CONTINUOUS SUBCUTANEOUS APOMORPHINE INFUSION EFFECTS ON PRIMARY MOTOR CORTEX ACTIVITY IN PEOPLE WITH PARKINSON'S DISEASE

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INTRODUCTION

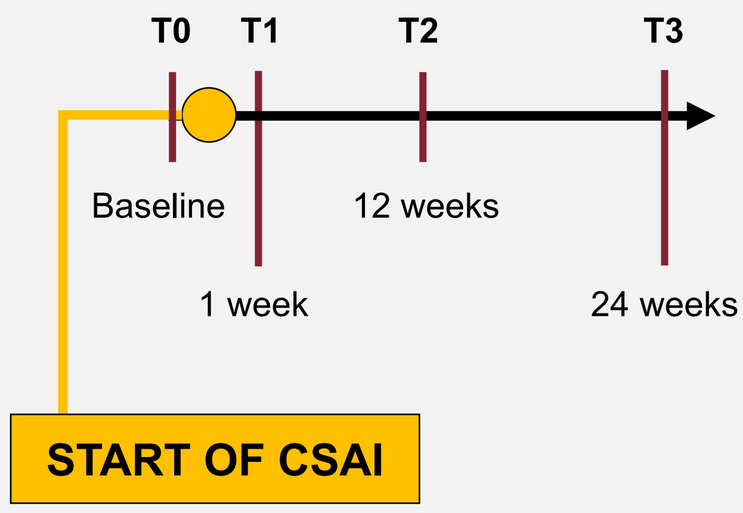
Transcranial magnetic stimulation (TMS) studies have consistently demonstrated that Parkinson's disease (PD) patients are characterized by abnormally increased excitability and reduced plasticity at primary motor cortex (M1) level[1]. PD plasticity changes play a pivotal role in PD pathophysiology, being closely associated with motor symptoms and complications appearance[2]. Levodopa-induced presynaptic dopaminergic stimulation can partially restore M1 function in the early stages, but its efficacy depends on the integrity of dopaminergic neurons, which are progressively lost over the course of the disease[3].

AIM

Continuous subcutaneous apomorphine infusion (CSAI) provides sustained, postsynaptic dopaminergic stimulation via both D1 and D2 receptors, and may represent an optimal strategy for modulating abnormal plasticity as the disease progresses. The aim of our study is to investigate the effects of apomorphine on excitability and plasticity in the M1 cortex of PD patients by conducting a TMS study.

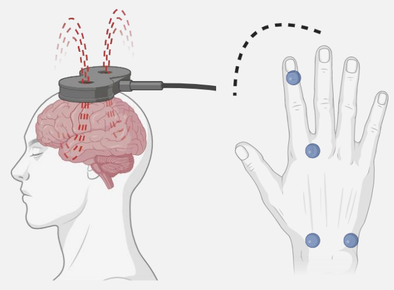
METHODS

21 FLUCTUATORS PD PATIENS



CLINICAL ASSESSMENT

UPDRS part I, II, III, IV; H&Y scale; NMSS; NoMoFa; PDQ-39; MoCA.

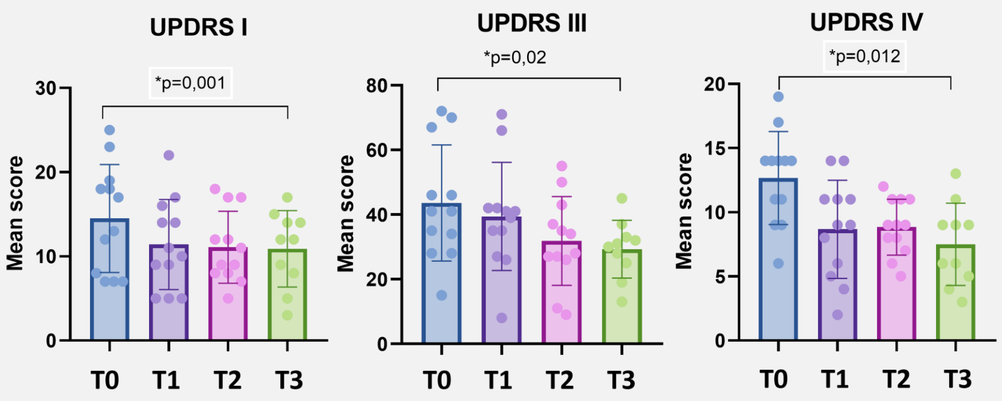


NEUROPHYSYOLOGICAL ASSESSMENT OF CORTICAL EXCITABILITY AND PLASTICITY (during ON-state)

