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Effect of Repeated Sessions of Transcranial Direct Current Stimulation on Functional Balance in Parkinson's Disease: A Pilot Randomized Controlled Study

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Abstract

Background: Trans cranial direct current stimulation is a new treatment for neuromodulation and in several studies showed positive effect on Parkinson's disease especially motor symptoms. The aim of this study was to assess additive effects of consecutive sessions of tDCS on functional balance in patients with PD.

Method: In this pilot randomized double blind parallel study, 23 patients with Parkinson's disease (PD) divided in two groups of real Trans Cranial Direct Current Stimulation plus occupational therapy and sham Trans Cranial Direct Current Stimulation plus occupational therapy and the effects of therapeutic sessions (8 sessions Trans Cranial Direct Current Stimulation with 0.6 mA/cm² current, 20 minute on dorsolateral prefrontal cortex) were evaluated on balance just after therapeutic course and in 3 months follow-up.

Results: There was no significant time-Group interaction in any time point showing that behavior of experimental and sham groups didn't differ regarding changes in BBS (df=1.44, F=0.91, p=0.38).

Conclusion: Based on the results of the present study there is no significant effect of tDCS on functional balance in patients with PD at any time point.

Keywords: Transcranial direct current stimulation; Parkinson's disease; Balance; Occupational therapy

Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder, primarily characterized by motor symptoms (MS) such as tremor, rigidity, bradykinesia, stiffness, slowness and impaired equilibrium [1] and non- motor symptoms (NMS) include fatigue, autonomic dysfunction, cognitive/ neurobehavioral disorders, and sensory and sleep abnormalities [2]. Postural instability is one of the cardinal symptoms of PD and Studies have shown subclinical manifestation of postural instability and balance dysfunction in the early stage of PD [3].

There is a high fall incidence, even in optimally-medicated, early-stage PD (40–70%). However, balance problems and resulting falls are major factors determining quality of life, morbidity, and mortality in individuals with PD [4,5]. Impairment of postural control in Patients with PD is due to different causes including rigidity, bradykinesia of postural responses, impaired kinesthesia for sensory integration, bradykinetic gait with freezing, and less automaticity of gait and balance [5]. Balance dysfunction is a clinical concern since they are not easily amenable to treatment neither with medication nor by surgical method in the form Deep brain stimulation [6,7].

Transcranial direct current stimulation (TDCS) is a noninvasive technique for inducing prolonged functional changes in the human cerebral cortex [8]. Previous studies have shown the benefit of TDCS on motor function, bradykinesia, gait, working memory, executive function and fatigue in patients with PD [9-14].

Significant motor improvement after right dorsolateral prefrontal cortex (DLPFC) stimulation [10] and reduced bradykinesia, and increased walking speed after TDCS of the motor and prefrontal cortices have been reported [9]. Also,

anodal stimulation of TDCS has produced significant improvement of gait with reduction in number and duration of freezing of gait episodes along with a significant reduction in the Unified Parkinson's Disease Rating Scale score [11].

TDCS can modulate cortical excitability and prefrontal dopamine release and enhance neurophysiological mechanisms that compensate for impaired learning in PD and affect motor performance. TDCS has the potential to enhance rehabilitation effects in the elderly and in patients with neurological diseases [13,15,16]. However, preliminary evidence regarding benefit of combining TDCS and physical training on gait [17,18] and effect of TDCS on balance is conflicting [18,19]. The aim of this study was to assess additive effects of consecutive sessions of TDCS on functional balance in patients with PD.

Materials and Methods

Study setting

This pilot double-blind controlled trial was conducted at Physical Medicine and Rehabilitation department, Firoozgar Hospital in Tehran, Iran.

Participants

Eligible participants were Twenty three patients (9 women and 14 men) aged between 36 and 80 years (mean age 63 years) with idiopathic Parkinson's who were in stage 2 or 3 of Parkinson disease based on Hoehn and Yahr criteria diagnosed by a neurologist; were under stable pharmacological regime at least 30 days before entrance the study; have stable clinical condition; have a good primary response to Levo-DOPA or DOPA agonists; have normal MRI.

