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Snips from the Journals

Updates in neuropsychiatric manifestations of Parkinson's disease

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Parkinson's disease (PD) is a progressive neurological disorder resulting from the dopaminergic dysfunction in the nigrostriatal system. Apart from its characteristic motor syndrome, PD is associated with a range of neuropsychiatric symptoms, including depression, anxiety, apathy, psychosis, cognitive impairment, and impulse control disorders, which greatly affect the patient's quality of life. Being the second most common neurodegenerative disorder and having a prevalence of approximately 572 cases per 100,000 people at 45 years of age or older, PD has become one of the significant challenges for clinicians (1).

Depression

Depression is one of the most common non-motor disorders in PD, affecting approximately 30-40% of PD patients, which is two to four times higher than that in the general population (2). Depressive disorder is present across all disease stages of PD, also being an important prodromal (pre-motor) syndrome, with a significant impact on the quality of life of the patients. It is associated with longer disease duration, disease severity, and several motor and non-motor symptoms (3).

According to the widely used Unified Parkinson's Disease Rating Scale (UPDRS), there are two motor subtypes of PD: tremor-dominant (TD) and postural instability and gait difficulty (PIGD). Cong et al, 2022, explain in their systematic review that the PIGD subtype has a positive correlation with depression, and the TD subtype does not show such an association (3).

Depression in PD is commonly associated with the non-motor symptoms of cognitive impairment and anxiety, and there is a notable overlap seen with fatigue, apathy, and insomnia. The clinical symptomatology of depression is largely similar to the general population; however, patients with PD feel less guilty, have less self-hatred, and have less loss of libido compared to the general population. Interestingly, in PD, alexithymia (defined as difficulty in identifying, describing, and communicating emotions) and anhedonia (defined as the difficulty in experiencing pleasure in previously pleasurable activities) are two key features noted with depressive disorder (4).

The current evidence on the neurobiology of depression in PD is complex and yet to be fully understood. There are dysfunctions noted in the striatal-thalamic-prefrontal cortex circuit, in the baso-temporal-limbic circuit, and alterations in the brainstem dopaminergic, serotonergic and noradrenergic systems (4). There is also evidence that patients carrying the GBA1 L444P mutation, rather than the LRRK2 G2019S mutation and the SNCA rs356219 polymorphism, were more likely to be depressed (3). In addition to biological mechanisms, psychosocial factors, positive family history of depression, and lower education levels have also been associated with depressive disorder (4).

The pharmacological management of depressive disorder in PD is an area that needs more attention from researchers. According to the most recent update from the 'Evidence-Based Medicine in Movement Disorders Committee', only the dopamine agonist pramipexole and the selective serotonin norepinephrine reuptake inhibitor (SNRI) venlafaxine are labelled as 'efficacious' and 'clinically useful' for the treatment of depression in PD. Other antidepressants, such as tricyclic antidepressants and selective serotonin reuptake inhibitors, have provided some positive results in randomised controlled trials, but the level of evidence collected is not adequate to recommend their use (4). Considering the non-pharmacological management, psychoeducation, support groups, information on self-help, behavioural activation, cognitive behaviour therapy, and involvement and support of family and/or carers have shown modest evidence (4,5).

Anxiety disorders

Anxiety disorders (AD) are a significant non-motor symptom group in PD with high prevalence and impact on patients' quality of life, but the clinical and research interest in this area is lacking. They seem to be more common in PD than in other medical conditions. The commonest ADs known to be associated with PD are generalised anxiety disorder (GAD), panic disorder, social phobia, and unspecified anxiety disorder. However, obsessive-compulsive disorder, agoraphobia, and phobic disorders have also been recorded in PD patients. Like other non-motor symptoms, anxiety also can be present as chronic or episodic (4).

ADs are commonly associated with other non-motor symptoms, mainly depressive disorders, and with sleep disturbances, cognitive impairment, and fatigue. Anxiety is also triggered in freezing gait, motor fluctuations, motor disability, fear of falling, needing help from others, and complications of dopaminergic therapy (4).

