

The Future of Transcranial Direct Current Stimulation (tDCS) in Rehabilitation: Applications for Depression, Stroke, and Improving Memory and Attention

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Abstract. Transcranial Direct Current Stimulation (tDCS) is a method of brain stimulation involving the placement of positive and negative electrodes over focal brain areas with the intent of modifying neuronal activity within the brain with the electrodes' current. tDCS is an exception to other brain stimulation approaches as it is completely noninvasive, relatively inexpensive, and has no known long-term side effects. Although currently approved only for investigational use, tDCS has potential for eventual use in rehabilitation settings as an augment to or replacement for various forms of pharmacological and/or non-pharmacological treatments for a variety of neural-related problems and disorders. The purpose of this paper, therefore, is to illuminate possible future applications of tDCS in rehabilitation practice, with particular emphasis on treating the prevalent disorders of depression and stroke and improving the critical cognitive functions of memory and attention.

As a result of advances in neuroimaging techniques, such as functional magnetic resonance imaging (fMRI) and single-photon emission computerized tomography (SPECT), knowledge of brain regions that can be targeted to induce changes in cognitive, emotional, motor, and other neural-related functions has greatly increased in the last twenty years (Semrud-Clikeman & Ellison, 2009). Given the knowledge gained from brain imaging, brain stimulation techniques have advanced for examining cortical activity and cognitive processes in both healthy and clinical samples (Been, Ngo, Miller, & Fitzgerald, 2007). These advances are particularly useful for rehabilitation practitioners as they seek to increase the quality of life of individuals with disabilities, many of whom are affected by neural-related disorders, such as depression and stroke, or have other neural-related problems that produce deficits in critical areas of cognitive functioning, such as memory and attention.

Unlike other brain stimulation techniques, such as transcranial magnetic stimulation (TMS), electroconvulsive therapy (ECT), and deep brain stimulation (DBS), which are typically expensive, invasive, and

have potential for serious adverse side effects (National Institute of Mental Health [NIMH], n.d.a), transcranial direct current stimulation (tDCS) is a noninvasive and relatively inexpensive brain stimulation technique (Nitsche & Paulus, 2000; Priori, A, 2003; Priori, Hallett, & Rothwell, 2009; Schlaug & Renga, 2008). Additionally, tDCS has no known long-term negative side effects (Poreisz, Boros, Antal, & Paulus, 2007; Schlaug & Renga, 2008). tDCS involves applying a very weak electrical current (0.5 – 2 mA) into the brain through the scalp (Nitsche et al., 2003; Wagner, Valero-Cabre, & Lascual-Leone, 2007). The procedure results in simultaneous excitatory and inhibitory brain activity, which can lead to various beneficial changes in cognition, mood, motor skills, and other functions, such as improvements in memory and attention of individuals with mild to moderate traumatic brain injury (TBI) (Lesniak, Polanowska, Seniow, & Czlonkowska, 2013) and improvements in gross motor function of individuals recovering from stroke (Kasashima et al., 2012; Ochi, Saeki, Oda, Matsushima, & Hachisuka, 2013). Although the procedure is currently approved for investigational use

only, tDCS has potential for eventual use in rehabilitation settings as an augment to or replacement for various forms of pharmacological and/or non-pharmacological treatments for a variety of neural-related problems and disorders. The purpose of this paper, therefore, is to illuminate possible future applications of tDCS in rehabilitation practice, with particular emphasis on treating the prevalent disorders of depression and stroke and improving the critical cognitive functions of memory and attention.

Rudiments of tDCS

Function

tDCS entails sending a weak direct current (DC) to the brain through the scalp across a positive electrode (anode) to a negative electrode (cathode), thereby causing simultaneous increase in brain activity in the region of the anode and decrease in brain activity in the region of the cathode (Soterix Medical, 2014). Different from other brain stimulation techniques, such as TMS, ECT, and DBS, tDCS is strictly neuromodulatory, only altering nerve activity without eliciting neuronal action potentials (Brunoni et al., 2012; Priori, Hallett, & Rothwell, 2009; Wagner et al., 2007). The current, through its effects on resting membrane potentials, can lead to increased or decreased neuronal excitability, depending upon the polarity and spatial arrangement of the electrodes. Generally, the anode increases brain activity by neuronal depolarization while the cathode decreases brain activity by neuronal hyper-polarization (Nitsche & Paulus, 2000; Nitsche et al., 2008; Schlaug & Renga, 2008).

