

Repetitive transcranial magnetic stimulation (rTMS) of the left dorsolateral prefrontal cortex (IDLDFC) in patients with Parkinson's disease and comorbid treatment-resistant depression: a pilot case study.

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Introduction

Parkinson's disease (PD) is a neurodegenerative movement disorder characterized by postural instability, slow movements, muscle rigidity and tremors. Clinical developments in the field have led to recognition of non-motor symptoms of PD. Different aspects of the disease can exert a significant burden on the quality of life of patients and their caregivers.

Behavior and mood alterations (e.g. depression, anxiety and apathy) are more common in PD without cognitive impairment than in the general population, and are usually present in PD with dementia. Establishing the diagnosis of depression within the context of Parkinson's disease is complicated by similar symptoms that often occur in Parkinson's disease itself, including executive dysfunction, decreased facial expression, slowed movement, a state of indifference and quiet speech. Many Parkinson's disease patients' symptoms of depression do not improve with conventional antidepressive therapy.

Repetitive transcranial magnetic stimulation (rTMS) is a non-invasive, well tolerated technique of brain stimulation based on electromagnetic induction for stimulating neurons via brief magnetic pulses delivered by a special coil placed on the scalp (see illustrative Figure 1). The rTMS machine delivers a strong current in a short period of time, the current in the coil then produces a magnetic field, which, if changing rapidly enough, will induce an electric field sufficient to change the resting membrane potential and/or stimulate spiking of neurons in the underlying cortex¹.

A recent meta-analysis² revealed a small demonstrable antidepressant effect of rTMS, with better results in subjects with treatment-resistant depression. rTMS of the left DLPFC is considered to be a particularly promising intervention for treatment-resistant depression^{3,4}. Additional studies confirmed that high-frequency rTMS (5-20 Hz) delivered to the left DLPFC for 2-4 weeks was able to produce potent antidepressant, anxiolytic and cognitive effects in PD patients while being functionally equivalent to pharmacological treatment with fluoxetine^{5,6}.

The present small-scale pilot study is part of an ongoing larger research project labeled „Clinical and therapeutic applications of repetitive transcranial magnetic stimulation (rTMS) of the dorsolateral prefrontal cortex (DLPFC) in patients with Parkinson's disease“ which seeks to better understand the underlying effects and mechanisms of rTMS in the described group of patients.

