Open Access

OBM Geriatrics

LIDSEN Publishing Inc.

Case Report

Sleep Disorders in Older People with Special Focus on Parkinson's Disease

Roy G Beran [1, 2, 3, 4, 5, 6, *]

1. Neurology Department, Liverpool Hospital, Liverpool 2170, NSW, Australia; E-Mail: roy.beran@unsw.edu.au
2. Conjoint Professor, South Western Sydney Clinical School, University of NSW, Sydney, NSW, Australia
3. Ingham Institute for Medical Research, South Western Sydney Area Health Service, NSW, Australia
4. Professor, Griffith University, Southport, Qld, Australia
5. Professor, Chair, Sechenov Moscow First State University, Moscow, Russia
6. Conjoint Professor, Western Sydney University, Sydney, NSW, Australia

* **Correspondence:** Roy G Beran; E-Mail: roy.beran@unsw.edu.au

Academic Editor: Pietro Gareri

Special Issue: Sleep Disorders in Older People

OBM Geriatrics
2022, volume 6, issue 3
doi:10.21926/obm.geriatr.2203204

Received: July 01, 2022
Accepted: September 07, 2022
Published: September 13, 2022

Abstract

This paper examines sleep disorders in older people, focusing on Parkinson's disease (PD). It defines PD and explores those conditions associated with sleep disorders and their relationship to PD. It identifies specific conditions which cause sleep disoders in patients with PD, namely: REM sleep behaviour disorder (RDB) which may be a precursor to PD; obstructive sleep apnoea (OSA) which is very prevalent amongst people with PD; depression and mood disorders which both increase with age and are more common in people with PD; nocturia which increases with age and has a negative impact on those with PD; restless leg syndrome (RLS) which some argue is an accompaniment but others argue against this, due to the relationship to iron metabolism, although both respond to dopamine medications; and

excessive daytime sleepiness (EDS) which completes the picture. The paper offers suggestions to the approach to these conditions and offers suggestions for therapeutic intervention.

Keywords
Sleep disorders; Parkinson's disease; older people; REM behaviour disorder; obstructive sleep apnoea; Restless legs; nocturia

1. Introduction

Health problems rise at an exponential rate with advancing years [1, 2]. With aging comes the impact of cumulative molecular and cellular damage that evolves over time and causes a steady decline in physical and mental capacity which results in enhanced prevalence of diseases and their consequences [3-5]. It follows that problems with sleep are also more prevalent with aging [6, 7].

Conditions that increase with aging and which are also associated with sleep disorders include: Parkinson's disease (PD) [6, 8]; obesity [7, 9]; dementia [10, 11]; Prostatism (be it associated with prostatic cancer [12] or benign prostatic enlargement [13]); hormone imbalance in both women [14] and men [15]; Stroke (be it as consequence of obstructive sleep apnoea (OSA) [16] or from cardiac/embolic causes [16, 17]; and diabetes [18]. This list is far from exhaustive but is sufficient to show that the topic of 'Sleep disorders in older people' encompasses almost all of geriatric medicine and, to do it justice, would dictate a submission that was too vast to be encapsulated in a single paper and would require the preparation of a book, in its own right. That being the case, what follows will focus exclusively on sleep disorders encountered in Parkinson's disease but, in so doing, it will, of necessity, stray into many of the other areas touched upon in the list provided. It will use Parkinson's disease to consider 'Sleep disorders in older people' as many of these sleep disorders are associated with Parkinson's disease.

2. What is Parkinson's Disease?

Idiopathic PD is a clinical diagnosis based on the confirmation of concomitant features of bradykinesia, rigidity, tremor and gait instability and disturbance [19, 20], requiring at least 2 of these 4 features to establish its presence. There are those who believe that Idiopathic Parkinson's disease, in contrast to symptomatic Parkinsonism, is an expression of aging [21], with degeneration of the dopamine producing cells in the substantia nigra which, if ignored, leads to the wasting of the relevant receptors which translates to the late introduction of therapy, with L-Dopa, being problematic and thus advocating the very early introduction of pharmacotherapy to obviate subsequent resistance thereto [22, 23].