Unlike depressive disorder, the prevalence of ADs appears to be more stable throughout the PD course. As with depressive disorder, anxiety can also be observed at the prodromal state of PD. Anxiety is inversely associated with the age of onset of PD, where young-onset PD patients suffer from ADs more than in late-onset PD (4). Prevalence of ADs in PD is estimated to be around 31%, with GAD being the most frequent (14%), followed by social phobia (13.8%), anxiety not otherwise specified (13.3%), specific phobia (13.0%) and panic disorder with or without agoraphobia (6.8%). Thirty-one percent (31%) fulfil the criteria for multiple anxiety disorders (6).

The neurobiology related to anxiety disorders is less researched. As for the depression, the available studies show a linkage to many serotonergic, dopaminergic, and noradrenergic systems along with degeneration, functional alteration, and decreased DAT binding at the amygdala (3,4).

Pharmacological interventions for the ADs in PD have been less researched. The current recommendation is to integrate a multidisciplinary approach with anxiety-specific treatment, dopaminergic therapy optimization, along with non-pharmacological interventions. Dopaminergic therapy optimization assists in reducing the anxiety associated with OFF periods, dyskinesia, and motor fluctuations. There is no evidence to recommend a specific anxiolytic for specific ADs in PD. The non-pharmacological therapies, such as yoga, dance therapy, exercise programs, mindfulness-based interventions, and Cognitive Behavioural Therapy, have shown potential benefits in reducing anxiety in PD (4).

Apathy and fatigue

Apathy and fatigue are two common non-motor symptoms in PD that significantly contribute to functional decline and disability. They are not well studied and often go under-recognised in clinical practice. It can occur as an independent and clinically significant symptom or as a feature of another neuropsychiatric manifestation, such as depression or cognitive impairment. Due to lack of precise diagnostic criteria and the overlapping nature with symptoms of depression and cognitive impairment, the identification of apathy and fatigue as independent clinical entities in PD is challenging.

Apathy denotes a collection of symptoms characterised by reduced interest and motivation in goal-oriented activities, indifference, flattened affect, and lack of emotional responsiveness (7). This typically manifests as a lack of spontaneous engagement or early withdrawal from activities, a lack of concern for one's health, or reduced curiosity about others and new experiences. The prevalence of apathy in PD patients ranges from 17% to 70% and is influenced by the extent of depression and cognitive impairment (8). A systematic review and meta-analysis found that approximately 40% of PD patients have apathy. Among them, half did not have concomitant depression or cognitive impairment, suggesting apathy is a distinct clinical entity in PD patients (9).

In contrast to apathy, an observed phenomenon, fatigue is subjective and reported in nearly one-third of PD patients. Fatigue can even occur before motor symptoms, has a chronic or intermittent course, with increasing lifetime prevalence over time (8,10).

The neurobiological mechanisms underlying these clinical entities are poorly understood, but are largely attributed to basal ganglia pathology and disturbance of fronto-subcortical connections (8,11).

The treatment of apathy in PD patients is difficult, as they have an indifference to their health, and families often view apathy as a patient's character-related laziness. Non-pharmacological strategies such as providing a goal-directed, reality-based, individualised daily schedule and structure with varied activities and group experiences that maintain a satisfactory activity level are helpful in managing apathy (12). This can be carried out with the help of family members. The role of cholinesterase inhibitors, memantine, dopamine agonists, SSRIs, methylphenidate, modafinil, and testosterone has been studied as specific pharmacological options in the management of apathy in PD patients; however, the results are equivocal, and the evidence is insufficient to make treatment recommendations (8,11). Similarly, studies on treating fatigue in PD have also yielded mixed results (13).

Psychosis

A substantial proportion of PD patients experience psychotic symptoms, affecting up to 50% of patients when mild forms of psychotic symptoms are also included (14). The prevalence of psychosis appears to increase in the late stages of the disease (15). Psychosis in PD patients is associated with dementia, depression, greater caregiver strain, nursing home placement and earlier mortality. Psychosis frequently coexists with dementia, and having one predicts the development of the other condition (16).

