The Role of the Motor Cortex in the Parkinsonian Tremor Network: Is it Time for an Upgrade?

Dear Editors,

We have read with great interest the recently published article by Wilken and colleagues, showing the persistence of oscillatory activity in the basal ganglia even during the suppression of parkinsonian tremor induced by movement.[1] These findings are particularly intriguing as they suggest that tremor can be suppressed without directly modifying basal ganglia activity, prompting us to reconsider the significance of other regions within the network responsible for tremor genesis in Parkinson's disease (PD).

Tremor suppression with movements could reflect the temporary disengagement of the primary motor cortex (M1) from the tremor network due to the encoding of a voluntary movement.[2] To date, the major pathophysiological models of PD tremor have considered M1 as the final effector of the tremor network or, at most, as an integration node between basal ganglia (the "switch" that drives the tremor) and cerebello-thalamo-cortical loop (the "dimmer" that modulates its features)[3,4] Nonetheless, previous transcranial magnetic stimulation (TMS) and electroencephalography (EEG) investigations have already substantiated the pivotal role of M1 in the tremor oscillating network and its suppression during voluntary movements.[2,5] Furthermore, a recent study by Lauro and colleagues[6] demonstrated that recordings of M1 signals in patients with PD using EEG/electrocorticography provide more detailed information about tremor states than can be obtained from local field potentials recorded by deep brain stimulation (DBS). Accordingly, the sensorimotor cortex was recently found to drive connectivity within cerebello-thalamo-cortical structures during re-emergent tremors in PD.[7]

Together with Wilken's recent findings,[1] this evidence may lead to the upscale of M1's role in the dimmer-switch model, up to the point of acknowledging the motor cortex as a critical node in tremor genesis.

Nonetheless, we recognize that more data are needed to clarify the role of M1. In this vein, electrophysiological and non-invasive stimulation methods might prove instrumental due to their great temporal resolution. Some hints might come from tremor suppression during voluntary movement. For instance, tracking the dynamic connectivity changes between deep and cortical sources during movement-related tremor suppression may elucidate whether the M1 plays a motor-context-dependent role in tremor-generating network. Similarly, employing perturbational approaches such as TMS-EEG to further investigate M1 effective connectivity within the tremor-related network before, during, and after tremor onset might confirm its regulatory influence on tremor dynamics.

Gaining a deeper understanding of the role of M1 in tremor genesis and its suppression has relevant pathophysiological and therapeutic implications. At the time of writing, the most effective therapies for treating tremors in PD are basal ganglia and thalamus DBS and focused ultrasound-mediated lesioning. However, these procedures are burdened by significant invasiveness, high costs, and poor reversibility. In this context, clarifying the M1-tremor relationship could foster the development of non-invasive neuromodulation approaches designed to alleviate tremors in PD.

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Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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