Patients excluded from the study if they have dementia related to Parkinson's disease using Mini-Cog test and also, have parkinsonism related to drugs, history of epilepsy, any other neurological disorder or have metal implants in the head including deep brain stimulator or aneurysm clips. The study protocol was approved by the local ethics committee at Iran University of Medical Sciences and underwent in accordance with the ethical standards of the Helsinki Declaration. The procedure was explained to the patients and they signed written informed consent before participation in the study.

Intervention

Patients were allocated into real or sham treatment groups using a simple randomization method. Each patient received eight sessions of real or sham anodal tDCS in two weeks and occupational therapy just after each session.

12 patients were assigned to real tDCS group and 11 patients to sham tDCS group. Irrespective of more involved side of body, the anode electrode was positioned over left DLPFC area that is localized as 5 cm in front of C1 using

international 10-20 electroencephalogram system. Cathode electrode was placed over Right DLPFC.

A battery driven stimulator (Activadose II) generated direct electrical current with a maximum current output of 4 milliampere. Two pairs of 35 cm² rubber electrodes covered with 0.9% saline soaked sponges were used for transmission.

In both groups the direct current was ramped up to 0.6 mA/cm² during 30 s. Experimental group received 20 min of real stimulation with a current intensity of 0.6 mA/cm². After the initial ramp-up in sham group, the current was directly ramped down to 0 and patients and after initial tingling sensation patients didn't receive any stimulation in the remaining time. The ramp-down time was 4 seconds in both groups. The stimulator was placed out of sight of patients considering blindness.

Outcome

Berg Balance Scale (14 items, each 0-4, total score is mean of 14 items range 0-4, lower score_ increasing severity) was used as outcome measure to evaluate patient functional balance at baseline, just after treatments (after two weeks) and 3 months later. Participants and rater were both blinded to the treatment

Statistical analysis

Data analysis was performed by SPSS 22 software. A Greenhouse-Geisser correction was used for sphericity violation. "Kolmogorov Smirnov" test showed data had normal distribution so, parametric tests were used. Independent sample t-test and Chi-square test were used for analysis of Baseline characteristic. "Mixed design ANOVA" was used to explore the main and interaction effects of time and group on BBS. Statistical significance was defined at <0.05.

Results

A total of 40 patients were evaluated and based on inclusion criteria, 23 patients were enrolled in the study and all of them completed study. These patients (14 males and 9 females) were randomly allocated to real/sham groups. Baseline characteristic of experiment and sham groups are shown in **Table 1**.

Table 1 Baseline characteristics of experimental and sham groups.

Variables	Experimental (N=12)	Sham (N=11)	P-value
Age (years)	61.33	64.81	0.478 ^a
Gender (N)	7 female	7 female	1.000 ^b
BBS (mean ± SD)	45.08 ± 15.95	50.54 ± 9.61	0.337 ^a

Although Berg Balance Scale didn't change significantly in either group at any time point but the main effect of time was significant in a whole sample (experiment and sham groups)

between before and just after therapeutic course termination ($p=0.02$) but not after 3 months follow up (Table 2).

Table 2 Pair wise comparison of BBS in whole sample.

Different time points	Mean Difference	P- value	95% Confidence Interval for Difference	
			Lower bound	Upper bound
Just before v/s just after treatment	-3.28	0.022	6.163	-0.398
Just before v/s 3-month follow-up	-4.25	0.165	-9.694	1.194
Just after v/s 3-month follow-up	-0.97	1	-5.798	3.859

There was no significant time-Group interaction in any time point and behavior of groups didn't differ regarding changes in BBS ($df= 1.44$, $F= 0.91$, $p= 0.38$) (Figure 1).

