wakefulness \[18, 31\]. In PD, dopaminergic dysfunction and neuronal degeneration can destabilise this switch and its regulators, promoting rapid transitions to sleep intruding on wakefulness. However, speculation that dopaminergic medications produce sleepiness by reducing levels of the hypothalamic neuropeptide hypocretin 1, insufficiency of which is implicated in narcolepsy, was not confirmed by studies of cerebrospinal fluid in three patients with PD and excessive day-time sleepiness associated with dopamine agonist use \[38\].

**Treatment**

Evidence base for the treatment of sleep problems and other non-motor symptoms in PD is poor. A recent Movement Disorders Society Task Force publication focused on an evidence-based medicine review of the treatment of PD and listed no trials of dopaminergic agents for the treatment of non-motor symptoms in PD \[39\]. Randomised double-blind trials have only been reported in a small number of patients in PD using modafinil and melatonin (Table 3). Other trials addressing sleep disorders in PD comprise case-series-related observations and open-label trials which provide limited and often inadequate evidence base for treatment.

In spite of these drawbacks, a systematic and pragmatic approach to the treatment of night-time symptoms by careful history taking and use of tools such as the PDSS is important (Figure 2). Examining specific responses on the PDSS can help direct treatment; for example, patients with low scores for questions 10–13, indicating nocturnal motor symptoms, might benefit from an increased dosage of levodopa, combining levodopa with entacapone, using stalevo or treatment with sustained-release levodopa before bedtime. On the contrary, low scores in response to questions 6 and 7, indicating hallucinations, might warrant withdrawal of dopamine agonists or treatment with an atypical antipsychotic or clonazepam if RBD is suspected. A list of possible causes of excessive sleepiness in PD is illustrated in Figure 2. A summary of management strategies for sleep disturbances related to PD is outlined in Table 4.

Prior to pharmacological treatment, good sleep-related advice (sleep hygiene) is always useful. In the UK, the UK Parkinson’s disease society has excellent patient-related

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**Parkinson’s Disease Sleep Scale (PDSS)**

How would you rate the following, based on your experience during the past one week.

(Place a cross at the appropriate point on the line)

1. The overall quality of your night’s sleep is:
   - Awful
   - Excellent

2. Do you have difficulty falling asleep each night?
   - Always
   - Never

3. Do you have difficulty staying asleep?
   - Always
   - Never

4. Do you have restless legs or arms at night or in the evening causing disruption of sleep?
   - Always
   - Never

5. Do you fidget in bed?
   - Always
   - Never

6. Do you suffer from distressing dreams at night?
   - Always
   - Never

7. Do you suffer from distressing hallucinations at night (seeing or hearing things that you are told do not exist)?
   - Always
   - Never

8. Do you get up at night to pass urine?
   - Always
   - Never

9. Do you have incontinence of urine because you are unable to move due to “off” symptoms?
   - Always
   - Never

10. Do you experience numbness or tingling of your arms or legs which wake you from sleep at night?
    - Always
    - Never

11. Do you have painful muscle cramps in your arms or legs whilst sleeping at night?
    - Always
    - Never

12. Do you wake early in the morning with painful posturing of arms or legs?
    - Always
    - Never

13. Do you experience tremor?
    - Always
    - Never

14. Do you feel tired and sleepy after waking in the morning?
    - Always
    - Never

15. Have you unexpectedly fallen asleep during the day?
    - Frequently
    - Never

**Figure 1.** The Parkinson’s Disease Sleep Scale. Numerical scoring is carried out with a transparency that is placed over the printed scale after the patient or the patient’s partner has marked it. Adapted from Chaudhuri \[6\].
literature on sleep dysfunction in PD, fatigue, RLS, hallucinations and others, which is available on request. A hot bath about 2 h before bedtime, hot milk or a light snack at bedtime, handrails in bed and/or satin sheets to enable easier turning in bed, flexible bed times and reclining armchair for some and avoiding stimulants such as tea or coffee at bedtime are useful. Nocturia remains one of the commonest causes of sleep disruption in PD [6, 7]. This needs to be tackled by avoiding diuretics or tea/coffee at bedtime and the use of nasal spray of desmopressin in some patients. Some have suggested the use of combined D2/D1-receptor dopamine agonists such as pergolide, but this has not been established in clinical trials. In cases with the risk of urinary incontinence, condom catheters or a bedside urinal is essential to ensure a good-quality sleep with minimal interruption.

