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Transcranial direct current stimulation as treatment for Parkinson's disease and other movement disorders

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ABSTRACT

Movement disorders have been traditionally regarded as disorders affecting motor control that result from dysfunction in basal ganglia circuitry. Currently, treatment options are symptomatic medications or surgical intervention (i.e., deep brain stimulation). Motor rehabilitation represents another important treatment option for reducing motor dysfunction and improving quality of life. Several studies have highlighted the therapeutic potential of transcranial direct current stimulation (tDCS) in patients with neurological diseases, including dementia, epilepsy, post-stroke dysfunctions, movement disorders, and other pathological conditions. This brief review focuses on available data regarding the effects of tDCS on motor ability and cognition in people with movement disorders. Findings indicate that tDCS is a promising therapeutic tool especially for Parkinson's disease. However, its efficacy in treating other movement disorders appears limited given the current data. Future research efforts should be directed at identifying optimal stimulation parameters (e.g., site, electrode montage and size, duration, intensity, number of sessions, on-line vs. off-line, duration of treatment) for specific types of movement disorders and even for customization for individual patients.

Contents

1. Introduction

Movement disorders are a group of neurological conditions that affecting the ability to produce and control movement [1]. Aside from motor symptoms, movement disorders are associated with a number of other features, such as cognitive and behavioral

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impairments, that negatively impact quality of life [2]. Currently, treatment options are focused on pharmacological treatment of symptoms and motor rehabilitation that reduces motor dysfunction. Another potential treatment involves electrical stimulation with electrodes implanted in deep brain structures (deep brain stimulation) [1]. Several studies have highlighted the therapeutic potential of transcranial direct current stimulation (tDCS) in patients with neurological diseases, including dementia, epilepsy, post stroke dysfunctions, movement disorders, and other pathological conditions [2].

tDCS is a tool that uses weak direct current to manipulate neuroplasticity and modulate cortical functions [3,4]. Depending on the polarity of the current, neuronal firing rates can be made to increase or decrease. In most settings, anodal tDCS is excitatory, while cathodal tDCS is inhibitory [4,5]. The longer-term after-effects of tDCS on cortical excitability are modulated by *N*-methyl-D-aspartate (NMDA) receptor-dependent processes [6]. Weak tDCS can result in long-term potentiation (LTP)-like synaptic changes that normally accompany facilitatory effects on cortical excitability, neuroplasticity, and learning [3,5]. Both immediate effects and after-effects of tDCS are can be modulated by dopaminergic and serotonergic agents [7–9]. Given that studies have shown that tDCS can enhance motor and cognitive functions in healthy individuals and in clinical populations of neurological patients [2], this technique could represent a novel and low-risk therapeutic option for treating movement disorders.

In this brief review, we focus on the effects that tDCS has on motor function and cognition in people with movement disorders (Table 1).

1.1. Parkinson's disease (PD)

In later stages of PD many patients present severe clinical features that interfere with conventional therapies, thereby limiting their utility. A common invasive treatment in PD involves surgical intervention with implantable electrodes stimulating deep brain structures (i.e., deep brain stimulation); however, this invasive intervention is indicated in selected patients. Recent research has highlighted the potential of non invasive brain stimulation technique, such as tDCS to influence the abnormal cortical–subcortical network activity that occurs in PD.

Several studies have assessed the effects of tDCS over the primary motor cortex (M1) [10–15]. The work by Fregni et al. [10]. provided the first evidence that anodal tDCS to M1 might be beneficial for PD patients. They evaluated the effect of tDCS on motor function and corticospinal motor excitability. Motor function was indexed by the unified Parkinson's disease rating scale (UPDRS), simple reaction time (sRT), and Purdue Pegboard test, while motor excitability was assessed by motor evoked potentials (MEPs) using different electrode montages. To study the effects of DC stimulation on MEP characteristics, they recorded MEPs from the right first dorsal interosseous muscle during transcranial magnetic stimulation (TMS). TMS is a non-invasive technique for assessment of brain corticospinal excitability. When applied over the portion of M1 that corresponds to the target muscle, TMS depolarizes neurons in descending corticospinal pathways, eliciting an MEP. Significant improvement was only observed in UPDRS motor score and sRT, and only after anodal stimulation to M1. Furthermore, the results showed that tDCS has a polarity-dependent effect on cortical excitability; whereas MEP amplitude and area significantly increased after anodal stimulation of M1, they decreased after cathodal stimulation.