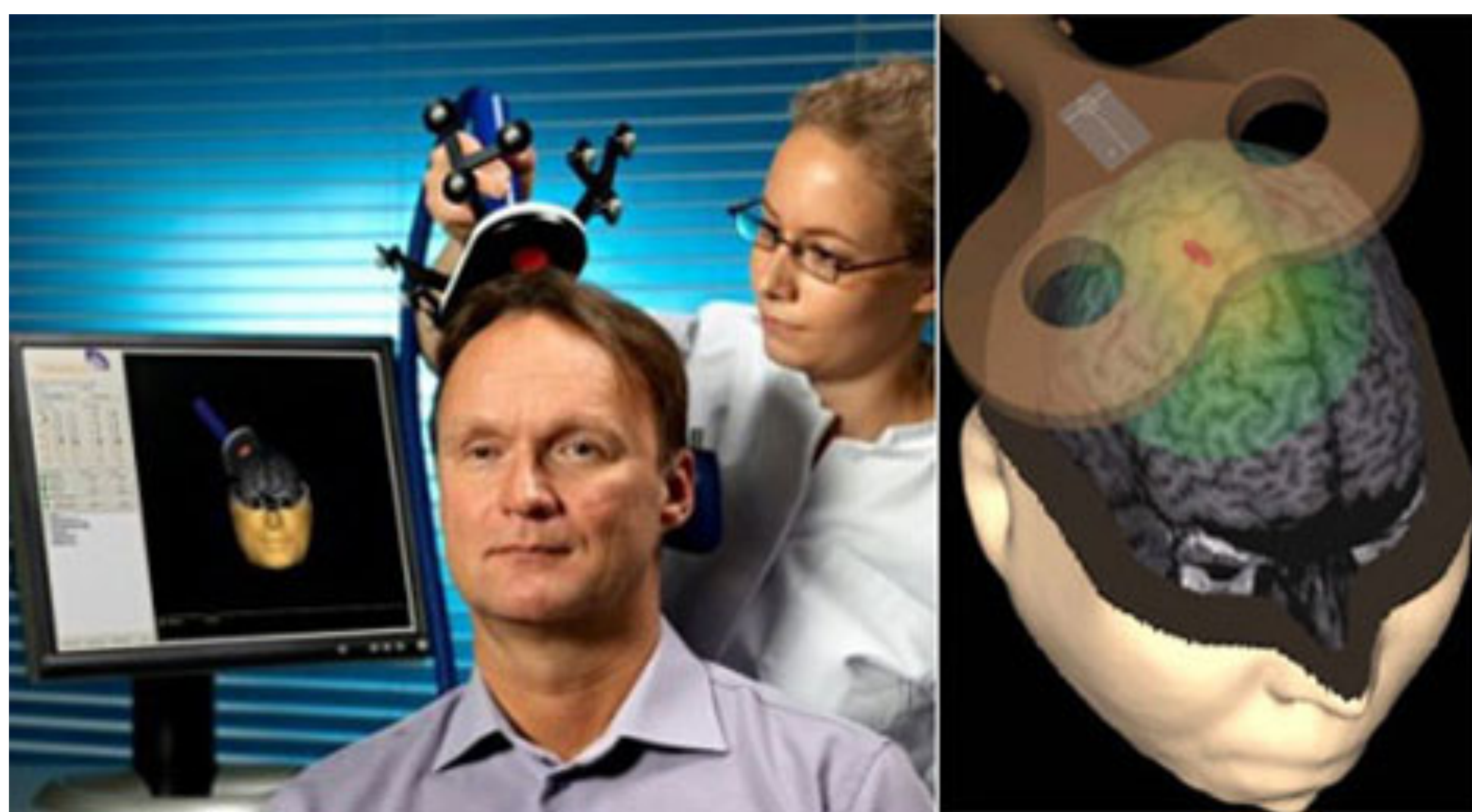


Figure 1. Transcranial magnetic stimulation

Methods

The subjects' inclusion criteria were as follows: Idiopathic PD diagnosis (according to UK Brain Bank criteria⁷); moderate or severe clinical depression (according to ICD-10); at least 2 previous AD trials; no implants, pregnancy, other CNS, neurological or psychiatric disorders and no dementia. Ethical approvals were obtained from the partaking Hospital and University Human Medical Research Ethics Committees.

The baseline assessment of the subjects consisted of a full neurological exam and neuropsychological evaluation, administered by a neurologist and clinical neuropsychologist, respectively. Patients were randomly assembled into one of two groups: sham (A) and stimulation (B). The study period of 3 weeks included baseline and Week 3 neurological and neuropsychological assessments and 6 stimulation sessions (frequency of twice a week). A Navigated TMS System with a 70mm-diameter Figure-8 Coil was used (Nexstim Ltd., Finland) to stimulate the left dorsolateral prefrontal cortex. Subjects were stimulated at 80% resting motor threshold (RMT) using a frequency of 10Hz. 500 impulses per trial were administered.

Severity of Parkinson's disease was assessed with the Hoehn-Yahr Scale⁸ and Schwab-England Scale⁹. To assess global cognitive functioning, the Montreal Cognitive Assessment Scale (MoCA¹⁰) was used. To assess depressive symptoms, the Beck Depression Inventory (BDI-II¹¹) and the Hamilton Depression Scale (HAM-D¹²) were used. To describe patients' quality of life, the Parkinson's Disease Questionnaire (PDQ-39¹³) was used.

Results

Three patients (n=3; 2F/1M) were investigated. Mean age of patients was 60,0 (SD=6,56). Patient characteristics are shown in Table 1. Beneficial effects were noted in the MoCA and PDQ scales for all subjects. In the context of depression, the results were mixed with a clear positive effect of rTMS for at least 1 of the subjects (S1; see Figure 2).

