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ACCEPTED MANUSCRIPT

Long Term Follow-Up Study of non-invasive brain stimulation (NBS) (rTMS and tDCS) in Parkinson's disease (PD). Strong Age-Dependency in the Effect of NBS.

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Highlights

- The NBS decreases the progression of Parkinson's disease.
- Both rTMS and rTMS plus tDCS was effective in patients \leq 65 years
- The yearly increment in different scores of UPDRS was zero during rTMS + tDCS
- NBS improved the pathological executive function > 65 years
- The effect of NBS on the progression is age and symptom dependent

Abstract

Background: Transcranial magnetic stimulation (rTMS) may influence the progression of PD compared with levodopa. The long term mind modification effect of repeated rTMS and tDCS is not known, nor are the predictors for the effect of NBS.

Objective/hypothesis: We hypothesized that the regularly repeated rTMS would decrease the development of PD. Later, the treatment protocol was completed with transcranial direct current stimulation (tDCS), supposing that there is an add-on effect. NBS may differently influence motor and mental aspects of the disease.

Methods: Thirty patients with PD were followed for 3.5 years in an open study. They were stimulated with 1 Hz rTMS every half year for 1.5 years. After that the tDCS was add to the stimulation over both sides of the cerebellum for the next 2 years. UPDRS, Trail Making Test and dual tests were used. The linear regression lines of score systems and percentage of yearly increment were counted, analyzed by ANOVA.

Results: The yearly progression rate for UPDRS total was 2 % for 3.5 years, $0.6\% \le 65$ years, 3.6% > 65 years. The increment was around zero during the rTMS + tDCS stimulations in patients ≤ 65 years. The slope of the equation showed the same tendency. The individual sensitivity to the NBS was high. tTMS and tDCS >65 yrs improved pathological executive function (p<0.0001).

Conclusion: The motor ability in PD was maintained at the same level in patients \leq 65 years with NBS for the 3.5 years in contrast to patients > 65 years. The cognitive function of patients > 65 yrs was favorable influenced by rTMS and tDCS. Age is the main predictor of the effect of NBS. rTMS and tDCS can slow the progression of PD without any side effects but in an age-dependent way.

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