This finding differed from the results obtained by Verheyden et al. [15], who evaluated the effect of anodal M1 stimulation on 20 patients who performed standardized clinical measurement tasks (sit-to-stand, functional reach, standing-start 180 degrees turning, timed up-and-go (TUG), and the 10-m walk test) to investigate postural stability and functional mobility. Results showed that tDCS had no effect, and indeed, possibly led to a decline in motor performance. This discrepancy likely resulted from both differences in methodologies (e.g., different measures, time of stimulation and patient age) and the medication status of the patients. In the Fregni et al. study, patients were tested in the "*off*" [10] phase of dopaminergic medication, while in Verheyden et al. they were tested in the "*on*" phases [15]. Thus, medication might interact with the effects of tDCS.

Freezing of gait (FOG) is a disabling motor complication that significantly impairs mobility and causes falls. To investigate how it is affected by tDCS, Valentino and colleagues [14] examined the efficacy of tDCS over M1. Ten patients with FOG in the "on" state underwent anodal and sham tDCS over M1. Delayed beneficial effects of anodal stimulation were present at the end of treatment and after 4 four weeks: anodal tDCS significantly reduced UPDRS score, and the number and duration of FOG episodes compared with sham stimulation.

Combining tDCS with physical training, Kaski et al. [12] aimed to improve gait velocity and the response on the pull test in patients with PD. Results showed that compared with the effects of tDCS alone, physical training combined with anodal tDCS to M1 significantly improved gait velocity and balance as showed by stride length, TUG, a 6-min walk test, and the pull test. In another case [11], tDCS was associated with tango dancing in one patient. Anodal bihemispheric stimulation over M1 and premotor cortices while the patient danced the tango improved trunk motion and balance. Peak trunk velocity was significantly greater during tDCS than during sham stimulation, implying less trunk rigidity and faster gait velocity. Improvement was also observed in gait performance, as measured by a reduction in time to complete motor task.

Salimpour et al. [13] used an isometric force-production task (bimanual and unimanual) to study the causal relationship between signal-dependent noise and motor cost in patients with PD. They found that cathodal tDCS over the M1 contralateral to the affected arm and anodal tDCS over opposite side reduced the lateralization of noise, increased the willingness to assign force to the affected arm, and produced significant reductions in motor symptoms measured by UPDRS.

Another cortical area to which researches have examined delivering tDCS is the prefrontal cortex [16–20]. Manenti et al. [19] used the TUG – an objective measurement of locomotor disturbance in PD – to evaluate the effects that tDCS to the dorsolateral prefrontal cortex (DLPFC) had on walking ability. Improvement as indexed by significantly lower sRT in the TUG occurred only after right DLPFC tDCS, and not after sham stimulation.

Because available studies in healthy participants showed that tDCS induced changes in cognitive functions, Boggio et al. [17] tested working memory (WM) in 18 PD patients during stimulation. They delivered anodal tDCS to the left DLPFC, anodal tDCS to M1, or sham tDCS. While WM accuracy significantly increased (by 20%) and error frequency decreased (by 35%) after anodal tDCS to the left DLPFC at 2 mA, the other stimulation conditions elicited no significant changes in task performance.

Benninger et al. [16] investigated whether anodal tDCS over motor and prefrontal cortices improves motor, cognitive, and psychological variables, and whether these effects persist over time. Evaluations were conducted for gait, bradykinesia, visuo-motor speed and procedural learning, mood, health and wellbeing. The motor tests and the UPDRS scores were assessed while patients were on and off dopaminergic medication. Gait improved significantly 24 h after tDCS, with walking time decreasing by 22%, and bradykinesia decreasing by 28% when patients were on medication and by 36% when they were off medication for longer