Visual hallucinations are the commonest psychotic symptom seen in PD patients. Other visuo-perceptual symptoms, such as illusions, passage phenomenon (vague, fleeting imaging in peripheral vision) and presence phenomenon (experience that someone is

present when nobody is there), are also common. The typical visual hallucinations consist of persons, and less frequently, animals or objects. They are often single or few in number, appear suddenly in dim light, and are complex and stereotyped. They commonly move and seem real to the patient and suddenly vanish when the patient attempts to verify their reality by approaching or touching them, or asking someone to confirm their presence. Lack of insight regarding the pathological nature of these phenomena is common in PD patients with cognitive impairment. Hallucinations in other modalities can also occur, usually in combination with visual hallucinations (8).

In addition to hallucinations, delusions of various types, commonly Capgras delusions, persecutory delusions and delusions of infidelity, also occur, usually linked with perceptual disturbances and are more frequent in relatively younger PD patients (8,17).

A complex interaction between multiple intrinsic and extrinsic factors leads to the development of psychosis in PD. In the majority of patients, dopaminergic anti-Parkinsonism medications, mainly dopamine agonists, contribute to inducing psychosis (18). Factors such as advanced disease stage, older age, presence of dementia, visuospatial impairment, pathological excitation of visual pathways and sleep disorders can also contribute to the occurrence of psychosis (8). Brain changes associated with psychosis in PD patients include cholinergic deficits and Lewy bodies in the temporal lobes (19).

The identification and optimum management of psychosis are essential to improve the outcome of PD patients. However, balancing the risks and benefits, it is not recommended to treat if psychotic symptoms are infrequent, not troublesome, and the patient has insight regarding their pathological nature (18). In other circumstances, patients need to be treated using a multidisciplinary approach. Non-pharmacological approaches in the management include psychoeducation, distraction or re-directing attention, improving light and providing visual aids to maximise orientation, and minimising problems associated with poor patient-caregiver interactions (20). Detection and management of medical factors that can lead to delirium (for example, pain, infection, dehydration, constipation, metabolic disturbances, sensory deficits, recent medication changes, etc.) are also important.

Pharmacologically, reducing the number of medications and making adjustments to anti-Parkinsonian medications are helpful in treating psychosis. It is recommended to reduce or stop anticholinergic medications and dopamine agonists prior to changing the dosage of levodopa, as anticholinergics and dopamine agonists seem to have a higher risk of inducing psychosis than levodopa or COMT inhibitors. Adjustments to anti-Parkinsonism medications need to be done carefully while monitoring for motor deterioration and with the aim of achieving the best balance between psychosis and mobility (18). The next step in pharmacological management is to consider an atypical antipsychotic medication. Clozapine is found to be effective in improving visual hallucinations without worsening motor symptoms (21). Low-dose quetiapine (25-200 mg per day) may have a marginal efficacy with good tolerability (22). Other atypical antipsychotic medications, such as olanzapine, aripiprazole and ziprasidone, are not useful due to no proven efficacy and high risk of adverse effects like worsening of motor symptoms, cognitive decline, drowsiness and confusion. Risperidone and typical antipsychotics are not recommended in the treatment (18). Antipsychotics need to be used in low doses with small dose increments while being cautious, particularly when using in elderly patients with dementia, due to an increased risk of cerebrovascular accidents, increased mortality and worsening cognition (23). A novel atypical antipsychotic, pimavanserin, a 5HT2A receptor inverse agonist, has been proven to be effective in the management of PD psychosis without worsening motor symptoms and increasing mortality (24). Cholinesterase inhibitors improve psychotic symptoms in PD patients, with a small effect size, particularly in patients with comorbid dementia (25). Psychotic and motor symptoms of PD usually respond well to electroconvulsive therapy (26), but the risk of inducing delirium in patients with pre-existing cognitive impairment limits its use in clinical practice.

