Predictors of improvement following excitatory repetitive transcranial magnetic stimulation with H-coil in Parkinson's disease

M. Fichera, F. Spagnolo, M.A. Volonté, G. Comi and L. Leocani

Scientific Institute University Hospital San Raffaele, INSPE - Institute of Experimental Neurology, Milan

Background and Objectives

Over the past years repetitive transcranial magnetic stimulation-rTMS has emerged as a possible add-on treatment for Parkinson's Disease-PD[1]. However, response to treatment may vary, often unpredictably. The aim of this work is to analyze which factors can influence clinical response to excitatory rTMS with H-coil in PD.

Methods

Fifty-nine patients with idiopathic PD were treated in our center in a randomized placebo-controlled study[2]. The protocol provided 12 sessions (3 sessions/wk) of 10Hz rTMS centered over primary motor cortex contralateral to the more affected side (M1) and prefrontal cortices bilaterally (PF). Patients were divided into 3 groups, specifically: M1r/PFr (real stimulation on M1 and PF), M1r/PFs (real stimulation on M1, sham stimulation on PF), Sham (apparent stimulation on both targets). Clinical evaluations (MDS-UPDRS part III and subscores) took place before the first and after the last session. Statistical analysys was conducted with an hierarchical order, considering first real stimulation (M1r/PFr + M1r/PFs; *Real* group) versus placebo and the M1r/PFr vs. placebo and M1r/PFs vs. placebo. At the end of the protocol a significant effect of real stimulation compared to placebo was demonstrated, for both UPDRS part III total score (p=0,04) and tremor subscore (p=0,01). A correlation analysis was then carried on to identify baseline characteristics related to improvement, including basal UPDRS scores and subscores, resting motor threshold – RMT, demographical characteristics (age, disease duration, Levodopa equivalent daily dose intake - LEDD, HY stage).

Results

A significant effect of stimulation was found at the end of the protocol comparing real and sham stimulation (Fig. 1). No significant correlation was identified between changes (both absolute and percentage) in the UPDRS part III scores at the end of the protocol with age, disease's duration, LEDD, HY stage, baseline resting motor threshold, lateralized and rigidity subscores. A significant correlation was identified between baseline tremor subscore and global improvement (rho 0,346; p=0,03 – Fig. 2) in the real group. A significant correlation was also present between tremor subscore at baseline and its improvement after rTMS in real (rho 0,326; p=0,04) but not in sham group (p=0,31)(Fig. 3).

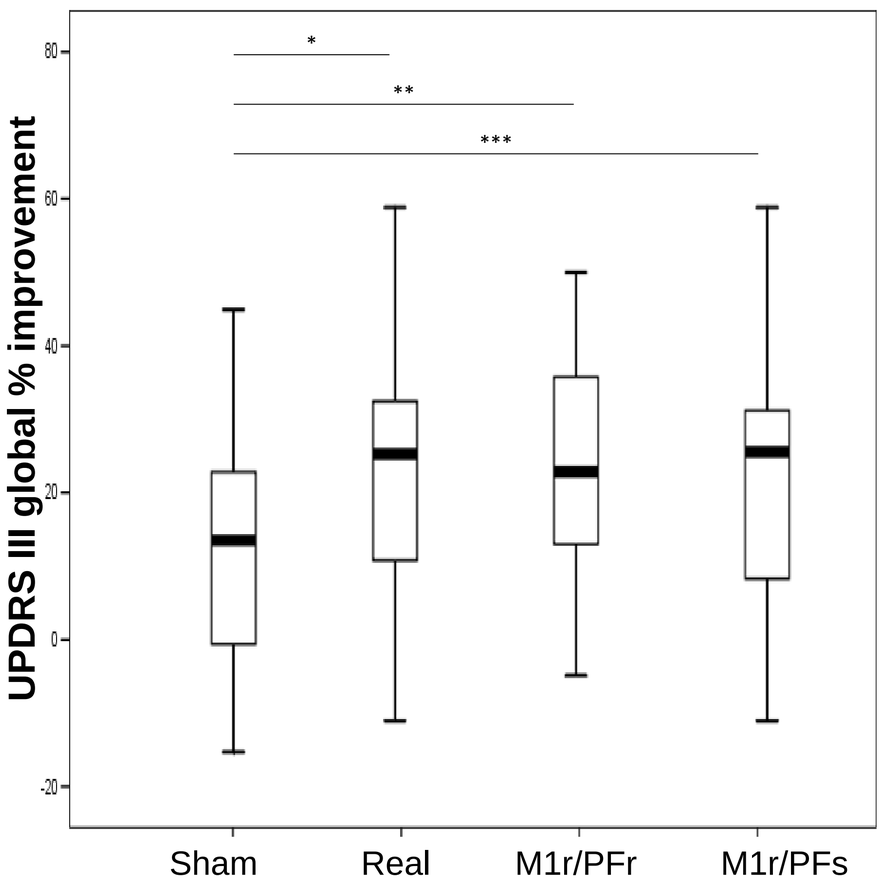

Figure 1.
UPDRS part III percentage improvement at the end of the protocol compare to baseline. *p<0,05 Merged vs. sham; ** p<0,05 M1r/PFr vs. sham; *** p<0,05 M1r/PFs vs. sham

