Letter to the Editor

Top-down Control of Dyskinesias in PD Using Brain Stimulation

An interesting proposal has been discussed in a letter by Cerasa and Quattrone on the potential mechanisms by which cortical repetitive transcranial magnetic stimulation (rTMS) may influence and possibly improve levodopa-induced dyskinesias (LID) in patients with Parkinson’s disease (PD). It is well established that different dysfunctional cortical regions may contribute to the development of LIDs in PD and among these regions, both the inferior frontal cortex (IFC) and pre-supplementary motor area (pre-SMA) certainly play an important role. As described in their letter, a well-defined basal ganglia model describes how cortico-subcortical interactions may account for the motor deficits observed in patients that develop LIDs. Thus, the application of rTMS in those cortical regions influencing response inhibition may be capable of modulating the fronto-striatal pathways that are relevant for action control.

We agree that modulating the ongoing top-down control of action may provide some help in PD patients with LIDs. TMS effects have shown to be capable of altering activity both in the striatum and subthalamic nucleus (STN) [1,2]. Thus, it seems a reasonable approach trying to apply rTMS over IFC and pre-SMA to evaluate possible compensatory mechanisms modulating unwanted behavior.

The indirect and hyperdirect pathways seem to interact when rapid and unexpected changes in behavior are required, a function attributed to the STN, the pre-SMA and the IFC [3,4]. The hyperdirect pathway is in theory activated in rapid and sudden inhibitory behavior (reactive inhibition), while the indirect pathway is involved in regulating and controlling predicted upcoming behaviors that may need to be canceled (proactive inhibition). The IFC tends to influence the STN via the hyperdirect pathway when rapid cancellation of actions are needed [3]. Instead, the pre-SMA by sending inputs to the striatum, via the indirect pathway [5] may favor proactive inhibition of actions. Thus, we could speculate that modulation of LIDs symptomatology may be obtained either by proactive mechanisms inherent in the indirect pathway or by the fast braking function linked to the hyperdirect pathway.

Previous chronic deep brain stimulation (DBS) studies of the STN [6,7] reported an influence on motor behavior involved in cancellation of action. From a cortical perspective, to modify either the hyperdirect or indirect pathway, one may need to apply a similar continuous stimulation paradigm which may be obtained using transcranial direct current stimulation (tDCS) proven to be useful in altering (increase or decrease) cortical and behavioral functions [8]. This stimulation approach could be a reasonable alternative for studying the causal role of the hyperdirect and indirect pathways on (i) inhibition of actions and (ii) possible influence on LID symptoms in PD patients.

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References