Cognitive impairment

Cognitive impairment represents a significant neuropsychiatric manifestation of PD, profoundly impacting both the quality of life and functional level. It is regarded as an integral aspect of the natural history of PD and occurs up to six times more frequently than in the healthy population (27). The cognitive decline may manifest at any stage of the disease. It exhibits a significant variability in clinical severity, the cognitive domains affected, and the rate of progression. Usually, the decline of cognitive functions is gradual and subtle; however, in certain instances, it can be rapid (28). The spectrum of cognitive impairment in PD ranges from subjective cognitive decline (SCD), mild cognitive impairment (MCI), to Parkinson's disease dementia (PDD). Typically, multiple cognitive domains such as memory, attention, visuospatial and executive functions are affected in PDD.

The cross-sectional data indicate that 24% to 31% of patients diagnosed with PD have dementia (29). The

cumulative prevalence of PDD is noted to be 17% at five years, 46% at ten years, and 83% at twenty years following the initial diagnosis (30-32). The rates of MCI are also higher in PD patients compared to the general population. Studies have demonstrated that nearly 20% of patients have MCI at the time of the PD diagnosis, a figure that increases to almost 50% after five years (33). Risk factors that are associated with increased risk of cognitive decline in PD include the presence of hallucinations, older age, severe motor symptoms, speech impairment, axial impairment, low education, depression and male sex (28). The neurobiological mechanisms that contribute to cognitive decline in PD remain largely unclear. Several mechanisms have been hypothesised, including widespread dopaminergic deficits in the brain, noradrenergic deficits in the locus coeruleus, and cholinergic deficits in the basal forebrain. Furthermore, alpha-synuclein deposition in Lewy pathologies, primarily in limbic (parahippocampal) and/or neocortical regions (frontal and temporal association areas), also contributes to the cognitive decline in patients with PD (34).

The assessment and treatment of cognitive impairment in PD is clinically challenging. For screening, MoCA is widely used in clinical practice, and based on the MoCA scores, a detailed neuropsychological assessment is indicated (28).

In pharmacological management, oral rivastigmine has been approved by the FDA for the treatment of mild to moderate PDD. The randomised controlled trial that demonstrated the efficacy of rivastigmine in treating PDD used rivastigmine 3-12 mg per day, and the results were assessed after 24 weeks of treatment (35). The evidence related to the effectiveness of donepezil, galantamine and memantine in the treatment of PDD is insufficient and inconsistent. There are no approved treatments for MCI in PD; however, several ongoing studies on pharmacological and non-pharmacological treatments for MCI in PD highlight the importance and need of slowing down its progression to PDD (28). The optimisation of anti-Parkinsonism medications is also essential in the management, as anticholinergic medications, such as benztropine and benzhexol, are associated with worsening cognitive functions in patients with PD (36). Therefore, liaising with the neurologist, stepwise simplification of anti-Parkinsonism medications, starting with withdrawing anticholinergics, needs to be considered.

Non-pharmacological approaches such as cognitive training, physical exercise and non-invasive brain stimulation may improve some cognitive abilities in PDD patients. Also, treating comorbid disorders (such as depression, psychosis, REM sleep behaviour disorder, obstructive sleep apnoea, vascular disease) and vascular risk factors (such as hypertension, diabetes mellitus, and dyslipidaemia) indirectly helps to improve the cognitive functions in PD (28).

Impulse-control and related behavioural disorders

During the course of PD, approximately 20% of patients experience impulse control and related behavioural disorders (ICBDs) (37,38). ICBDs that occur in PD include pathological gambling, compulsive sexual behaviours, compulsive shopping, compulsive hobbyism, binge eating, punding (non-goal-oriented repetitive activities such as sorting things, tidying, disassembling, or collecting objects, that are performed excessively in a stereotyped manner), and overuse of dopaminergic medications (dopamine dysregulation syndrome) (38,39). It is common for most patients to suffer from several ICBDs concurrently.