PD is associated with a host of sleep disorders, including: REM behaviour disorder (RBD) which may predate the diagnosis of PD [24]; OSA [25, 26]; depression and mood disorders [27, 28]; nocturnal motor disturbances [29]; nocturia [30]; restless leg syndrome [31, 32]; and excessive daytime sleepiness, from a variety of causes [33]. Even this list which is specifically related to PD is not exhaustive but it is sufficient to emphasise that PD is associated with many sleep disorders.

3. Rapid Eye Movement (REM) Sleep Behaviour Disorder (RBD)

RBD is a REM sleep phased parasomnia in which the person loses the usual atonia which is associated with REM sleep and [5] he experiences vivid, often frightening dreams that may be accompanied by either simple or complex behavioural disturbances which represent the acting out of those dreams [34, 35]. RBD may be more common in males [35, 36] although some studies have found it equally gender represented [37]. It has been reported to be increased with solvent exposure, head injury and obesity [36] and the use of antidepressant and antipsychotic medications and a history of smoking [36, 37], acknowledging that PD is one of the few conditions said to be less prevalent amongst smoker [38]. RBD and Glucocerebrosidase gene (GBA) gene mutations are both associated with Parkinson's disease [39]. GBA mutations carriers had an OR of 6.24 (10.2% in patients vs. 1.8% in controls, $P < 0.0001$) for RBD and among Parkinson's disease patients, the OR for mutation carriers to have probable RBD was 3.13 ($P = 0.039$) [39]. These results demonstrate that RBD is associated with GBA mutations, and combining genetic and prodromal data may assist in identifying individuals susceptible to PD [39]. While GBA mutations were more common in RBD, no leucine-rich repeat kinase 2 (LRRK2) mutations were found [36]. RBD patients are impaired across a range of clinical measures, consistent with prodromal PD, and suggestive of a more severe nonmotor subtype. Clinical risk stratification has the potential to select higher risk patients for neuroprotective interventions [36]. It is accepted that RBD has a prodromal association with both PD and PD plus (namely dementia with Lewy Bodies (DLB) and Multiple System Atrophy (MSA)) [35] with the vast majority have a α-synucleinopathy [40].

If those who experience RBD are woken during the occurrence they will usually have a full recollection of the dream content but, if allowed to remain 'asleep' during the occurrence, they will have no recollection of either the dream or that which took place during the RBD [35]. The violent behaviour that may occur in RBD may include hitting, kicking or even attempted strangulation with vocalisations including screaming, shouting or even laughing [34, 41]. In one study, a third of patients with RBD injured themselves and two thirds injured their sleeping partner [41]. There has been an English case in which a man killed his wife, during RBD, and was considered to be innocent, due to the RBD, which excluded the involvement of a guilty mind (*mens rea*) or guilty act (*actus rea*) [42].

There is a strong association between RBD and neurodegenerative disease, especially PD, in which the first manifestations of PD may be the RBD, necessitating careful follow-up of any patients presenting with RBD [41]. While routine neuroimaging, with magnetic resonance and computer tomography, is unlikely to contribute to the evaluation of RBD [41], more sophisticated evaluation, using [^{11}C]DTBZ PET imaging has shown that there is pathology, mainly involving the pontine nuclei [43] but it is unclear if those with RBD and PD have greater affected denervation of striatal dopamine when compared with PD patients who do not exhibit RBD [43]. Valli et al. [43] examined availability of vesicular monoamine transporter 2 (VMAT2) which is an index of nigrostriatal dopamine innervation and reported that those with PD and RBD had lower availability of VMAT2, than did healthy controls, within the putamen, ventral striatum and globus pallidus but not within the substantia nigra or subthalamus. When compared with those who had PD but not RBD, they concluded that VMAT2 and striatal dopamine denervation, in general, may not be a significant contributor to the pathophysiology of RBD in PD patients [43].

