Disinhibition of the motor cortex in Parkinson's disease

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Parkinson's disease is defined by a dysfunctional motor output due to striatal dopamine depletion. A key regulator of motor output is the balance between excitation and inhibition in the primary motor cortex. In humans, motor cortex excitability can be measured indirectly through transcranial magnetic stimulation (TMS) and a common measure to explore inhibitory mechanisms is the short-interval intracortical inhibition (SICI) induced by paired-pulse TMS stimuli. The disagreement between previously published studies raised doubts about the actual role of SICI in Parkinson's disease. Thus, our objective was to clarify whether SICI is altered in Parkinson's disease and whether and how the possible loss of inhibition, if any, may reflect the clinical state of patients and the evolution of the disease. Moreover, since motor symptoms, such as tremor, bradykinesia and rigidity, are lateralized in most patients with Parkinson's disease, we also wanted to examine the relationship between motor cortex excitability and lateralization of motor symptoms. To address all these issues, we studied a relatively large sample of patients with Parkinson's disease, using paired-pulse TMS protocols. Our results show that SICI is decreased in Parkinson’s disease compared to age-matched healthy controls. Moreover, cortical inhibition was similarly reduced in levodopa-naïve, non-dyskinetic and dyskinetic patients. The striking result was that this loss of cortical inhibition was already present in newly diagnosed patients in whom the less affected side was still minimally symptomatic. This result suggests that cortical disinhibition is a very early, possibly prodromal feature of Parkinson's disease.