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Long-term modulation of glutamatergic transmission in Parkinson's disease patients with and without L-dopa-induced dyskinesia

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Introduction: Abnormal glutamatergic neurotransmission in the primary motor cortex (M1) contributes to the pathophysiology of Parkinson's disease (PD) and is crucially related to L-dopa-induced dyskinesias (LID). The short-term modulation of glutamatergic neurotransmission improves the abnormally enhanced short-interval intracortical facilitation (SICF) in PD patients.

Objective: To examine whether the long-term modulation of SICF has beneficial effects on clinical measures, including LID severity, and whether these changes parallel an improvement in cortical plasticity mechanisms in PD.

Methods: We tested SICF before (S0) and after short- (14 days - S1) and long-term (12 months - S2) treatment with safinamide 100 mg/day, a drug with anti-glutamatergic properties, in patients with and without LID. Possible changes in M1 plasticity were assessed using intermittent theta-burst stimulation (iTBS). Finally, we correlated safinamide-related neurophysiological changes with possible modifications in clinical scores.

Results: SICF was abnormally enhanced at S0, and prominently in patients with LID. Safinamide normalized SICF at S1 and this effect persisted at S2. The iTBS-induced plasticity was impaired at S0 and safinamide restored this alteration at S2. There was a significant correlation between the degree of SICF and the amount of iTBS-induced plasticity at S0 as well as at S2. In patients with LID, the degree of SICF at S0 and S2 correlated with long-term changes in LID severity.

Conclusion: SICF alteration contributes to M1 plasticity impairment in PD. Safinamide-related long-term modulation of glutamatergic neurotransmission ameliorates both SICF and M1 plasticity. The abnormality in SICF-related circuits plays a relevant role in LID pathophysiology and its long-term modulation may prevent LID worsening over time in PD.