**Nocturnal akinesia**

One goal in the treatment of PD is to achieve 24 h control of PD symptoms with continuous dopaminergic stimulation. Overnight apomorphine infusion has had beneficial effects on nocturnal PD symptoms but is not practical for regular use. Sustained-release levodopa/benserazide significantly ($P<0.016$) improved night-time akinesia (ability to turn around in bed) in a 12-month open-label, non-comparative trial including 15 patients with PD and distressing nocturnal symptoms. Total time awake also significantly decreased from 2.13 to 0.67 h ($P=0.046$) [40]. Open-comparative trials in patients with severe sleep disruption because of motor causes suggest that cabergoline may be superior to levodopa or pergolide, another dopamine agonist in this respect [41, 42]. Trials investigating the efficacy of controlled-release formulations of agents such as ropinirole and rotigotine on nocturnal akinesia are underway.

**Sudden onset of sleep and EDS**

Sudden onset of sleep (sleep attacks) may warrant other measures, and those with high sleepiness scores should be advised to drive cautiously and not to drive alone or for

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**Table 3. List of trials of pharmacological and surgical interventions in sleep disorders in Parkinson’s disease**

<table>
<thead>
<tr>
<th>Drug/intervention</th>
<th>Study design</th>
<th>Patient number/duration</th>
<th>Mean dose</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Akinesia and sleep time</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Levodopa + Benserazide</td>
<td>Open label</td>
<td>15/12 months</td>
<td>CR levodopa (200 mg)</td>
<td>Improved total time awake ($P=0.046$)</td>
</tr>
<tr>
<td>2 Cabergoline</td>
<td>Retrospective, comparative with levodopa CR</td>
<td>25 (CBG) vs 15 (LD)/6 months</td>
<td>CBG (4 mg od) CR levodopa (200 mg)</td>
<td>Reduction of painful dyskinesias, early-morning akinesia ($P&lt;0.05$)</td>
</tr>
<tr>
<td>3 Melatonin</td>
<td>DBPC, crossover</td>
<td>40</td>
<td>Melatonin (50 mg)</td>
<td>Improved total sleep time (10 min, $P&lt;0.05$)</td>
</tr>
<tr>
<td><strong>RBD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Clonazepam</td>
<td>Open label</td>
<td>93/4.5 years</td>
<td>Clonazepam (0.25–1 mg)</td>
<td>RBD treatment completely or partially successful in 87% of patients</td>
</tr>
<tr>
<td>2 Melatonin</td>
<td>Case series</td>
<td>13/14 months</td>
<td>Seven patients on clonazepam (0.5–1.0) + melatonin (3–12 mg); 12 patients on melatonin</td>
<td>Eight patients reported continued benefit with melatonin for 1 year</td>
</tr>
<tr>
<td>3 Pramipexole</td>
<td>Case series</td>
<td>8 (idiopathic RBD and Periodic limb movements)</td>
<td>Pramipexole (1.5–4.5 mg)</td>
<td>Five patients reported reduction in REM sleeptime ($P=0.09$), and percentage of REM sleep ($P=0.07$)</td>
</tr>
<tr>
<td><strong>EDS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Modafinil</td>
<td>DBPC crossover study</td>
<td>15/4 weeks</td>
<td>Modafinil (100 mg 1st week, 200 mg 2nd week)</td>
<td>ESS significantly improved in all patients ($P=0.011$)</td>
</tr>
<tr>
<td>2 Modafinil</td>
<td>DBPC</td>
<td>21/6 weeks</td>
<td>Modafinil (200 mg/day)</td>
<td>Improvement in CGI for change ($P=0.07$) on Modafinil</td>
</tr>
<tr>
<td><strong>DBS</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Subthalamic nucleus stimulation (bilateral)</td>
<td>Five-year prospective study</td>
<td>49/5 years</td>
<td>Patient assessed at 1, 3 and 5 years with and without levodopa</td>
<td>Improved sleep and activities of daily living ($P&lt;0.001$)</td>
</tr>
<tr>
<td>2 Subthalamic nucleus stimulation (bilateral)</td>
<td>Observational study</td>
<td>386/3 months</td>
<td>NA</td>
<td>Decreased day-time somnolence and improved sleep quality</td>
</tr>
<tr>
<td>3 Subthalamic nucleus stimulation (bilateral)</td>
<td>Case–control</td>
<td>5/3 months</td>
<td>NA</td>
<td>Significant improvement in total mean PDSS score</td>
</tr>
</tbody>
</table>