The management of RBD has to focus on safety and the protection of both the patient and, where necessary, the sleep partner [35]. Some medications have been implicated, such as clomipramine, selegiline and phenelzine [44]. Clonazepam (Rivotril®) has confirmed efficacy [35, 41] as does melatonin MR [35] although both may exert unwanted adverse effects, such as daytime sleepiness, nocturnal confusion and potential for falls [35]. A recent study of melatonin was negative thereby endorsing clonazepam as the drug of choice [45]. Clonazepam is commenced at a low dosage of 0.25 mg nocte and titrated to need, up to 2gms nocte [35].

4. Obstructive Sleep Apnoea (OSA) and PD

Both OSA and PD become more prevalent with advancing years [46]. Oxidative stress and inflammation have been implicated in the aetiologically of both OSA and PD [47, 48]. There are conflicting data which are contradictory as some studies report an increase of OSA with PD [49, 50] while others dispute the increased co-existence [51, 52]. In a case controlled polysomnographic (PSG) study, in an Asian population, there was reduced sleep and altered sleep architecture in PD patients [52]. Reduced sleep time was associated with advancing age and levodopa (acknowledging that dosages of levodopa often increase with advancing years [53]) [52] but nocturnal arousals, primary sleep disorders and abnormal sleepiness were not increased in the Asian PD patients, raising questions concerning ethnic/genetic factors within this domain [52].

It is argued, by some, that OSA is not a clinically relevant concern with PD [51], claiming that excessive daytime sleepiness may be more related to nocturia and cognitive impairment which also increase with advancing years [54]. Personal clinical experience suggests that there is a significant increase in OSA amongst those with PD although detailed analysis, within a controlled study, suggested that PD patients had: lower sleep efficiency; shorter REM stage; and that the expression of excessive daytime sleepiness (EDS) is multifactorial and responds to clonazepam [50] resulting in less fatigue for PD patients [50], despite sleepiness being a recognised adverse effect of clonazepam therapy [35]. The converse is also advocated, suggesting that sleep breathing disorders, predominantly OSA, seem to be common in PD and those events correlate with the severity of the disease [49].

There is little debate that there remains a place for continuous positive air pressure (CPAP) in the management of those with PD and OSA [55]. CPAP proved effective in patients with PD and OSA leading to reduced arousal index, during 6 weeks follow up [55], and reduced EDS as measured with the multiple sleep latency test [55]. There is also emerging evidence to suggest that OSA is associated with an increase of non-motor symptoms in PD, especially cognitive dysfunction in which OSA may play a pivotal role adding to the groundswell that advocates PSG in patients with PD and early intervention [56].

5. Depression and Mood Disorders in PD

It is almost axiomatic that depression and mood disorders adversely affect sleep, especially restful sleep [57, 58]. It is also said that both depression and PD increase with advancing years [59]. Depression is acknowledged to influence many aspects of PD [59] as well as impact on quality of life of PD patients [59]. Early intervention, to curb the impact of depression and mood disorders, has a positive long term benefit for patients with PD [59]. There exists the argument, following a two decade follow-up study, that depression may even be a very early prodromal symptom of PD or a

causal risk factor [60]. In either case, early intervention, to treat the mood disorders, will have significant benefit on the sleep pattern for people with PD [61].

6. Nocturnal Motor Disturbance in PD

Almost 70% of those with PD report nocturnal disturbances [62]. These nocturnal disturbances may be considered within 4 main categories: 1) PD-related motor symptoms, such as nocturnal akinesia, early-morning dystonia, painful cramps, tremor, and difficulty rolling over in bed; 2) treatment-related nocturnal disturbances; 3) psychiatric symptoms, including hallucinations, vivid dreams, depression, dementia, insomnia, psychosis and panic attacks, some of which have already been described above; and 4) other sleep disorders, as described herein [62]. The nocturnal motor disturbances, encountered by people with PD, such as restless leg syndrome (RLS) and periodic limb movement in sleep (PLMS), may be controlled by dopaminergic medications while others, such as insomnia and EDS, may be improved by reducing the dopaminergic stimulation [62]. It follows that it is imperative for the clinician to critically evaluate both the symptomatology and likely aetiology of the predominant nocturnal disturbance to provide the optimal intervention.