Impact and Adjustment of Administration

Adjustment to the placement of the anode and cathode and changes to the intensity and duration of the DC allow for various neuromodulatory configurations of tDCS application (Brunoni et al., 2012; Nitsche & Paulus, 2000; Priori, A., 2003; Priori, Hallett, & Rothwell, 2009; Schlaug & Renga, 2008). In addition to changing the DC intensity of tDCS by the amount of current administered (Nitsche et al., 2008; Wagner et al., 2007), DC intensity also can be altered by changing the distance between the electrodes, with intensity decreasing with interelectrode distance (Miranda, Lomarev, & Hallett, 2006). The size of the electrodes also can be modified, with smaller sizes enhancing the current's regional specificity (Nitsche et al., 2008; Priori, Hallett, & Rothwell, 2009). The direction of the electrodes' current determines the effect of the DC, with the anodal-to-cathode current causing hyper-polarization under the anode at its placement (Brunoni et al., 2012; Nitsche et al., 2008; Schlaug & Renga, 2008). An "anode only" configuration can be

used with the anode placed on the head and the cathode placed on the shoulder or arm (extracephalic placement) to still allow for necessary anode-to-cathode current flow (Soterix, 2014). The currents used in tDCS are weak (Brunoni et al., 2012; Priori, Hallett, & Rothwell, 2009), with a significant sum of the electrodes' current never fully penetrating brain tissue (Miranda, Lomarev, & Hallett, 2006).

Applications of tDCS for Depression, Stroke, and Improving Memory and Attention

Depression

Depression is the most common of all mental disorders, affecting an estimated 1 out of 10 adults in the United States and includes a range of symptoms, such as lack of interest and pleasure, lethargy, inattention, and feelings of worthlessness (American Psychological Association [APA], 2014; Centers for Disease Control [CDC], 2011). Treatments for depression commonly include a combination of cognitive-behavioral therapy and medication (APA, 2014; NIMH, n.d.b), which are typically aimed at managing the condition; thus, remission is usually partial with the treatment ([American Psychiatric Association] APA, 2013). Furthermore, 20% to 40% of individuals affected by depression are resistant to pharmacological antidepressant treatments (Lan-dau, Chakravarty, Clark, Zis, & Doudet, 2011). Noninvasive brain stimulation techniques, such as tDCS and TMS offer viable alternatives for treatment of depression.

TMS was approved by the Federal Drug Administration (FDA) for treatment of depression in 2008 (NIMH, n.d.a). The procedure is based on the premise that individuals with depression experience reduced activity in the prefrontal cortex, particularly in the left half, along with other abnormal activity (Grimm et al., 2008). A repetitive application of TMS (rTMS), thus, offers a means to increase neuronal excitability in the left half of the prefrontal cortex, which can alleviate some symptoms of depression (Demirtas-Tatlidede, Vahabzadeh-Hagh, & Pascual-Leone, 2013). tDCS is similar to TMS with respect to its impact on neuronal activity (George et al., 2009) for the treatment of depression. Like TMS treatments for depression, tDCS treatments are based on the assumption that individuals with depressive symptoms have an inter-hemispheric imbalance with lower brain activity in the left hemisphere and higher brain activity in the right hemisphere (Brunoni et al., 2012; Brunoni et al., 2011; Koenigs & Grafman, 2009). For this reason, anodal tDCS is typically placed over the left dorsolateral prefrontal cortex (DLPFC), with cathodal tDCS typically placed over the right DLPFC in order to increase and decrease brain activity, respectively (Brunoni et al., 2012; Brunoni et al., 2011; Brunoni,

Ferrucci, Fregni, Boggio, & Priori, 2012; Dell'Osso et al., 2012; Miranda, Lomarev, & Hallett, 2006).

tDCS treatments have been found to successfully treat depressive and melancholic symptoms in patients with major depressive disorder (MDD) and bipolar disorder (BD) with a depressive episode when treatment entails two twenty-minute sessions separated by four-hour intervals for five consecutive days (Brunoni et al., 2012; Brunoni et al., 2011; Brunoni, Ferrucci, Fregni, Boggio, & Priori, 2012; Dell'Osso et al., 2012). A study by Palm et al. (2012) found that daily twenty-minute sessions of anodal tDCS over the left DLPFC and cathodal tDCS over contralateral supraorbital regions failed to show an improvement in depressive symptoms when compared to active and sham tDCS groups, the study, nevertheless, found an increase in positive emotions and a decrease in negative emotions in active versus sham cathodal stimulation conditions, indicating that, although short of serving as a therapeutic treatment for depression, tDCS may still be effective in influencing emotional regulation.