CR, controlled release; DBPC, double-blind placebo controlled; DBS, deep brain stimulation; ESS, Epworth Sleepiness Scale; NA, not applicable; PDSS, Parkinson’s Disease Sleep Scale.
long distances [7, 18]. Dopamine agonists when started should be titrated up slowly especially in older patients, and patients with excessive day-time sleepiness may respond to an alternative agonist. In patients with severe EDS, concurrent medications that may be sedating should be eliminated or reduced. Formal sleep studies may be required in some patients, and in those with a narcolepsy-like phenotype, modafinil (100–400 mg) may be useful. Modafinil, a sleep–wake cycle activator, is non-stimulating and is the only drug which has shown efficacy in improving EDS without detrimental effect on PD when examined in double-blind placebo-controlled trials [43, 44]. A 7-week double-blind placebo crossover study of 200 mg modafinil followed by a 4-week open-label extension (200 and 400 mg) study by Adler et al. [44] showed significant improvement in ESS with modafinil and improvement in clinical global impression scores for wakefulness in the open-label arm. Where EDS is thought to be secondary to the use of dopamine agonists, modafinil may allow the continuation of dopamine agonist therapy.

Neuropsychiatric problems

Depression affects ~40% of patients with PD and may contribute to sleep disturbances [6, 7], necessitating active treatment with sedating antidepressants (e.g. trazodone) or SSRIs. Panic attacks can occur in both ‘on’ and ‘off’ periods and need to be treated accordingly. Successful treatment of the neuropsychiatric problems often leads to the improvement of sleep quality in PD.

RBD and RLS

The treatment of choice for RBD is clonazepam, a benzodiazepine; BDZ, short-acting benzodiazepine; BTX, botulinum toxin therapy; DA, dopamine agonist; ESS, Epworth Sleepiness Scale; OSA, obstructive sleep apnea; PDSS, Parkinson’s Disease Sleep Scale; PLM, periodic limb movements of sleep/resting wakefulness; PSG, polysomnography. Adapted from Chaudhuri [6].
Table 4. Management strategies for symptoms contributing to nocturnal disturbance in Parkinson’s disease [6, 7]

<table>
<thead>
<tr>
<th>Symptom Category</th>
<th>Comorbid Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insomnia symptoms</td>
<td>Lewy body demyelination; multisystem atrophy; progressive supranuclear palsy; restless legs syndrome.</td>
</tr>
<tr>
<td>Non-pharmacologic measures</td>
<td>Use of alcohol, caffeine, and tobacco.</td>
</tr>
<tr>
<td>Pharnmacologic strategies</td>
<td>Clonazepam, temazepam, diazepam.</td>
</tr>
<tr>
<td>Motor symptoms</td>
<td>Use of alcohol, caffeine, and tobacco.</td>
</tr>
<tr>
<td>Non-pharmacologic measures</td>
<td>Use of alcohol, caffeine, and tobacco.</td>
</tr>
<tr>
<td>Pharmacologic strategies</td>
<td>Clonazepam, temazepam, diazepam.</td>
</tr>
<tr>
<td>REM behaviour disorder</td>
<td>Clonazepam, pramipexole, melatonin.</td>
</tr>
<tr>
<td>Neuropsychiatric symptoms</td>
<td>Consider alternative diagnosis: MSA, LBD, and PSP.</td>
</tr>
<tr>
<td>Non-pharmacologic measures</td>
<td>Use of alcohol, caffeine, and tobacco.</td>
</tr>
<tr>
<td>Pharmacologic strategies</td>
<td>Quetiapine, atypical neuroleptics.</td>
</tr>
<tr>
<td>Urinary symptoms</td>
<td>Nocturia.</td>
</tr>
<tr>
<td>Non-pharmacologic measures</td>
<td>Reduction of evening fluid intake.</td>
</tr>
<tr>
<td>Pharmacologic strategies</td>
<td>Low-dose amitriptyline.</td>
</tr>
</tbody>
</table>