Nocturnal motor disturbance is a common cause for impaired sleep pattern and negative impact on quality of life for people with PD [63]. The appropriate treatment for the nocturnal motor disturbance is determined by the nature and diagnosis of the cause. As stated above, there may be competing factors that underpin the expression of the disturbance and it behoves the clinician to have an open mind and to best ascertain the exact cause, before embarking on the appropriate intervention [63].

7. Nocturia

Nocturia is a prominent cause of disturbed sleep, especially in older men with prostatism and in post menopausal women [64], an age group which encompasses the bulk of those with PD. Nocturia is defined as needing to void at least nightly, during sleep period [64] and is clinically relevant if occurring at least twice nightly [64]. It is reported to affect 28-62% of those aged 70-80 years old [64]. This directly affects quality of life and impedes good quality sleep [64]. The pathophysiology of nocturia is multifactorial and typically is related to polyuria (either global or nocturnal), reduced bladder capacity or increased fluid intake [64].

It is one of the most common non-motor symptoms of PD [64] and has similar causes to those listed for the general community [64, 65]. In exactly the same way, the assessment of patients with PD and nocturia are comparable, requiring proper history and examination, urinalysis and possibly ultrasonography and urodynamic studies to help assess the aetiology for the lower urinary tract symptoms and to exclude concomitant pathologies, such as bladder outlet obstruction [65]. Antimuscarinic medications are the first-line treatment for the overactive bladder; acknowledging that caution is required when using these agents in patients predisposed to cognitive impairment which includes people with PD. Desmopressin is effective for managing nocturnal polyuria [66]. It follows that the management of nocturia, in patients with PD, is an individualised approach depending on a clear understanding of the complete picture [66].

8. Restless Leg Syndrome (RLS)

RLS and PD represent common neurological disorders with debate regarding whether there is an aetiological link between the two [67], there being a common response to treatment with dopaminergic medications [67]. There is evidence suggesting that the nigrostriatal system, primarily involved in PD, is also affected in RLS [67] with a possible association with the parkin mutation genetic link [67]. One of the most conflicting pieces of evidence which may contradict the association is the differing roles of iron for RLS and PD [67]. It is known that elevated iron, in the substantia nigra, contributes to the oxidative stress in PD while RLS is associated with relative iron deficiency [67] in which ferritin levels and iron replacement are used to monitor intervention [68]. PSG may confirm the presence of periodic limb movement in sleep (PLMS) which will also disrupt the sleep pattern and is common in patients with PD but may just co-exist rather than being related [69].

9. Excessive Daytime Sleepiness (EDS)

EDS is a frequent accompaniment of PD [33] and, at times, has almost narcolepsy-like features [33]. Poryazova et al studied 30 consecutive patients with PD, including Epworth Sleepiness Scale (ESS) and the Multiple Sleep Latency (MSL) Test (MSLT), together with video-PSG and, in 3 patients, cerebro-spinal fluid hypocretin-1 levels [33]. They found that >50% had an ESS <10 (17 patients); MSL in the MSLT was <5 minutes in 11 patients (>35%); there was negative correlation between ESS and MSL; none of the 11 with MSL <5 minutes had sleep onset REM patterns; and all 3 hypocretin levels were within the normal range [33]. Those with EDS had higher medication dosages, suggestive of more significant disease, great apnoea scores and had more frequent wearing-off symptoms also suggestive of more advanced PD [33]. They concluded that EDS, in PD, was multifaceted, unassociated with narcolepsy and represented more advanced PD [33].

