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GABAergic and glutamatergic alterations in prodromal and early Parkinson's disease

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Introduction: Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation technique able to detect the impairment of specific neurotransmitter circuits in vivo. The aim of this study was to detect alterations within GABAergic and glutamatergic circuitries in Parkinson's disease (PD) patients, including *de novo* PD (naïve), and prodromal Parkinson's disease, namely rapid eye movement (REM) sleep behaviour disorder (RBD) patients.

Methods: The study enrolled consecutive patients with PD, polysomnography-confirmed RBD and age-matched healthy controls. Each subject underwent an extensive motor and cognitive assessment and a TMS paired-pulse protocol evaluating GABA A ergic circuits (short interval intracortical inhibition, SICI), and glutamatergic circuits (intracortical facilitation, ICF).

Results: Seventy-seven subjects entered the study, namely 46 PD patients (including 24 drug-naïve and 22 under dopaminergic treatment), 13 RBD and 18 age-matched healthy controls (HC). Compared to HC, SICI and ICF resulted significantly impaired in PD (both drug-naïve and under dopaminergic treatment). All RBD subjects exhibited impaired SICI, whereas ICF was reduced in 6 and increased in 7 subjects.

Conclusions: GABAergic and glutamatergic alterations are a prominent feature of PD from prodromal stages. The differences observed in ICF patterns in subset of RBD might indicate divergent risk of conversion to PD or dementia with Lewy bodies (DLB). Further longitudinal studies are thus warranted to extend these findings.