SOUTHERN BRAZILIAN JOURNAL OF CHEMISTRY 2021 VIRTUAL CONFERENCE

TRANSCRANIAL DIRECT STIMULATION IN THE NEUROMODULATION OF CONTROLLING MAIN SYMPTOMS OF PARKINSON'S DISEASE: A CASE STUDY

SOUZA, Alice Medeiros de¹; AMADEU, Lilian Campos¹; VOSNIADOU, Eleni¹; CORRÊA, Fernanda Ishida¹; DALL'AGNOL, Letizzia^{1*};

¹ Universidade Nove de Julho, Faculdade de Fisioterapia

*Letizzia Dall'Agnol
e-mail: fisioterapiador@gmail.com

Received 20 September 2021; received in revised form 30 December 2021; accepted 10 January December 2022

ABSTRACT

Parkinson's disease (PD) is a central nervous system neurodegenerative disorder that primarily affects the motor system, decreasing motor coordination, balance and generating tremors, and a progressive loss of everyday mobility, including walking. This study was conducted to verify the effects of Transcranial Direct Current Stimulation (tDCS) on balance, motor control, and the quality of life in Parkinson's disease patients. The patient received three treatments consisting of 10 sessions of 20 minutes each and a one-week interval between treatments. Active stimulation was applied on the primary motor cortex (M1), the dorsolateral prefrontal cortex (DLPFC), and the dorsolateral prefrontal cortex (D Sham-tDCS). DLPFC stimulation produced the best improvements in terms of motor control, balance, gait, and overall PD symptoms, as evaluated by different scales and questionnaires. As a result, active stimulation of the DLPFC produced superior outcomes and may contribute to treating Parkinson's disease.

Keywords: *Parkinson's disease, tDCS, Motor Control, Rest Tremor, Quality of Life.*

1. INTRODUCTION

Parkinson's disease (PD) is a progressive neurodegenerative disorder of the central nervous system that mainly affects the motor system, impairing motor coordination, balance, causing tremors with progressive loss of everyday movement, including walking (de Lau, 2006). Epidemiological studies indicate that PD currently affects about 1% of the population of the world over 60 years of age (Marttila, 1981). However, it can affect young adults and, in rare cases, individuals under 40 years of age (Darweesh, 2017). Furthermore, the incidence increases with age, and the disease symptoms appear more frequently after age 55 (Olanow, 1999).

The main characteristic of PD is the progressive loss of predominantly dopaminergic neurons found in the gray matter located in the midbrain. These neurons are part of the extrapyramidal system, which is directly related to the motor system (de Lau, 2006). Neurotransmitter dopamine acts directly on the

basal nuclei to facilitate voluntary automatic movement of the body. PD becomes evident at the loss of approximately 80% of the dopaminergic neurons, and PD patients begin to present a great variety of symptoms, mainly related to a lack of motor control (Jankovic, 2020).

Brain neuromodulation therapies, such as transcranial direct current stimulation (tDCS), are known to improve symptoms associated with PD (Ferrucci, 2016; Fateme, 2021). tDCS can induce significant improvement in motor function when applied to the primary motor cortex (M1) (Elsner, 2016) and also a significant antidepressant effect when applied over the dorsolateral prefrontal cortex (DLPFC) (Dinkelbach, 2017). However, very few studies currently demonstrate the effects of tDCS on the overall improvement in motor function and quality of life in patients with PD. Therefore, we conducted a study to verify the effects of tDCS on balance, motor control, and the quality of life of patients with PD.

2. MATERIALS AND METHODS

2.1. Participant

After signing the Informed Consent Form, the patient participating in the study, a 72-year-old male, was recruited voluntarily through the Supervised Clinical Practice in Neurology at Universidade Nove de Julho. Unfortunately, by the time the study started, the participant could not receive any sort of motor rehabilitation that may interfere with the results to be included in the research.