The approach to EDS is similar to all medical management in that it relies heavily on the taking of a proper history, including examination of issues such as: sleep hygiene; insomnia, from whatever cause; symptoms suggestive of OSA, such as snoring; RBD with vivid dreams or acting out; circadian rhythm changes; emotional status (looking for depression and mood alterations); and asking about RLS or PLMS with uncontrollable impulse to move the legs, either in waking or sleep [32]. Once the diagnosis has been made, appropriate remedies may be adopted, including: light therapy which may improve motor function and depression, in addition to pharmacotherapy; advice on sleep hygiene; and the careful use of dopaminergic drugs and hypnosedatives, where appropriate [32]. There have been very few controlled studies upon which to make informed recommendations for the evidence-based management of sleep-wake disturbances in PD which relies heavily on its management in other areas of the management of sleep disorders [32].

10. Conclusions

PD provides the perfect vehicle with which to assess sleep disorders in older people, especially acknowledging that idiopathic PD is essentially a condition of older people. This review has highlighted the extensive interface between various sleep disorders in people who have PD, including RBD, OSA, mood disorders, nocturia and EDS and has offered some insight into their management.

Author Contributions

The author did all the research work of this study.

Competing Interests

There is nothing to declare.

References

1. Maresova P, Javanmardi E, Barakovic S, Barakovic Husic J, Tomsone S, Krejcar O, et al. Consequences of chronic diseases and other limitations associated with old age–A scoping review. BMC Public Health. 2019; 19: 1431.
2. Dovenmuehle RH, Busse EW, Newman EG. Physical problems of older people. J Am Geriatr Soc. 1961; 9: 208-217.
3. Liguori I, Russo G, Curcio F, Bulli G, Aran L, Della-Morte D, et al. Oxidative stress, aging, and diseases. Clin Interv Aging. 2018; 13: 757-772.
4. Li Z, Zhang Z, Ren Y, Wang Y, Fang J, Yue H, et al. Aging and age-related diseases: From mechanisms to therapeutic strategies. Biogerontology. 2021; 22: 165-187.
5. Franceschi C, Garagnani P, Morsiani C, Conte M, Santoro A, Grignolio A, et al. The continuum of aging and age-related diseases: Common mechanisms but different rates. Front Med. 2018; 5: 61.
6. Wolkove N, Elkholy O, Baltzan M, Palayew M. Sleep and aging: 1. Sleep disorders commonly found in older people. CMAJ. 2007; 176: 1299-1304.
7. Lavoie CJ, Zeidler MR, Martin JL. Sleep and aging. Sleep Sci Pract. 2018; 2: 3.
8. Suzuki K, Miyamoto M, Miyamoto T, Iwanami M, Hirata K. Sleep disturbances associated with Parkinson's disease. Parkinsons Dis. 2011; 2011: 219056.
9. Beccuti G, Pannain S. Sleep and obesity. Curr Opin Clin Nutr Metab Care. 2011; 14: 402-412.
10. Kinnunen KM, Vikhanova A, Livingston G. The management of sleep disorders in dementia: An update. Curr Opin Psychiatry. 2017; 30: 491-497.
11. Rose KM, Lorenz R. Sleep disturbances in dementia: What they are and what to do. J Gerontol Nurs. 2010; 36: 9-14.
12. Sigurdardottir LG, Valdimarsdottir UA, Mucci LA, Fall K, Rider JR, Schernhammer E, et al. Sleep disruption among older men and risk of prostate cancer. Cancer Epidemiol Biomarkers Prev. 2013; 22: 872-879.
13. Chartier-Kastler E, Leger D, Comet D, Haab F, Ohayon MM. Prostatic hyperplasia is highly associated with nocturia and excessive sleepiness: A cross-sectional study. BMJ Open. 2012; 2: e000505.
14. Pengo MF, Won CH, Bourjeily G. Sleep in women across the life span. Chest. 2018; 154: 196-206.
15. Wittert G. The relationship between sleep disorders and testosterone in men. Asian J Androl. 2014; 16: 262-265.
16. McDermott M, Brown DL, Chervin RD. Sleep disorders and the risk of stroke. Expert Rev Neurother. 2018; 18: 523-531.