Stroke

Stroke, caused by a blockage of blood to the brain, is the leading cause of death in the United States and includes symptoms varying in severity and combination, such as speech deficits, loss of memory and motor function, and emotional problems (CDC, 2013; Miniño, Murphy, Xu, & Kochanek, 2011). Ideally, stroke rehabilitation occurs almost immediately after the condition is stabilized and includes treatments to promote movement in the days following stroke to long-term work with a variety of rehabilitation professionals to reestablish normal life routines as much as possible (National Institute of Neurological Disorders and Stroke [NINDS], 2013). tDCS may be an effective augment to traditional stroke therapies (Im, Jung, Choi, Lee, & Jung, 2008; Priori, Hallett, & Rothwell, 2009; Schlaug & Renga, 2008). Given that much of the limited mobility after stroke is due to unbalanced transcallosal inhibitory influences of the unaffected hemisphere that ultimately inhibits activity within the affected hemisphere (Nair, Renga, Lindenberg, Zhu, & Schlaug, 2011; Ochi, Saeki, Oda, Matsushima, & Hachisuka, 2013; Priori, Hallett, & Rothwell, 2009; Schlaug & Renga, 2008), the anodal and cathodal neuronal excitability in tDCS can be successfully applied in stroke recovery by exciting action in the affected hemisphere while simultaneously inhibiting activity in the unaffected area. This will permit the affected area to regain normal excitability by freeing it from the inhibitory influence of the unaffected area (Nair et al., 2011; Ochi, Saeki, Oda, Matsushima, & Hachisuka, 2013; Priori, Hallett, & Rothwell, 2009; Schlaug & Renga, 2008).

In a study of healthy participants and participants recovering from stroke, anodal and sham tDCS were placed over the affected motor cortex while participants took part in mu event-related desynchronization (ERD) with motor imagery of a finger, the affected finger for those recovering from a stroke (Kasashima et al., 2012). Anodal tDCS was found to improve mu ERD in both treatment groups of participants, with the sham condition failing to elicit such improvement. Other studies utilizing Anodal tDCS stimulation over the Wernicke's area (Sparing, Dafotakis, Meister, Thirugnanasambandam, & Fink, 2008), left frontal cortex (Baker, Rorden, & Fridriksson, 2010; Fridriksson, Richardson, Baker, & Rorden, 2011), and left dorsolateral (Fertonani, Rosini, Cotelli, Rossini, & Miniussi, 2010) and left dorsal (Wirth et al., 2011) prefrontal cortex have shown that tDCS improves expressive and receptive language functions in both individuals with aphasia due to stroke or other condition and healthy samples.

Similarly, cathodal tDCS has been shown to be effective. Ochi, Saeki, Oda, Matsushima, and Hachisuka (2013), utilized cathodal tDCS with a robot-assisted arm training in stroke patients recovering from moderate-to-severe paresis. Ochi and colleagues found that participants with damage to the right hemisphere benefitted the most from cathodal tDCS applied to the unaffected left hemisphere than when anodal tDCS was applied to the affected area; however, participants with damage to the left hemisphere showed similar improvement in the Modified Ashworth Scale (MAS) scores when cathodal tDCS was applied to the unaffected area as well as when anodal tDCS was applied to the affected area.

Indeed, the effects of tDCS treatment may be an effective supplement to rehabilitation therapy, given that concurrent focal brain stimulation of the targeted motor area during rehabilitation will ultimately lead to improvement in synaptic plasticity and motor skills, thus enhancing the efficacy of each treatment (Schlaug & Renga, 2008). For example, Nair et al., 2011 in a randomized, double blind trial in which tDCS was paired with occupational therapy (OT) found that combining a central and peripheral stimulation protocol using cathodal tDCS and OT enhanced motor function in chronic stroke patients with moderate to severe motor impairment, more than a similarly intense protocol involving sham tDCS and occupational therapy. The chief conclusions of the study suggested that the benefits of tDCS combined with OT are induced if the ipsilesional motor cortex is depolarized, the contralesional motor cortex is hyperpolarized, or both approaches are utilized simultaneously.

Memory and Attention

Because application of tDCS increases cortical excitability and sustains the long-term potentiation re-

quired for learning, the procedure can be used to modulate memory and attention when supplementing other types of rehabilitation (Lesniak, Polanowska, Seniow, & Czlonkowska, 2013). Lesniak, Polanowska, Seniow, and Czlonkowska (2013) found that repeated applications of anodal tDCS supplementing a cognitive training program improved the memory and attention of individuals with some forms of TBI, possibly because anodal tDCS increases cortical excitability and sustains the long-term potentiation. Although findings from the study did not support the use of anodal tDCS in conjunction with cognitive rehabilitation to improve attention and memory in individuals recovering from severe TBI, the results did, nevertheless, suggest an overall positive response to the use of anodal tDCS to improve attention and memory in individuals with mild to moderate forms of TBI.