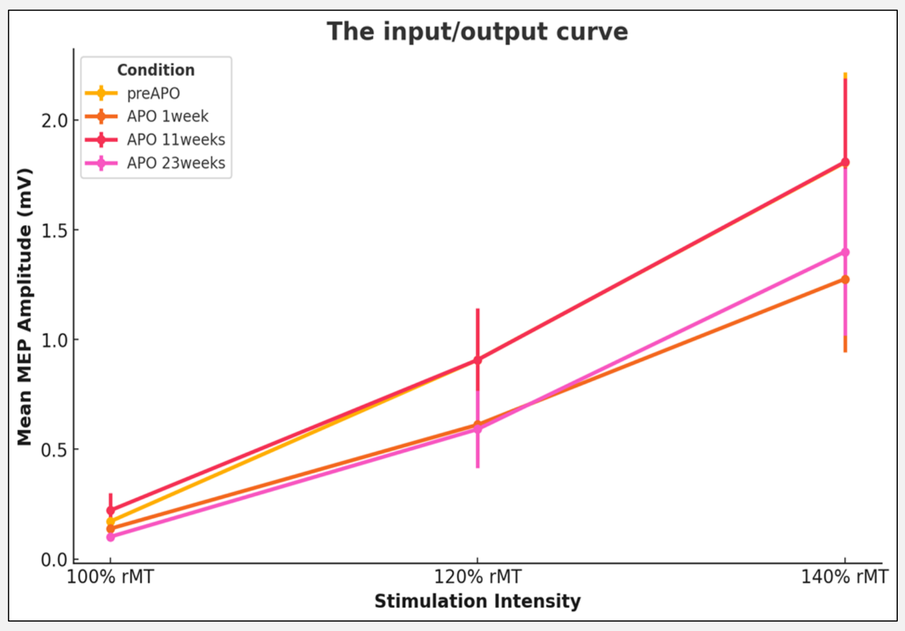
Single TMS paradigm
Input/output curve, cortical silent period (CSP)
Paired TMS paradigms
Short-interval intracortical inhibition (SICI), intracortical facilitation (ICF)
Repetitive TMS protocol
Intermittent theta burst stimulation (iTBS)
Kinematic Analysis of Movement (ballistic movement of the index finger)

UPDRS: MDS-Unified Parkinson's Disease Rating Scale; **H&Y**: Hoehn and Yahr scale;
NMSS: Non-Motor Symptoms Scale; **NoMoFa**: Non-Motor Fluctuation Assessment;
PDQ-39: Parkinson's Disease Questionnaire-39; **MoCA:** Montreal Cognitive Assessment.

RESULTS

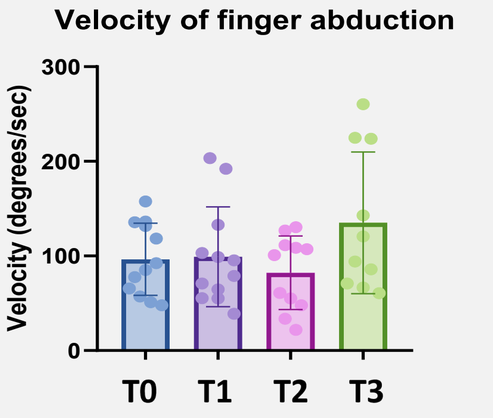


Clinical Assessment
A significant improvement in UPDRS I; III and IV score was observed from T0 vs T3.