2.2 tDCS protocol

The participant received three treatments, consisting of 10 sessions of 20 minutes each and a one-week interval in between treatments. Treatments were randomized, resulting in the following order: (1) active tDCS over M1, (2) active tDCS over DLPFC, and (3) Sham tDCS. For both M1 and DLPFC, we used the intensity of 2mA. During the sham-tDCS treatment, the participant stayed for 20 minutes with the electrodes in the same locations as in the a-tDCS condition. However, the device was turned off after 30 seconds of active stimulation. Adverse effects of the stimulation were minor and not persistent (skin redness and tingling during active stimulation and drowsiness/sleepiness during Sham).

2.3 Outcome measures

The following scales and questionnaires were used to assess the effectiveness of the treatments: Timed up and go test (TUG), e Unified Parkinson's Disease Rating Scale (UPDRS), Scales for Outcomes in Parkinson's Disease - Motor Function (SCOPA-M), Berg Balance Scale (BBS), State-Trait Anxiety Inventory (STAI), Pittsburgh Sleep Quality Index (PSQI), Parkinson's Disease Questionnaire (PDQ-39), and Beck Depression Inventory (BDI). Before and after each treatment, all scales and questionnaires were used to analyze the participant (Table 1).

3. RESULTS AND DISCUSSION

After active tDCS stimulation over M1, the patient showed an increase in motor control, a decrease in rest tremors, a broader range of motion in the upper limbs, hands, and fingers, and considerably improved control of pinch motions as measured by the UPDRS (16%) and SCOPA (9%) scales.

Stimulation over DLPFC presented the highest motor control improvement, balance, and gait, as well as a reduction in symptoms

associated with PD, according to an improvement of results in TUG (50%), BBS (20%), UPDRS (38,18%) and SCOPA (36%). On the other hand, sham intervention, in comparison to DLPFC stimulation, showed a decrease in TUG (12,5%), UPDRS (8%), and BBS (3%), thus demonstrating a worsening in the condition of the patient. (see Table 1 for results).

While analyzing the results, we found that, in regards to the quality of sleep and levels of anxiety, the patient presented worsening after active stimulation over M1 according to increased values of PSQI (71%), PDQ-39 (19%), and BDI (50%). However, it is essential to note that these results correspond with the period when the physician of the patient adjusted the prescription for Parkinson's disease (Pramipexole), which caused hallucinations and worsened sleep quality before reverting to the initial dosage of medicine. Although it was not possible to come to conclusive findings in relation to the anxiety levels of the patient, DLPFC stimulation showed the highest results, demonstrating improvement in quality of sleep, as shown on the PSQI (60%).

While not conclusive, our results suggest that active M1 and DLPFC stimulation might improve parkinsonian symptoms, such as resting tremor, loss of motor control and balance. This goes along with the review (Broeder, 2015), showing the efficacy of M1 stimulation in improving motor function and indicating that DLPFC stimulation benefited executive function. However, it is unclear which form of stimulation delivers the best results. According to (Lattari, 2016) substantial findings were obtained when comparing the influence of left DLPFC stimulation on balance and functional mobility.

Regarding the results on DLPFC stimulation, we could find significance on the TUG, UPDRS, SCOPA, BBS, and PSQI results. This corroborates with the findings of (Manenti, 2014), showing a substantial motor improvement following DLPFC stimulation compared to Sham-tDCS.

As additional information, the patient reported increasing resting tremors and rigidity during the one-week intervals in between treatments. Also, the patient had insomnia at the time he was receiving active stimulation but had hypersomnolence when receiving Sham stimulation, during and after each session, being represented by the increase of the PSQI (50%), PDG-39 (29%), and BDI (13%) scales during Sham-tDCS.

4. CONCLUSIONS

In this study, DLPFC stimulation showed the highest improvements in motor control, balance, gait, and overall PD symptoms. Additionally, improved sleep quality was observed on the PSQI scale during DLPFC stimulation and Sham-tDCS. Thus, active stimulation over DLPFC has better results than stimulation over M1 and Sham-tDCS.

One limitation of the present study was the absence of investigation of further long-lasting effects of the therapy. In addition, future research investigating cortical excitability in its relation to controlling the main symptoms of PD might provide more explanations for our findings. Finally, this study was a case study involving only one patient, and we hope studies with larger sample sizes might better explore the present study results.

