P131

Assessing the role of motor network excitability alterations in Parkinson's disease, a TMS-EEG study

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Background: Motor impairment in Parkinson's disease (PD) reflects changes in the basal gangliathalamocortical circuit converging on the primary motor cortex (M1) and supplementary motor area (SMA). In a previous study, using transcranial magnetic stimulation coupled with electroencephalography (TMS-EEG), we showed how moderate PD patients off medication had lower M1 and higher pre-SMA excitability, as reflected by alterations in early TMS-EEG responses [1]. These abnormalities were reverted by dopaminergic therapy. In this study, we aimed at understanding the pathophysiological and clinical meaning of these alterations by studying TMS-EEG responses in de novo (DNs) and early (EA) PD patients.

Objectives: To understand the role of pre-SMA and M1 excitability alterations in PD patients.

Methods: We compared TMS-evoked cortical potentials (TEPs) from M1 and pre-SMA contralateral to the most affected side between 15 de-novo (i.e. newly diagnosed, not taking dopaminergic medications) and 15 early (< 1 yr of history) PD patients tested off medications and 15 healthy controls (HCs). Also, a kinematic assessment of bradykinesia was performed on the most affected side and correlated to TEPs.

Results: When stimulating M1, DNs and EAs showed lower P30 than HCs, while DNs showed a less pronounced N45 than DNs. When stimulating pre-SMA, only EAs, but not DNs, showed a more negative N40 than HCs. No correlation was found between kinematic-based bradykinesia assessment and TEPs.

Conclusions: Here we confirmed a reduced M1 excitability from the early stages of PD patients that may offer a new disease biomarker. Also, we validated the finding of increased pre-SMA excitability in PD, which seems to parallel disease progression. Although dopaminergic medications reverted both abnormalities, these do not seem to be directly correlated with bradykinesia mechanisms.

References:

[1] Leodori G, De Bartolo MI, Guerra A, Fabbrini A, Rocchi L, Latorre A, Paparella G, Belvisi D, Conte A, Bhatia KP, Rothwell JC, Berardelli A. Motor Cortical Network Excitability in Parkinson's Disease. Mov Disord. 2022 Apr;37(4):734-744. doi: 10.1002/mds.28914. Epub 2022 Jan 9. PMID: 35001420.