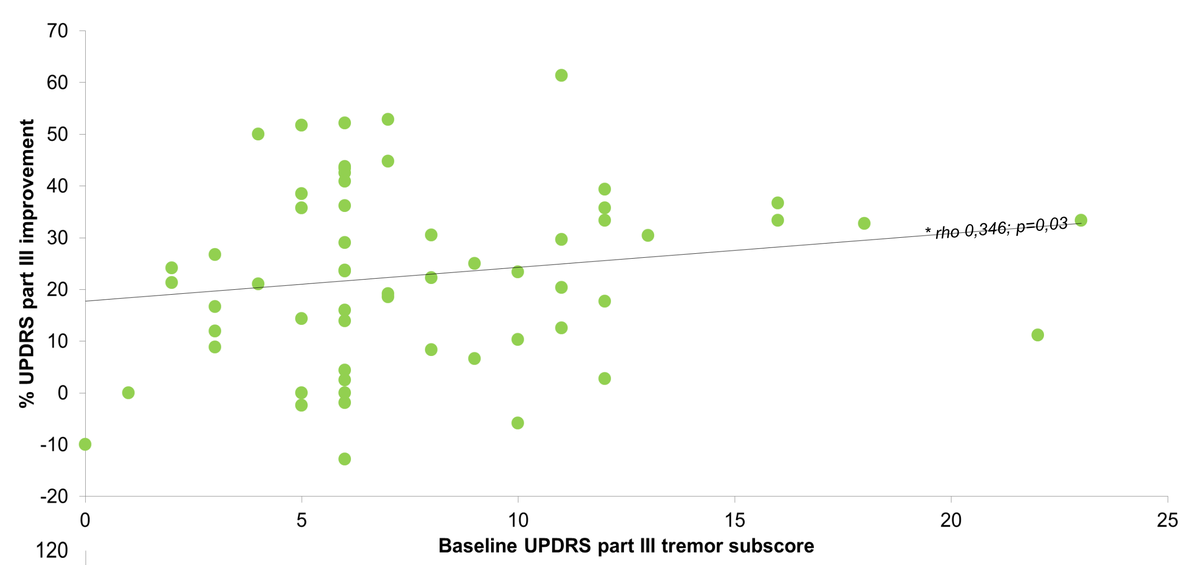

Figure 2.
Correlation between UPDRS part III tremor subscore and % total UPDRS part III improvement at the end of the protocol. Positive values indicate reduction in severity.

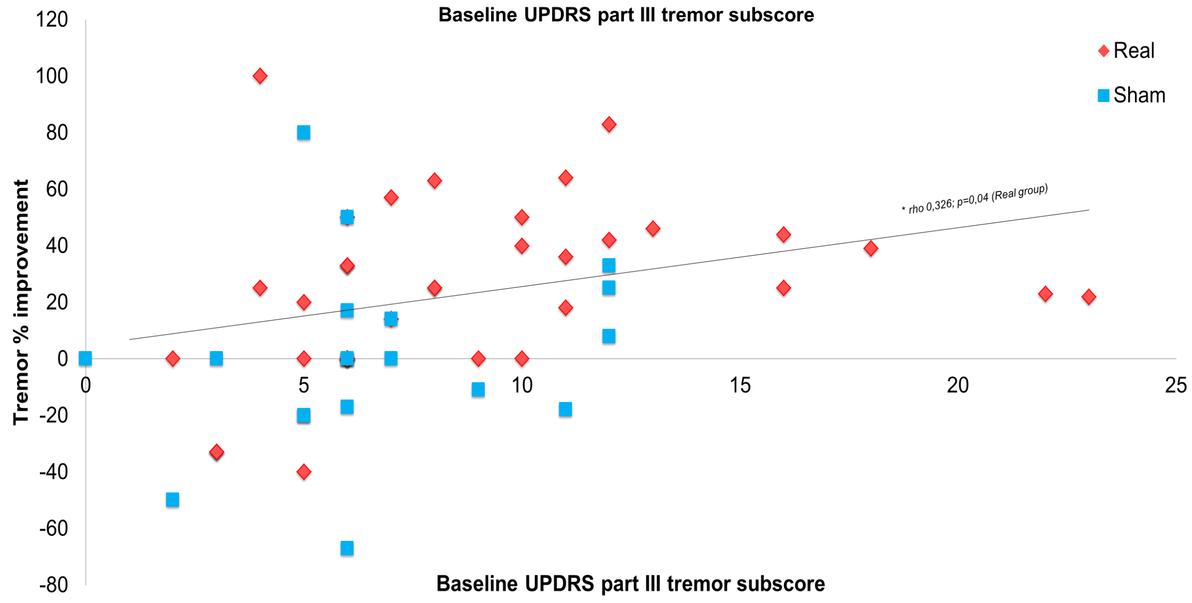

Figure 3.
Correlation between UPDRS part III tremor subscore and % tremor improvement at the end of the protocol. Positive values indicate reduction in tremor.

Conclusions

In our cohort of patients data suggests that higher amount of tremor is related to higher clinical improvement following excitatory rTMS with H-coil. The absence of the correlation between tremor and improvement in the sham group, despite a significant amount of placebo effect, may indicate that other non-dopamine related mechanisms, such as volitional, can account for placebo-effect in PD.

References

1. Wagle Shukla A et al. 2016; Repetitive Transcranial Magnetic Stimulation Therapy in Parkinson Disease: A Meta-Analysis.
2. Spagnolo F et al.; Repetitive transcranial magnetic stimulation with H-coil in Parkinson's Disease: a double-blind, placebo-controlled study . Article in preparation