17. Ferre A, Ribó M, Rodríguez-Luna D, Romero O, Sampol G, Molina CA, et al. Strokes and their relationship with sleep and sleep disorders. Neurologia. 2013; 28: 103-118.
18. Mikołajczyk-Solińska M, Śliwińska A, Kosmalski M, Drzewoski J. The phenotype of elderly patients with type 2 diabetes mellitus and poor sleep quality. Int J Environ Res Public Health. 2020; 17: 5992.
19. Massano J, Bhatia KP. Clinical approach to Parkinson's disease: Features, diagnosis, and principles of management. Cold Spring Harb Perspect Med. 2012; 2: a008870.
20. Marsili L, Rizzo G, Colosimo C. Diagnostic criteria for Parkinson's disease: From James Parkinson to the concept of prodromal disease. Front Neurol. 2018; 9: 156.
21. Beran RG. Is Parkinson's disease truly a disease or simply an indication of a long life. Neurol Neurosurg. 2020; 4: 1-2.
22. Beran RG. What is required when developing a new application for an older medication - Using Parkinson's disease as an example. Nov Appro Drug Des Dev. 2021; 6: NAPDD.MS.ID.555677.
23. Chow-Chuen J, Beran RG. An independent clinical audit of an alternative treatment paradigm for the management of Parkinson's Disease. Clin Neuro Neurological Res Int J. 2019; 2: 180008.
24. Tekriwal A, Kern DS, Tsai J, Ince NF, Wu J, Thompson JA, et al. REM sleep behaviour disorder: Prodromal and mechanistic insights for Parkinson's disease. J Neurol Neurosurg Psychiatry. 2017; 88: 445-451.
25. Yeh NC, Tien KJ, Yang CM, Wang JJ, Weng SF. Increased risk of Parkinson's disease in patients with obstructive sleep apnea: A population-based, propensity score-matched, longitudinal follow-up study. Medicine. 2016; 95: e2293.
26. Shafqat MN, Aadil M, Shoaib M. Sleep apnea leading to Parkinson's disease-an important association. Neuropsychiatr Dis Treat. 2017; 13: 1491-1492.
27. Borek LL, Kohn R, Friedman JH. Mood and sleep in Parkinson's disease. J Clin Psychiatry. 2006; 67: 958-963.
28. Kay DB, Tanner JJ, Bowers D. Sleep disturbances and depression severity in patients with Parkinson's disease. Brain Behav. 2018; 8: e00967.
29. Zuzuárregui JR, During EH. Sleep issues in Parkinson's disease and their management. Neurotherapeutics. 2020; 17: 1480-1494.
30. Batla A, Phé V, De Min L, Panicker JN. Nocturia in Parkinson's disease: Why does it occur and how to manage? Mov Disord Clin Pract. 2016; 3: 443-451.
31. Suzuki K, Okuma Y, Uchiyama T, Miyamoto M, Sakakibara R, Shimo Y, et al. Impact of sleep-related symptoms on clinical motor subtypes and disability in Parkinson's disease: A multicentre cross-sectional study. J Neurol Neurosurg Psychiatry. 2017; 88: 953-959.
32. Bruin VM, Bittencourt LR, Tufik S. Sleep-wake disturbances in Parkinson's disease: Current evidence regarding diagnostic and therapeutic decisions. Eur Neurol. 2012; 67: 257-267.
33. Poryazova R, Benninger D, Waldvogel D, Bassetti CL. Excessive daytime sleepiness in Parkinson's disease: Characteristics and determinants. Eur Neurol. 2010; 63: 129-135.
34. Boeve BF. REM sleep behavior disorder: Updated review of the core features, the REM sleep behavior disorder-neurodegenerative disease association, evolving concepts, controversies, and future directions. Ann N Y Acad Sci. 2010; 1184: 15-54.
35. Hu MT. REM sleep behavior disorder (RBD). Neurobiol Dis. 2020; 143: 104996.