Parkinson's disease patients undergoing dopaminergic treatment are at an increased risk of developing ICBDs (40). Receiving treatment with a dopamine agonist that has a higher affinity for the D3 receptor in the mesolimbic pathways is the main risk factor for developing ICBDs in PD patients (41). Other risk factors include younger age at disease onset, longer disease duration, motor fluctuations, male gender, apathy, depression, cognitive impairment, smoking, personal or family history of gambling, and having novelty seeking and impulsivity in their personality (37,42,43).

The management of the ICBDs in PD is clinically challenging due to the lack of evidence-based treatment recommendations (37). NICE guidelines, 2017, recommend seeking advice from a healthcare professional with specialist expertise in PD, discussing the impact of ICBDs with patients and families, modifying dopaminergic therapy by gradually reducing dopamine agonists while monitoring for dopamine agonist withdrawal syndrome and offering cognitive behaviour therapy for ICBDs in PD (43).

Pharmacologically, naltrexone and amantadine have been studied as adjunctive medications to treat ICBDs in PD; however, the results were insufficient to recommend their use as a treatment modality. The efficacy of clozapine, quetiapine and selective serotonin reuptake inhibitors has been highlighted in few case reports. Subthalamic nucleus deep brain stimulation and continuous apomorphine infusions have also been studied and used by some clinicians (37,43,44). Blocking credit cards, restricting access to places of gambling and mobile applications, and supervising medication use by family members are common-sense approaches that can be used in clinical practice.

