

# Restless Legs Syndrome and Impulse Control Disorders in Patients with Parkinson's Disease: An Intricate Association

Parkinson's disease (PD) is the second most common neurodegenerative disorder in the world and is characterized by loss of dopaminergic neurons in the substantia nigra leading to bradykinesia, rigidity, tremors, and a large number of motor and non-motor symptoms.<sup>[1,2]</sup> It is a complex disorder with pathology showing Lewy body deposition in the brain.<sup>[1,2]</sup> The main treatment option consists of dopaminergic therapy.<sup>[2]</sup> Restless legs syndrome (RLS), a sensorimotor disorder described several centuries ago by Willis and Ekbom, was also found in patients with PD.<sup>[3]</sup> The patients with RLS respond to dopaminergic therapy.<sup>[3]</sup> As per the current understanding, the response to dopaminergic therapy in patients with RLS is linked to D1 and D3 receptors in the spinal cord's dorsal and ventral horns.<sup>[3]</sup> The reports of augmentation of symptoms of RLS with dopamine (DA) agonists started coming in the early twenty-first century, and soon, it was found that these were very distressing and created a difficult situation for the treating physician.<sup>[3,4]</sup> The reasons for augmentation were proposed to be the upregulation and sensitization of dopaminergic receptors in the putamen.<sup>[3,4]</sup>

However, as PD is a DA deficiency state and the patients are always treated with dopaminergic drugs.<sup>[2]</sup> With the discovery of DA agonists for treating PD, an important therapeutic tool was added for physicians.<sup>[5]</sup> The DAs were soon found to possess a unique adverse effect known as impulse control disorders (ICDs) due to DA receptor dysregulation.<sup>[6]</sup> Compulsive shopping, binge eating, hypersexuality, Internet addiction, and punting were all identified as ICDs.<sup>[6]</sup> As the common denominator between RLS and ICD is DA receptor-related, the association also has been identified in a subgroup of patients with PD.<sup>[3,4,7]</sup> Marques *et al.*<sup>[8]</sup> conducted a study on fifty patients with PD with and without ICDs and performed suggested immobilization tests, video polysomnography, and other sleep and neuropsychological assessments. They found that the patients with ICDs had significantly higher subjective discomfort during suggested immobilization test (SIT) than those without ICDs. They found ICDs as an independent predictor of the SIT in PD. They proposed that the restlessness and discomfort captured by SIT seen in patients with ICDs were another reflection that the SIT is not only abnormal in RLS but in ICDs, and they both may have a common basis. Additionally, they found no differences in RLS frequency in patients with and without ICD.<sup>[8]</sup>

Another study by Voon *et al.*<sup>[9]</sup> evaluated the cross-sectional prevalence of ICDs in RLS and its associated factors. They detected ten patients of ICDs of 140 patients with RLS. Binge eating, pathological gambling, punting, and hypersexuality were found in this cohort. They concluded that the patients with RLS on DA agonists should be educated about the risk

of developing ICDs, and the higher dose of DAs, young age at RLS onset, female gender, and family history of gambling were the identified risk factors.<sup>[9]</sup> Schreglmann *et al.* analyzed the frequency and clinical features of ICDs and patients with RLS on transdermal rotigotine patches. Of the 28 patients of RLS, six had developed features of ICDs on rotigotine treatment.<sup>[10]</sup>

The recent study published by Paul, *et al.* sought to find any correlation between the ICDs and RLS in a cohort of patients with PD in a tertiary care hospital in north India and if there is any specific behavioral abnormality associated with it. In addition to recording the demographic details and PD stage, the authors used validated scales such as Questionnaire for Impulsive–Compulsive Disorders in Parkinson's Disease (QUIP) for ICDs and RLS by standard diagnostic criteria.<sup>[11]</sup> They summarized that 11% of PD patients on treatment could have coexisting RLS and ICDs. Of the 105 patients with PD, 51 patients were detected to have at least one ICD, and 18 patients had RLD in the same cohort. Of the 18 patients with RLS, 12 had at least one ICD. The common ICDs found in this group were gambling in five patients and compulsive eating in eight patients. Another critical finding that they reported was that in the cohort with PD and ICD/RLS, they found statistically significant more extended duration of disease and higher levodopa equivalent daily dosage (LEDD).<sup>[11]</sup> There was no difference in the rest of the parameters tested.<sup>[11]</sup>

These findings further support the association of DA receptor dysregulation in the clinical features of these two disorders in patients with PD. The neuro-physicians should be alert and aware of this coexistence and take suitable measures to manage the risk factors accordingly.

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## REFERENCES

- Gibb WR, Lees AJ. The relevance of the Lewy body to the pathogenesis of idiopathic Parkinson's disease. *J Neurol Neurosurg Psychiatry* 1988;51:745-52.
- Kalia LV, Lang AE. Parkinson's disease. *Lancet* 2015;386:896-912.
- Allen RP, Picchiotti D, Hening WA, Trenkwalder C, Walters AS, Montplaisi J, *et al.* Restless legs syndrome: Diagnostic criteria, special considerations, and epidemiology. A report from the restless legs syndrome diagnosis and epidemiology workshop at the National Institutes of Health. *Sleep Med* 2003;4:101-19.
- Trenkwalder C, Allen R, Högl B, Clemens S, Patton S, Schormair B,

- et al.* Comorbidities, treatment, and pathophysiology in restless legs syndrome. *Lancet Neurol* 2018;17:994-1005.
5. Kalia LV, Lang AE. Parkinson's Disease. Vol 386, The Lancet. Lancet Publishing Group; 2015. p. 896-912.
  6. Weintraub D. Impulse control disorders in Parkinson's disease: A 20-year odyssey. *Mov Disord* 2019;34:447-52.
  7. Khoo TK, Yarnall AJ, Duncan GW, Coleman S, O'Brien JT, Brooks DJ, *et al.* The spectrum of nonmotor symptoms in early Parkinson disease. *Neurology* 2013;80:276-81.
  8. Marques A, Figorilli M, Lambert C, Pereira B, Vidal T, Montplaisir J, *et al.* The urge to move: From restless legs syndrome to impulse control disorders in Parkinson's disease. *J Sleep Res* 2021;30:e13127.
  9. Voon V, Schoerling A, Wenzel S, Ekanayake V, Reiff J, Trenkwalder C, *et al.* Frequency of impulse control behaviours associated with dopaminergic therapy in restless legs syndrome. *BMC Neurol* 2011;11:117.
  10. Schreglmann SR, Gantenbein AR, Eisele G, Baumann CR. Transdermal rotigotine causes impulse control disorders in patients with restless legs syndrome. *Parkinsonism Relat Disord* 2012;18:207-9.
  11. Paul BS, Aggarwal S, Paul G, Khehra AS, Jain A. Impulse-control disorders and restless leg syndrome in Parkinson's disease: Association or coexistence. *Ann Indian Acad Neurol* 2023;26:161-6.

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