Inflammation and Synaptic Plasticity in Parkinson's Disease: A Multicenter TMS Study

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Objectives: To investigate long term potentiation (LTP)-like plasticity using transcranial magnetic stimulation (TMS) in a large cohort of patients with Parkinson's disease (PD), specifically assessing the relationship with clinical characteristics and inflammatory biomarkers.

Clinical, molecular and electrophysiological profiling of Parkinsons Disease: the role of non-pharmacological therapies

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Methods:

- This study included a group of consecutive PD patients recruited from four Italian centers. Inclusion criteria: Age (30-80), stable dopaminergic treatment for ≥3 months, H&Y (1–3), no contraindications to TMS, no history of oncological, autoimmune or other neurological disorders
- LTP-like plasticity was evaluated using the intermittent theta burst stimulation (iTBS) TMS protocol[1]. Motor evoked potential (MEP) amplitudes were recorded before and after iTBS.
- Peripheral blood samples were collected (total a-syn, NfL, BDNF, IL-1B, IFNg, TNF, IL-4, IL-5, IL-6, IL-10, IL-17)

Results:

	PD patients (N = 156)	Control group (N = 54)
Age	68 (58.5-73)	63 (53.3-72)
Sex, M (N, %)	112 (72%)	33 (61.1)
Disease duration (y)	2 (1-6)	-
LED	400 (200–600)	-
TUG test (s)	9.5 (7.6-14)	-
H & Y	2 (1-2)	-
UPDRS-III	22 (14-29.75)	-

* Median (IQR). No significant differences In age and sex distribution

1. iTBS-induced LTP-like plasticity is reduced in PD patients compared to controls ($F_{(1,194)}$=54.66, p<0.01).

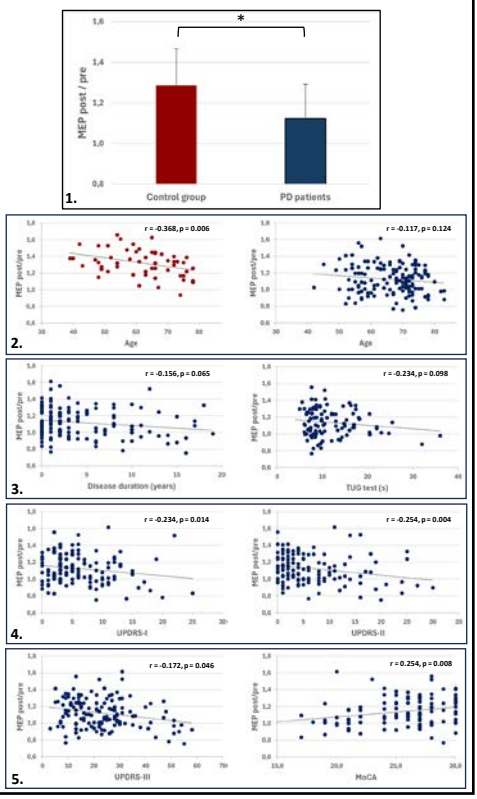
2. A significant correlation was found between LTP-like response and age in the control group (Spearman's Rho= -0.368; p=0.006). No significant correlation was found in the PD group (Spearman's Rho= -0.117; p=0.124).

3. No significant correlations were found between iTBS response and disease duration (Spearman's Rho= -0.156; p=0.065), LED (Spearman's Rho= -0.104; p=0.241), TUG test (Spearman's Rho= -0.234; p=0.098).

4. Significant negative correlations were found beteween LTP-like plasticity and UPDRS-I (Spearman's Rho= -0.234; p=0.014), UPDRS-II (Spearman's Rho= -0.254; p=0.004), UPDRS,-III (Spearman's Rho= -0.196; p=0.021), H&Y (Spearman's Rho= -0.172; p=0.046),

5. A significant correlation was found beteween LTP-like plasticity and MoCA (Spearman's Rho= 0.254; p=0.008)

6. The analysis of blood samples ongoing.



Conclusions:

Our multicenter TMS study demonstrates a significant reduction of LTP-like plasticity in PD patients compared to healthy controls. These findings suggest that impaired cortical plasticity may serve as an early marker of disease and a potential therapeutic target for neuroprotective strategies.

References: 1. Huang, et al., 2005. Theta burst stimulation of the human motor cortex. *Neuron*, *45*(2), 201–206. 2. Stampanoni Bassi, et al., 2017. Neurophysiology of synaptic functioning in multiple sclerosis. *Clinical neurophysiology 128*(7), 1148–1157. 3. Calabresi et al., 2023. Alpha-synuclein in Parkinson's disease and other synucleinopathies: from overt neurodegeneration back to early synaptic dysfunction. *Cell death & dis*, *14*(3), 176.