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Connectome and molecular pharmacological dopaminergic differences in RLS: plastic changes and neuroadaptations that may contribute to augmentation

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Highlights

- Long-term treatment of RLS dopamine D2/D3 receptor agonists leads to augmentation
- Augmentation may be a consequence of a hyper-dopaminergic state
- Protein tyrosine phosphatase D (PTPRD) may play a role in the reconfiguration of neural circuits
- Alterations in direct and indirect interactions between D1 and D3 receptors might be involved
- New treatment options for RLS may reach beyond the dopamine system itself

Abstract

Restless Legs Syndrome (RLS) is primarily treated with levodopa and dopaminergics that target the inhibitory dopamine receptor subtypes D3 and D2. The initial success of this therapy led to the idea of a hypo-dopaminergic state as the mechanistic origin underlying RLS. However, multiple lines of evidence suggest that this simplified concept of a reduced dopamine function as the basis of RLS is incomplete. Moreover, long-term medication with