5. REFERENCES

1. Broeder, S., Nackaerts, E., Heremans, E., Vervoort, G., Meesen, R., Verheyden, G., and Nieuwboer, A. (2015). Transcranial direct current stimulation in Parkinson's disease: Neurophysiological mechanisms and behavioral effects. *Neuroscience and biobehavioral reviews*, 57, 105–117.
2. Darweesh, S. K., Verlinden, V. J., Stricker, B. H., Hofman, A., Koudstaal, P. J., and Ikram, M. A. (2017). Trajectories of prediagnostic functioning in Parkinson's disease. *Brain: a journal of neurology*, 140(2), 429–441.
3. de Lau, L. M., and Breteler, M. M. (2006). Epidemiology of Parkinson's disease. *The Lancet. Neurology*, 5(6), 525–535.
4. Dinkelbach, L., Brambilla, M., Manenti, R., and Brem, A. K. (2017). Non-invasive brain stimulation in Parkinson's disease: Exploiting crossroads of cognition and mood. *Neuroscience and biobehavioral reviews*, 75, 407–418.
5. Elsner, B., Kugler, J., Pohl, M., and Mehrholz, J. (2016). Transcranial direct current stimulation for improving idiopathic Parkinson's syndrome. An abridged version of a Cochrane review. *European journal of physical and rehabilitation medicine*, 52(6), 902–906.
6. Ferrucci, R., Mameli, F., Ruggiero, F., and Priori, A. (2016). Transcranial direct current stimulation as treatment for Parkinson's disease and other movement disorders. *Basal ganglia*, 6, 53–61.
7. Jankovic, J., and Tan, E. K. (2020). Parkinson's disease: etiopathogenesis and treatment. *Journal of neurology, neurosurgery, and psychiatry*, 91(8), 795–808.
8. Lattari, E., Costa, S. S., Campos, C., de Oliveira, A. J., Machado, S., and Maranhao Neto, G. A. (2017). Can transcranial direct current stimulation on the dorsolateral prefrontal cortex improves balance and functional mobility in Parkinson's disease?. *Neuroscience letters*, 636, 165–169.
9. Manenti, R., Brambilla, M., Rosini, S., Orizio, I., Ferrari, C., Borroni, B., and Cotelli, M. (2014). Time up and go task performance improves after transcranial direct current stimulation in patients affected by Parkinson's disease. *Neuroscience letters*, 580, 74–77.
10. Marttila, R. J., and Rinne, U. K. (1981). Epidemiology of Parkinson's disease an overview. *Journal of neural transmission*, 51(1-2), 135–148.
11. Olanow, C. W., and Tatton, W. G. (1999). Etiology and pathogenesis of Parkinson's disease. *Annual review of neuroscience*, 22, 123–144.
12. Pol, F., Salehinejad, M. A., Baharlouei, H., and Nitsche, M. A. (2021). The effects of transcranial direct current stimulation on gait in patients with Parkinson's disease: a systematic review. *Translational neurodegeneration*, 10(1), 22.
13. Rizzo, G., Copetti, M., Arcuti, S., Martino, D., Fontana, A., and Logroscino, G. (2016). Accuracy of clinical diagnosis of Parkinson disease: A systematic review and meta-analysis. *Neurology*, 86(6), 566–576.

Table 1. Scores for motor, balance, quality of life, and quality of sleep scales before and after each transcranial direct current stimulation (tDCS) protocol over M1, DLPFC, and sham tDCS, respectively.

Scales	tDCS over M1			tDCS over DLPFC			Sham tDCS		
	before	after	%	before	after	%	before	after	%
TUG	3	3	0	22	33	50	32	36	12.5
UPDRS	75	63	-16	55	34	-38	37	34	-8
SCOPA	45	41	-9	33	21	-36	16	16	0
BBS	7	7	0	25	30	20	31	32	3
STAI-Y1	32	32	0	30	28	-7	29	30	3
STAI-Y2	34	33	-3	32	31	-3	27	27	0
PSQI	7	12	71	10	4	-60	4	2	-50
PDQ-39	72	86	19	95	89	-6	59	4	-29
BDI	4	6	50	7	7	0	8	7	-13