References

1. Tanner CM, Ostrem JL. Parkinson's Disease. N Engl J Med. 2024; 391(5): 442-52.
2. Angelopoulou E, Stanitsa E, Karpodini CC, Bougea A, Kontaxopoulou D, Fragkiadaki S, et al. Pharmacological and Non-Pharmacological Treatments for Depression in Parkinson's Disease: An Updated Review. Medicina (Kaunas). 2023; 59(8): 1454.
3. Cong S, Xiang C, Zhang S, Zhang T, Wang H, Cong S. Prevalence and clinical aspects of depression in Parkinson's disease: A systematic review and meta-analysis of 129 studies. Neurosci Biobehav Rev. 2022; 141: 104749.
4. Batzu L, Podlewska A, Gibson L, Chaudhuri KR, Aarsland D. A general clinical overview of the non-motor symptoms in Parkinson's disease: Neuropsychiatric symptoms. Int Rev Neurobiol. 2024; 174: 59-97.
5. Wu X, Shi M, Lian Y, Zhang H. Cognitive behavioral therapy approaches to the improvement of mental health in Parkinson's disease patients: a systematic review and meta-analysis. BMC Neurol. 2024; 24(1): 352.
6. Broen MPG, Narayen NE, Kuijf ML, Dissanayaka NNW, Leentjens AFG. Prevalence of anxiety in Parkinson's disease: A systematic review and meta-analysis. Mov Disord. 2016; 31(8): 1125-33.
7. Marin RS. Differential diagnosis of apathy and related disorders of diminished motivation. Psychiatric Annals. 1997; 27(1): 30-3.
8. Aarsland D, Marsh L, Schrag A. Neuropsychiatric symptoms in Parkinson's disease. Mov Disord. 2009; 24(15): 2175-86.
9. den Brok MGHE, van Dalen JW, van Gool WA, Moll van Charante EP, de Bie RMA, Richard E. Apathy in Parkinson's disease: A systematic review and meta-analysis. Mov Disord. 2015;3 0(6): 759-69.
10. Alves G, Wentzel-Larsen T, Larsen JP. Is fatigue an independent and persistent symptom in patients with Parkinson disease? Neurology. 2004 Nov 23;63(10):1908-11.
11. Maher S, Donlon E, Mullane G, Walsh R, Lynch T, Fearon C. Treatment of Apathy in Parkinson's Disease and Implications for Underlying Pathophysiology. J Clin Med. 2024 Apr 11;13(8):2216.
12. Campbell III JJ, Duffy JD. Treatment strategies in amotivated patients. Psychiatric Annals. 1997; 27(1): 44-9.
13. Rissardo JP, Jayasinghe M, Rashidi M, Rashidi F, Moharam H, Khalil I, et al. Exploring Fatigue in Parkinson's Disease: A Comprehensive Literature Review. Cureus [Internet]. 2025 Mar 25 [cited 2025 Jun 9];17(3). Available from: https://www.cureus.com/articles/344799-exploring-fatigue-in-parkinsons-disease-a-comprehensive-literature-review
14. Mack J, Rabins P, Anderson K, Goldstein S, Grill S, Hirsch ES, et al. Prevalence of psychotic symptoms in a community-based Parkinson disease sample. Am J Geriatr Psychiatry. 2012; 20(2): 123-32.
15. Chendo I, Fabbri M, Godinho C, Moiron Simões R, Severiano Sousa C, Coelho M, et al. High frequency of psychosis in late-stage Parkinso?s disease. Clinical Parkinsonism & Related Disorders. 2021; 5: 100119.
16. Factor SA, Feustel PJ, Friedman JH, Comella CL, Goetz CG, Kurlan R, et al. Longitudinal outcome of Parkinson's disease patients with psychosis. Neurology. 2003; 60(11): 1756-61.
17. Kiziltan G, Ozekmekçi S, Ertan S, Ertan T, Erginöz E. Relationship between age and subtypes of psychotic symptoms in Parkinson's disease. J Neurol. 2007; 254(4): 448-52.
18. Taylor DM, Barnes TRE, Young AH. The Maudsley Prescribing Guidelines in Psychiatry [Internet]. Wiley; 2025. (The Maudsley Prescribing Guidelines Series). Available from: https://books.google.co.uk/books?id=iqdNEQAAQBAJ
19. Onofrj M, Thomas A, Bonanni L. New approaches to understanding hallucinations in Parkinson's disease: phenomenology and possible origins. Expert Rev Neurother. 2007; 7(12): 1731-50.
20. Diederich NJ, Pieri V, Goetz CG. Coping strategies for visual hallucinations in Parkinson's disease. Mov Disord. 2003; 18(7): 831-2.
21. Parkinson Study Group. Low-dose clozapine for the treatment of drug-induced psychosis in Parkinson's disease. N Engl J Med. 1999; 340(10): 757-63.
22. Yunusa I, Rashid N, Seyedin R, Paratane D, Rajagopalan K. Comparative Efficacy, Safety, and Acceptability of Pimavanserin and Other Atypical Antipsychotics for Parkinson's Disease Psychosis: Systematic Review and Network Meta-Analysis. J Geriatr Psychiatry Neurol. 2023; 36(5): 417-32.
23. Ballard C, Waite J. The effectiveness of atypical antipsychotics for the treatment of aggression and psychosis in Alzheimer's disease. Cochrane Database Syst Rev. 2006; 2006(1): CD003476.
24. Sarva H, Henchcliffe C. Evidence for the use of pimavanserin in the treatment of Parkinson's disease psychosis. Ther Adv Neurol Disord. 2016; 9(6): 462-73.
25. d'Angremont E, Begemann MJH, van Laar T, Sommer IEC. Cholinesterase Inhibitors for Treatment of Psychotic Symptoms in Alzheimer Disease and Parkinson Disease: A Meta-analysis. JAMA Neurol. 2023; 80(8): 813-23.
26. Takamiya A, Seki M, Kudo S, Yoshizaki T, Nakahara J, Mimura M, et al. Electroconvulsive Therapy for Parkinson's Disease: A Systematic Review and Meta-Analysis. Mov Disord. 2021; 36(1): 50-8.
27. Aarsland D, Andersen K, Larsen JP, Lolk A, Nielsen H, Kragh-Sørensen P. Risk of dementia in Parkinson's disease: a community-based, prospective study. Neurology. 2001; 56(6):730-6.
28. Aarsland D, Batzu L, Halliday GM, Geurtsen GJ, Ballard C, Ray Chaudhuri K, et al. Parkinson disease-associated cognitive impairment. Nat Rev Dis Primers. 2021; 7(1): 47.