COMT, catechol O-methyl-transferase; CR, controlled release; LBD, Lewy body dementia; MSA, multisystem atrophy; PSP, progressive supranuclear palsy; RLS, restless legs syndrome.
Sleep disturbances are a key aspect of the non-motor anatomical substrates responsible for the sleep–wake cycle uncontrolled motor symptoms, degeneration of the neurologic system, and under-treated. They may result from recognition in recent years, they remain under-treated. Sleep disorders in patients with PD are common, and in particular Parkinson’s disease (PD). Pathophysiological and observational studies will also help devise better treatment strategies for nocturnal parasomnias such as RBD, RLS and sleep-disordered breathing. Currently, apart from a few small trials addressing EDS in PD, there are no robust trials addressing the treatment of various sleep disabilities in PD. In terms of evidence base of treatment, therefore, robust double-blind randomised trials specifically investigating sleep dysfunction in PD are required, and some related to nocturnal akinesia using oral or non-oral formulations of dopamine agonists are already planned.

The future

Research into the causation and treatment of sleep dysfunction in PD is required. A key area of interest is to unravel the role of hypocretin and other hormones such as neuronal activity-related pentraxin in the causation of sleep dysfunction (if any) in PD. Pathophysiological and observational studies will also help devise better treatment strategies for nocturnal parasomnias such as RBD, RLS and sleep-disordered breathing. Currently, apart from a few small trials addressing EDS in PD, there are no robust trials addressing the treatment of various sleep disabilities in PD. In terms of evidence base of treatment, therefore, robust double-blind randomised trials specifically investigating sleep dysfunction in PD are required, and some related to nocturnal akinesia using oral or non-oral formulations of dopamine agonists are already planned.

Conclusion

Sleep disorders in patients with PD are common, and in spite of recognition in recent years, they remain under-diagnosed and under-treated. They may result from uncontrolled motor symptoms, degeneration of the neuroanatomical substrates responsible for the sleep–wake cycle or unwanted medication side-effects. Routine assessment of patients with PD should include enquiry regarding the quality of sleep and sleep-related symptoms. The use of simple clinical tools such as the PDSS, SCOPA-SLEEP and ESS offer a subjective, semi-quantitative means not only to assess the presence or absence of sleep disruption but also to guide treatment. Uncontrolled nocturnal motor symptoms may be ameliorated by long-acting dopaminergic agents, whereas other sleep disruptions such as hallucinations or RBD require a different approach. In resistant cases, patients may need to undergo polysomnography and/or multiple sleep latency test so as not to miss sleep-disordered breathing, RBD or secondary narcolepsy. Targeted treatment should result in improved sleep for patients with PD.

Key points

- Sleep disturbances are a key aspect of the non-motor symptom complex of PD and affect health-related quality of life.
- Sleep disturbances occur in over 80% of PD patients and may complicate early or advanced disease.
- Sleep problems are multifactorial and needs systematic assessment using validated tools such as the PDSS that is easy to administer.
- Specific issues such as RBD, obstructive sleep apnoea and restless legs need particular attention.
- Once recognised and categorised, many sleep problems of PD can be treated with targeted therapy such as nocturnal dopaminergic therapy.

References

15. Shouse MN, Siegel JM. Pontine regulation of REM sleep components in cats: integrity of the pedunculopontine tegmentum (PPT) is important for phasic events but unnecessary for atonia during REM sleep. Brain Res 1992; 571: 50–63.
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