Neurophysiological mechanisms in LRRK2 gene mutation in Parkinson's Disease: a TMS study

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INTRODUCTION

Parkinson's Disease (PD) is a neurodegenerative disorder that affects dopaminergic neurons of the substantia nigra pars compacta. The etiology of PD has long been thought to involve both genetic and environmental factors. Recent genetic studies have identified that mutations in **leucine-rich repeat kinase 2** (**LRRK2**) are the most common cause of hereditary PD. **Transcranial Magnetic Stimulation** (TMS) is a non-invasive brain stimulation method able to explore intracortical inhibitory and excitatory neural circuits in the primary motor cortex (M1) and to investigate pathophysiology of neurodegenerative disorders. The aim of our study is to test the functional deficits of multiple brain areas that are known to be associated with PD, using TMS measurements in different experimental designs in two groups of PD patients with LRRK2 gene mutation and sporadic (non-familial) forms compared to a group of age-matched Healthy Control (HC).

METHODS

Ten patients with LRRK2 gene mutation, ten patients with non-familial form PD according to the UK PD Society Brain Bank Criteria was evaluated in ON and OFF medication. In both conditions, all patients were clinically assessed by Unified Parkinson's Disease Rating Scale (UPDRS). Moreover, We studied short intracortical inhibition and facilitation (**SICI-ICF**), short latency afferent inhibition (**SAI**), long latency afferent inhibition (**LAI**), cortical silent period (**CSP**) and long-term potentiation (LTP) mechanisms applying intermittent theta burst stimulation protocol (**iTBS**) on primary motor cortex, in both pharmacological conditions (ON *vs* OFF) on the clinically less affected side.

RESULTS

A significant decrease intra-cortical inhibition in PD patients with LRRK2 mutation compared to those with sporadic form PD or HC. Conversely, LTP-like cortical plasticity was significantly increased in LRRK2 PD group (**p<0.05**) compared to sporadic PD and HC. No effect was found for SLAI, LAI and CSP protocols. No significant difference was found in UPDRS assessments between two groups also in both conditions.

CONCLUSION

The current findings suggest a **gabaergic** (GABA-A mediated) impairment probably due to an altered neurotransmitter release and an impairment of vesicular trafficking in LRRK2 patients. The "hyperplastic" response iTBS-induced in LRRK2 could depend by an increased susceptibility to levodopa administration compared to sporadic form of PD. Although LRRK2 and sporadic PD patients have clinical similarities, neurophysiological examinations have shown considerable differences in intra-cortical networks and in motor cortex plasticity.

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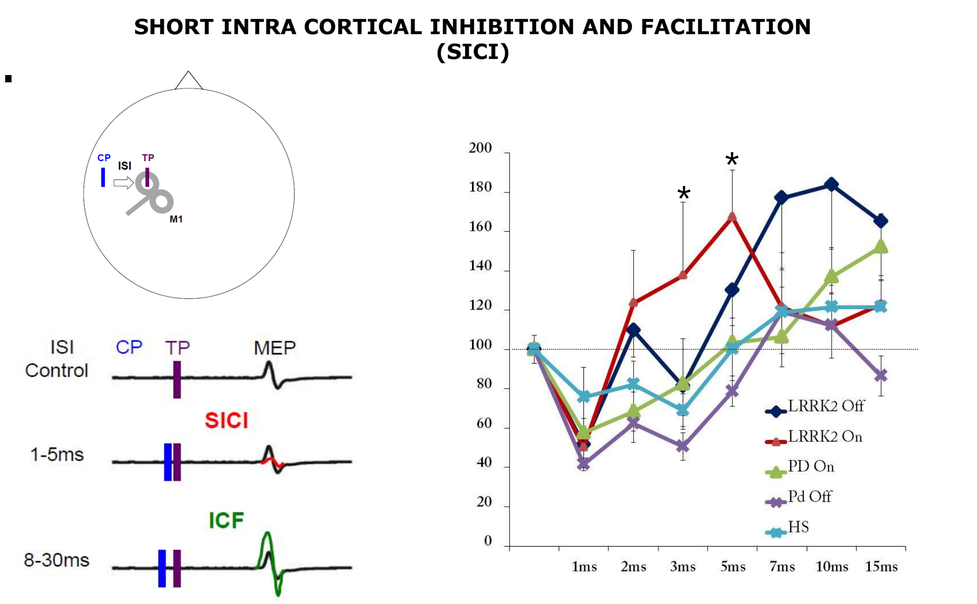