36. Barber TR, Lawton M, Rolinski M, Evetts S, Baig F, Ruffmann C, et al. Prodromal parkinsonism and neurodegenerative risk stratification in REM sleep behavior disorder. Sleep. 2017; 40: zsx071.
37. Haba-Rubio J, Frauscher B, Marques-Vidal P, Toriel J, Tobback N, Andries D, et al. Prevalence and determinants of rapid eye movement sleep behavior disorder in the general population. Sleep. 2018; 41: zsx197.
38. Mappin-Kasirer B, Pan H, Lewington S, Kizza J, Gray R, Clarke R, et al. Tobacco smoking and the risk of Parkinson disease: A 65-year follow-up of 30,000 male British doctors. Neurology. 2020; 94: e2132-e2138.
39. Gan-Or Z, Mirelman A, Postuma RB, Arnulf I, Bar-Shira A, Dauvilliers Y, et al. GBA mutations are associated with rapid eye movement sleep behavior disorder. Ann Clin Transl Neurol. 2015; 2: 941-945.
40. Boeve BF, Silber MH, Ferman TJ, Lin SC, Benarroch EE, Schmeichel AM, et al. Clinicopathologic correlations in 172 cases of rapid eye movement sleep behavior disorder with or without a coexisting neurologic disorder. Sleep Med. 2013; 14: 754-762.
41. Olson EJ, Boeve BF, Silber MH. Rapid eye movement sleep behaviour disorder: Demographic, clinical and laboratory findings in 93 cases. Brain. 2000; 123: 331-339.
42. Morris S. Devoted husband who strangled wife in his sleep walks free from court–Prosecution drops case against chronic sleep disorder sufferer who killed wife during bad dream on holidays [Internet]. London: Guardian; 2009 [cited date 2022 June 30]. Available from: https://www.theguardian.com/uk/2009/nov/20/brian-thomas-dream-strangler-tragedy.
43. Valli M, Cho SS, Uribe C, Masellis M, Chen R, Mihaescu A, et al. VMAT2 availability in Parkinson's disease with probable REM sleep behaviour disorder. Mol Brain. 2021; 14: 165.
44. Hoque R, Chesson Jr AL. Pharmacologically induced/exacerbated restless legs syndrome, periodic limb movements of sleep, and REM behavior disorder/REM sleep without atonia: Literature review, qualitative scoring, and comparative analysis. J Clin Sleep Med. 2010; 6: 79-83.
45. Gilat M, Coeytaux Jackson A, Marshall NS, Hammond D, Mullins AE, Hall JM, et al. Melatonin for rapid eye movement sleep behavior disorder in Parkinson's disease: A randomised controlled trial. Mov Disord. 2020; 35: 344-349.
46. Sheu JJ, Lee HC, Lin HC, Kao LT, Chung SD. A 5-year follow-up study on the relationship between obstructive sleep apnea and Parkinson disease. J Clin Sleep Med. 2015; 11: 1403-1408.
47. Miller RL, James-Kracke M, Sun GY, Sun AY. Oxidative and inflammatory pathways in Parkinson's disease. Neurochem Res. 2009; 34: 55-65.
48. Lavie L. Intermittent hypoxia: The culprit of oxidative stress, vascular inflammation and dyslipidemia in obstructive sleep apnea. Expert Rev Respir Med. 2008; 2: 75-84.
49. Maria B, Sophia S, Michalis M, Charalampos L, Andreas P, John ME, et al. Sleep breathing disorders in patients with idiopathic Parkinson's disease. Respir Med. 2003; 97: 1151-1157.
50. Shpirer I, Miniovitz A, Klein C, Goldstein R, Prokhorov T, Theitler J, et al. Excessive daytime sleepiness in patients with Parkinson's disease: A polysomnography study. Mov Disord. 2006; 21: 1432-1438.
51. De Cock VC, Abouda M, Leu S, Oudiette D, Roze E, Vidailhet M, et al. Is obstructive sleep apnea a problem in Parkinson's disease? Sleep Med. 2010; 11: 247-252.