Table 1. Subject characteristics

Subject	S1	S2	S3
Group	B	A	B
Sex	M	F	F
Age	54	67	59
Education (yrs)	11	17	13,5
MoCA at Baseline	25	26	19
Schwab-England at Baseline	80	80	70
Hoehn & Yahr Stage at Baseline	2,5	3	3

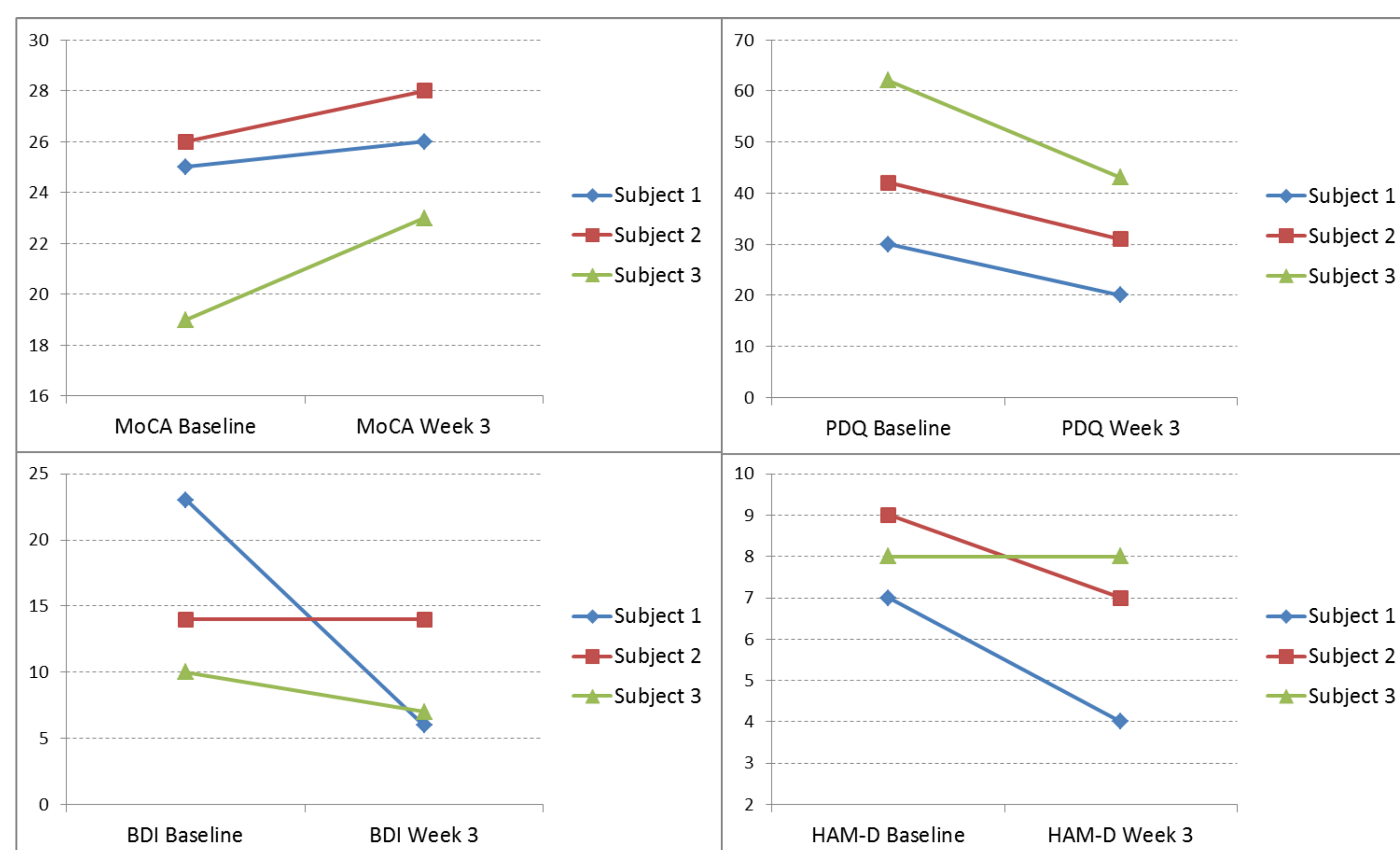


Figure 2. Patients' results in cognitive, quality of life and depression measures.

Discussion

Repetitive transcranial magnetic stimulation (rTMS) is a relatively new and promising technique in alleviating symptoms of treatment-resistant depression in patients with Parkinson's disease. Preliminary results of the present small-scale pilot study show that in specific instances, symptoms of depression lessen after a brief period of high-frequency rTMS to the left DLPFC and there is implication for benefit in overall cognitive functioning and quality of life. Our findings are not in contrast with previous studies and warrant further examination with a larger sample and a longer stimulation period. Emphasis should be placed on repeated measures of depression and overall functioning as well as incorporating additional measures for mood (incl. anxiety) and cognition (incl. tests for measuring working memory, attention, psychomotor speed and executive functioning).

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