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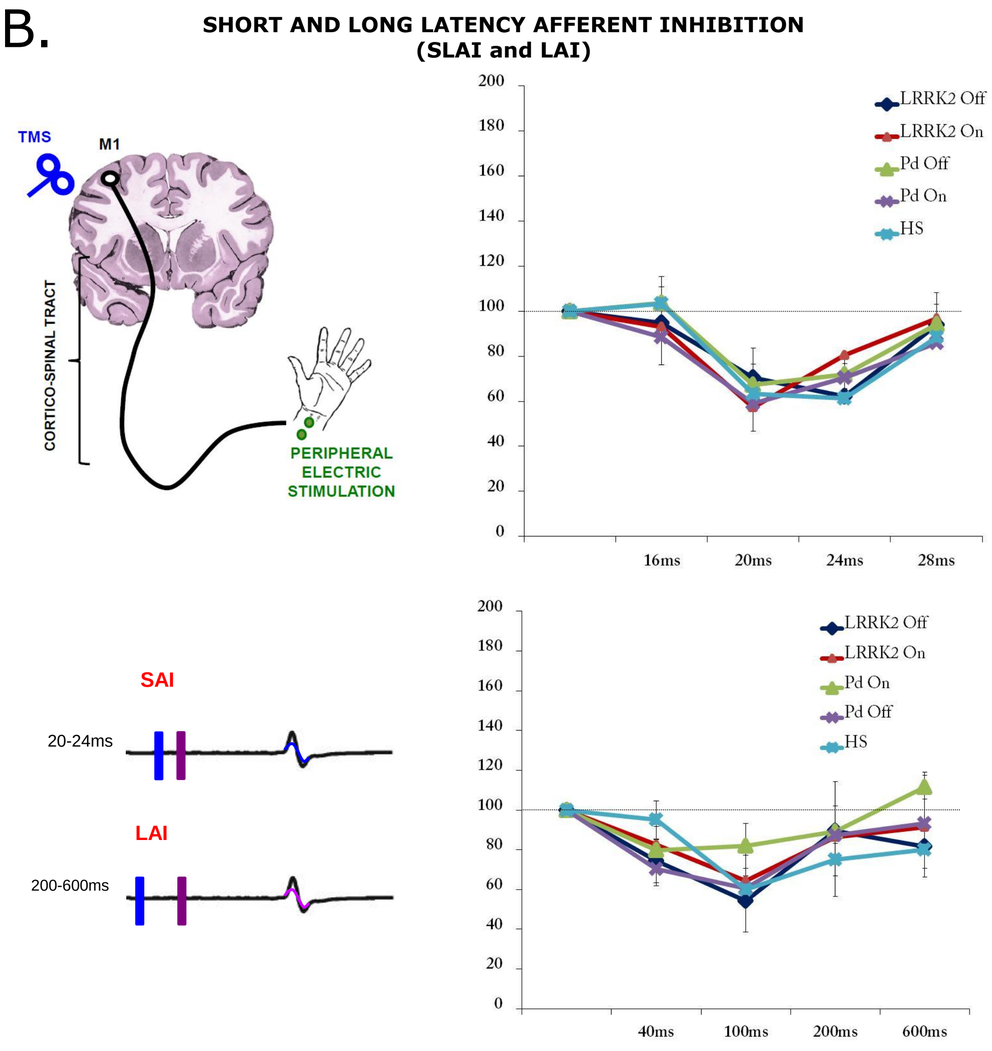