29. Aarsland D, Zaccai J, Brayne C. A systematic review of prevalence studies of dementia in Parkinson's disease. Mov Disord. 2005; 20(10): 1255-63.

30. Williams-Gray CH, Evans JR, Goris A, Foltynie T, Ban M, Robbins TW, et al. The distinct cognitive syndromes of Parkinson's disease: 5 year follow-up of the CamPaIGN cohort. Brain. 2009; 132(Pt 11): 2958-69.

31. Williams-Gray CH, Mason SL, Evans JR, Foltynie T, Brayne C, Robbins TW, et al. The CamPaIGN study of Parkinson's disease: 10-year outlook in an incident population-based cohort. J Neurol Neurosurg Psychiatry. 2013; 84(11): 1258-64.

32. Hely MA, Reid WGJ, Adena MA, Halliday GM, Morris JGL. The Sydney multicenter study of Parkinson's disease: the inevitability of dementia at 20 years. Mov Disord. 2008 Apr 30;23(6):837-44.

33. Pedersen KF, Larsen JP, Tysnes OB, Alves G. Natural course of mild cognitive impairment in Parkinson disease: A 5-year population-based study. Neurology. 2017; 88(8): 767-74.

34. Smith C, Malek N, Grosset K, Cullen B, Gentleman S, Grosset DG. Neuropathology of dementia in patients with Parkinson's disease: a systematic review of autopsy studies. J Neurol Neurosurg Psychiatry. 2019; 90(11): 1234-43.

35. Emre M, Aarsland D, Albanese A, Byrne EJ, Deuschl G, De Deyn PP, et al. Rivastigmine for dementia associated with Parkinson's disease. N Engl J Med. 2004; 351(24): 2509-18.

36. Ehrt U, Broich K, Larsen JP, Ballard C, Aarsland D. Use of drugs with anticholinergic effect and impact on cognition in Parkinson's disease: a cohort study. J Neurol Neurosurg Psychiatry. 2010; 81(2): 160-5.

37. Debove I, Paschen S, Amstutz D, Cardoso F, Corvol JC, Fung VSC, et al. Management of Impulse Control and Related Disorders in Parkinson's Disease: An Expert Consensus. Mov Disord. 2024 Feb;39(2):235-48.

38. Baig F, Kelly MJ, Lawton MA, Ruffmann C, Rolinski M, Klein JC, et al. Impulse control disorders in Parkinson disease and RBD. Neurology. 2019; 93(7): e675-87.

39. Warren N, O'Gorman C, Lehn A, Siskind D. Dopamine dysregulation syndrome in Parkinson's disease: a systematic review of published cases. J Neurol Neurosurg Psychiatry. 2017; 88(12): 1060-4.

40. Marques A, Lewis S. Impulse control disorders in Parkinson's disease: What's new? J Neurol. 2025; 272(2): 138.

41. Béreau M, Krack P, Brüggemann N, Münte TF. Neurobiology and clinical features of impulse control failure in Parkinson's disease. Neurological Research and Practice. 2019; 1(1): 9.

42. Barone P, Antonini A, Stanzione P, Annoni K, Asgharnejad M, Bonuccelli U. Risk factors for impulse control disorders and related behaviors in Parkinson's disease: secondary analyses of the ICARUS study. J Drug Assess. 2019; 8(1): 159-66.

43. National Institute for Health and Care Excellence (NICE). Managing and monitoring impulse control disorder as an adverse effect of dopaminergic treatment. In: Parkinson's disease in adults: diagnosis and management [Internet]. National Institute for Health and Care Excellence (NICE); 2017 [cited 2025 Jun 8]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK535838/

44. Zhang JF, Wang XX, Feng Y, Fekete R, Jankovic J, Wu YC. Impulse Control Disorders in Parkinson's Disease: Epidemiology, Pathogenesis and Therapeutic Strategies. Front Psychiatry. 2021; 12: 635494.