52. Yong MH, Fook-Chong S, Pavanni R, Lim LL, Tan EK. Case control polysomnographic studies of sleep disorders in Parkinson's disease. PloS One. 2011; 6: e22511.
53. Brooks DJ. Optimizing levodopa therapy for Parkinson's disease with levodopa/carbidopa/entacapone: Implications from a clinical and patient perspective. Neuropsychiatr Dis Treat. 2008; 4: 39-47.
54. Haddad R, Monaghan TF, Joussain C, Phé V, Bower W, Roggeman S, et al. Nocturia in patients with cognitive dysfunction: A systematic review of the literature. BMC Geriatr. 2020; 20: 230.
55. Neikrug AB, Liu L, Avanzino JA, Maglione JE, Natarajan L, Bradley L, et al. Continuous positive airway pressure improves sleep and daytime sleepiness in patients with Parkinson disease and sleep apnea. Sleep. 2014; 37: 177-185.
56. Kaminska M, Lafontaine AL, Kimoff RJ. The interaction between obstructive sleep apnea and Parkinson's disease: Possible mechanisms and implications for cognitive function. Parkinsons Dis. 2015; 2015: 849472.
57. Li M, Cui J, Xu B, Wei Y, Fu C, Lv X, et al. Sleep Disturbances and Depression Are Co-morbid Conditions: Insights from animal models, especially non-human primate model. Front Psychiatry. 2021; 12: 827541.
58. Franzen PL, Buysse DJ. Sleep disturbances and depression: Risk relationships for subsequent depression and therapeutic implications. Dialogues Clin Neurosci. 2022; 10: 473-481.
59. Marsh L. Depression and Parkinson's disease: Current knowledge. Curr Neurol Neurosci Rep. 2013; 13: 409.
60. Gustafsson H, Nordström A, Nordström P. Depression and subsequent risk of Parkinson disease: A nationwide cohort study. Neurology. 2015; 84: 2422-2429.
61. Chikatimalla R, Dasaradhan T, Koneti J, Cherukuri SP, Kalluru R, Gadde S. Depression in Parkinson's disease: A narrative review. Cureus. 2022; 14: e27750.
62. Barone P, Amboni M, Vitale C, Bonavita V. Treatment of nocturnal disturbances and excessive daytime sleepiness in Parkinson's disease. Neurology. 2004; 63: S35-S38.
63. Menza M, Dobkin RD, Marin H, Bienfait K. Sleep disturbances in Parkinson's disease. Mov Disord. 2010; 25: S117-S122. doi: 10.1002/mds.22788.
64. Oelke M, De Wachter S, Drake MJ, Giannantoni A, Kirby M, Orme S, et al. A practical approach to the management of nocturia. Int J Clin Pract. 2017; 71: e13027.
65. Smith M, Seth J, Batla A, Hofereiter J, Bhatia KP, Panicker JN. Nocturia in patients with Parkinson's disease. Mov Disord Clin Pract. 2015; 3: 168-172. doi: 10.1002/mdc3.12279.
66. Rezakhaniha B, Arianpour N, Siroosbakhat S. Efficacy of desmopressin in treatment of nocturia in elderly men. J Res Med Sci. 2011; 16: 516-523.
67. Peeraully T, Tan EK. Linking restless legs syndrome with Parkinson's disease: Clinical, imaging and genetic evidence. Transl Neurodegener. 2012; 1: 6.
68. Trotti LM, Becker LA. Iron for the treatment of restless legs syndrome. Cochrane Database Syst Rev. 2019. doi:10.1002/14651858.CD007834.pub3.
69. Sieminski M, Pyrzowski J, Partinen M. Periodic limb movements in sleep are followed by increases in EEG activity, blood pressure, and heart rate during sleep. Sleep Breath. 2017; 21: 497-503.

Enjoy *OBM Geriatrics* by:

1. Submitting a manuscript
2. Joining in volunteer reviewer bank
3. Joining Editorial Board
4. Guest editing a special issue

For more details, please visit:
http://www.lidsen.com/journals/geriatrics