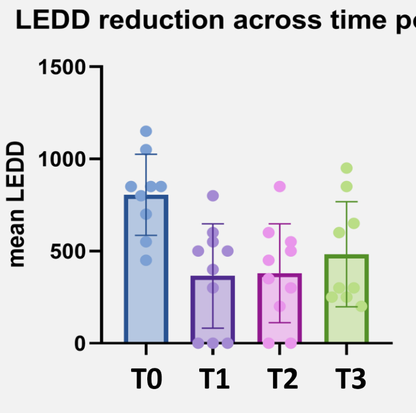


Primary motor cortex excitability.

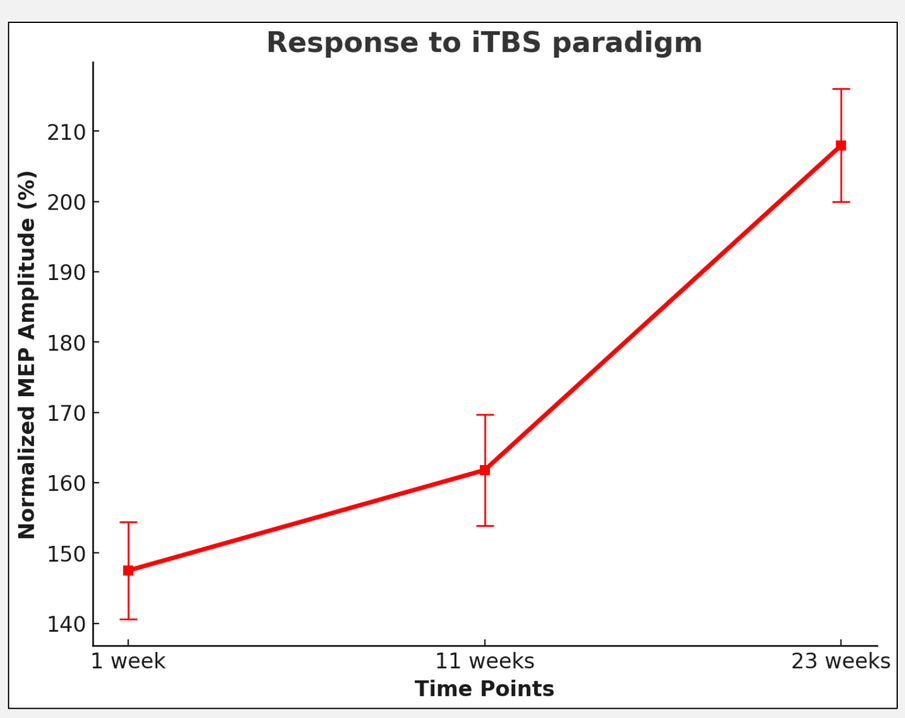
Significant difference across time points for the mean amplitude of the MEP at 140% of RMT (χ^2=8.486, p=0.037) stimulation intensity.



Kinematic evaluation of motor performance
Significant improvement in motor performance, as evidenced by a increase in the "VELOCITY" variable from T0 to T3.



Therapy changes across time points
A significant reduction in LEDD was observed from T0 vs T1, T2 and T3.



Primary motor cortex plasticity.

A significant effect of the iTBS paradigm was observed 23 weeks after the initiation of apomorphine therapy (χ^2=6.33, p=.043).

CONCLUSIONS

CSAI was able to induce a significant improvement of abnormal M1 excitability and plasticity in PD patients. These effects may be mediated by continuous stimulation of post-synaptic dopamine receptors and could contribute to CSAI clinical effects on motor symptoms and complications in PD patients.

Continuous post-synaptic dopaminergic stimulation via apomorphine infusion appears to improve motor cortical activity in PD Patients, potentially contributing to its therapeutic benefits. These findings support the role of apomorphine not only in symptom management but also in modulating underlying cortical dysfunction.

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2. Morgante F et al. Motor cortex plasticity in Parkinson's disease and levodopa-induced dyskinesias. Brain. 2006 Apr;129(Pt 4):1059-69. doi: 10.1093/brain/awl031
3. Calabresi P, Ghiglieri V, Mazzocchetti P, Corbelli I, Picconi B. - Levodopa induced plasticity: a double edged sword in Parkinson's disease? - Philos Trans R Soc Lond B Biol Sci - 2015 - 370 - 167