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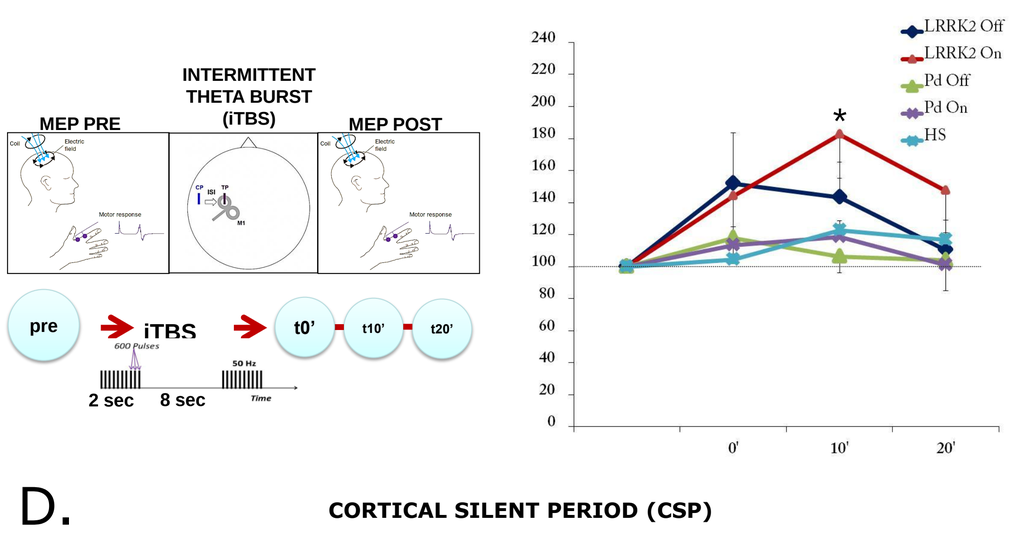

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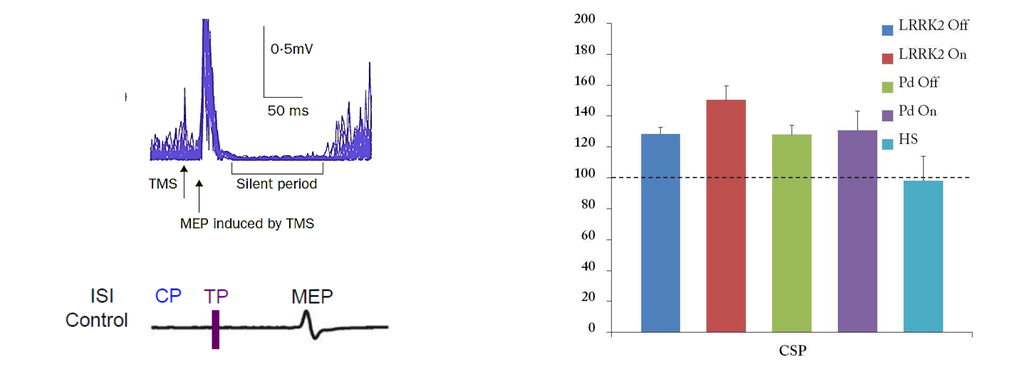

- **REFERENCES**
- Friedman LG, Lachenmayer ML, Wang J, He L, Poulose SM, Komatsu M, Holstein GR, Yue Z (May 2012). Disrupted autophagy leads to dopaminergic axon and dendrite degeneration and promotes presynaptic accumulation of α-synuclein and LRRK2 in the brain. J. Neurosci. 32 (22): 7585–93. doi:10.1523/JNEUROSCI.5809-11.2012
- Morgante F, Espay AJ, Gunraj C, Lang AE, Chen R. Motor cortex plasticity in Parkinson's disease and levodopa-induced dyskinesias. Brain 2006;129:1059–69.

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