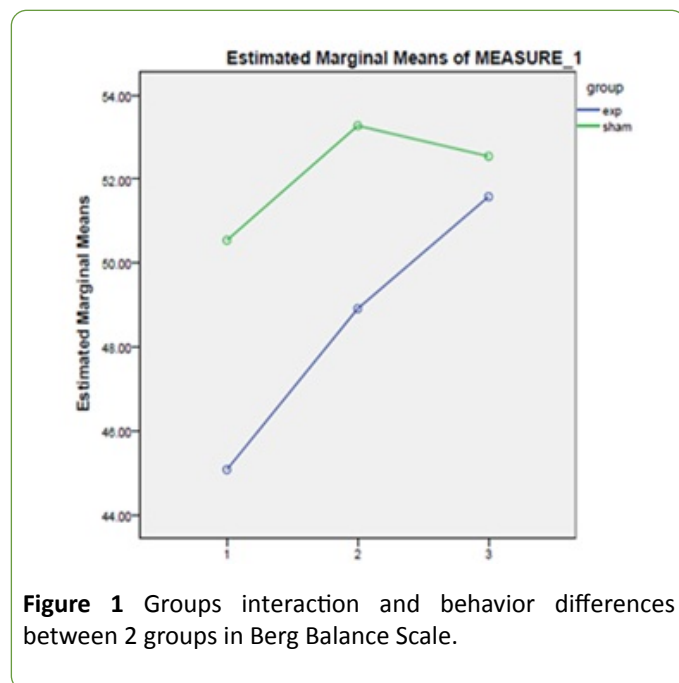


Figure 1 Groups interaction and behavior differences between 2 groups in Berg Balance Scale.

Discussion

Parkinson's disease is a progressive neurodegenerative disorder characterized by motor and non-motor symptoms [1]. Postural instability is one of the four cardinal symptoms of PD [3] which may be present sub clinically in the early stage of the disease [5]. It is known that the executive functions and attention supported by the DLPFC play a key role in walking speed, especially in the elderly and frontal areas are functional during locomotion [20]. TDCS may modulate prefrontal dopamine release, thus affecting motor performance [11].

Preliminary findings showed benefits of TDCS in multiple aspects of PD such as working memory, cognitive ability, motor function, walking ability and freezing of gait and fatigue [9-14]. Motor rehabilitation may be regarded as a process of relearning how to move to satisfy personal needs; practice and training lead to effective motor learning thus improving skills and motor performance. PD subjects demonstrate a relatively preserved ability in motor learning, but consolidation of

learned material is defective and translation to the clinical setting may be critical [21].

General physiotherapy (stretching, muscle strengthening, balance and postural exercises), occupational therapy, and treadmill training, are frequently adopted to improve specific aspects of mobility [20]. Occupational therapy is a conventional effective treatment in motor function improvement and fall prevention in patients with PD performed from the past till to date [22,23].

Results of this study showed, the main effect of time was significant in both groups and there was a significant difference between before and just after therapeutic course termination, but behavior of groups didn't differ regarding changes in BBS at any time point. Therefore, TDCS cannot have any additive effect than which has occupational therapy as the common effective intervention. In line with this study, Costa-Ribeiro et al. [17] compared the effects of a-TDCS (anode placed in Cz) combined with gait training versus sham-TDCS combined with training on functional mobility of individuals with PD. Both groups displayed similar improvements on gait-related outcome measures. However, in another study, combining TDCS on primary motor and premotor cortex with physical training showed positive effects on gait and balance in patients with PD but TDCS alone did not [18].

In contrast, a recent study showed the acute positive effect of left dorsolateral prefrontal cortex (DLPFC) TDCS on balance and functional mobility over to sham- TDCS measured by Berg Balance Scale, Dynamic Gait Index and Timed Up and Go. Participants in this study were Seventeen patients with PD who all received one session of two conditions (TDCS and sham- TDCS) at least 48 h apart [19].

Conclusion

Although the findings of this pilot study couldn't show positive effects of TDCS on function balance in patients with PD, but one explanation may be due to high score of baseline BBS in our patients. Future studies with more sample size and severe balance dysfunction and longer follow up duration should be conducted. Furthermore, using objective measures of balance by force plate may be useful in detection of minimal changes especially in patients with subclinical balance dysfunction.

Based on the results of the present study there is no significant effect of TDCS on functional balance in patients with PD at any time point.

Conflict of Interest

The authors declare that they have no conflict of interest.

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