Fregni and colleagues (2005) first investigated the effects of tDCS on working memory among healthy individuals in their seminal study in which they found that anodal, but not cathodal, tDCS stimulation over the DLPFC cortex enhanced working memory performance among healthy individuals. Andrews, Hoy, Enticott, Daskalakis, and Fitzgerald (2011) found application of anodal tDCS over the left DLPFC cortex to improve working memory as measured by performance on a digits forward task among healthy individuals when combined with a cognitive activity but not performance on a digits backward task. Javadi and Cheng (2012) applied anodal tDCS to participants to assess the effects of tDCS on long-term verbal memory. To specifically study the effect of the anodal tDCS on word recall, the researchers applied sham, cathodal, as well as anodal tDCS to three different groups during the entire word recognition phase and compared results to a control group that underwent the recognition phase without tDCS stimulation. In this study, improved performance in the delayed recall phase was only seen in the group who received anodal tDCS during the recognition phase, with cathodal and sham tDCS producing equally ineffective results on later word recall. Regarding the expected excitatory nature of anodal tDCS, this finding was somewhat expected.

In a study by Gladwin, Uyl, Fregni and Wiers (2012), anodal tDCS was applied to the DLPFC for 10 minutes during a Sternberg task with distracters as a means to examine the effect of anodal tDCS on selective attention. Selective attention was chosen as a representation of a subcomponent of working memory in which the researchers believed would be more likely to be activated in a complex span task as opposed to a simple span task such as Sternberg tasks without distracters. Important to note is that increases in response time were only present when distracters were used as the incorrect option in the Sternberg task. These findings are similar to the results from Javadi and Cheng (2012), which indicated that tDCS en-

hances memory performance only when past memories are reactivated. In sum, these studies suggest that anodal tDCS applied to the DLPFC has the potential to improve the selective-attention component of memory, mainly when stimulation is applied early in the encoding phase and/or memory is reactivated during recognition or recall.

Anodal tDCS has also been found to be applied over the right inferior frontal cortex (IFC) in an attempt to enhance attention. Coffman, Trumbo and Clark (2012), applied anodal tDCS to the right IFC during the training phase of the Attention Networks Test (ANT). The training session was used to help familiarize the participants with detecting hidden objects in a complex environment. The researchers hypothesized that anodal tDCS stimulation to the right IFC would improve the participants' alerting, orienting and/or executive attention in the ANT. Although the anodal tDCS led to a faster alerting reaction time during the participants' completion of the ANT, there was no impact on orienting or executive attention. The researchers concluded that anodal tDCS of the right IFC improved performance in a difficult hidden object task by enhancing alerting attention as opposed to signal detection.

Jacobson, Goren, Lavidor and Levy (2012) applied anodal tDCS to a substrate of selective attention located within the intraparietal sulcus/superior parietal cortex (IPS/SPL) and cathodal tDCS to a substrate of orienting located within the right inferior parietal cortex (IPC). The researchers hypothesized that this particular application of tDCS would enhance participants' recognition of verbal material, based on the theoretical underlining that the attentional state is a dual process, consisting of one attentional system for selective attention (located within the IPS/SPL) and another attentional system for orienting (located within the right IPC). The findings of this study supported that increased excitability within IPS/SPL overpowered the competition of orientation located within the right IPC leading to enhanced selective attention performance. These findings are complementary to the study by Coffman, Trumbo, and Clark (2012) that found anodal tDCS to the right IFC to enhance alerting attention but not orientation.

Safety and Side Effects

The key benefits of using tDCS are its portability, safety, and noninvasiveness (Brunoni et al., 2012; Nitsche & Paulus, 2000; Priori, Hallett, & Rothwell, 2009; Schlaug & Renga, 2008). tDCS can be battery powered or operated by a power source (Priori, Hallett, & Rothwell, 2009; Schlaug & Renga, 2008). Negative side effects of tDCS, when present, are typically mild and short-term, and include fatigue, tingling, itching, and warming sensations under the electrodes

placed on the scalp (Poreisz, Boros, Antal, & Paulus, 2007; Schlaug & Renga, 2008). Factors, such as age, health, and target stimulation area may predispose some participants to the mild side effects (Gandiga, Hummel, & Cohen, 2006; Poreisz, Boros, Antal, & Paulus, 2007; Priori, 2003).

To reduce the potential of side effects associated with tDCS, a common recommendation is to soak electrodes in a saline solution or apply an electrode cream and continuously monitor the current during application (Nitsche et al., 2008; Priori, Hallett, & Rothwell, 2009; Schlaug & Renga, 2008). Another popular recommendation to reduce the potential of negative sensations associated with tDCS is using current ramping, applying a slight increase in current at the beginning and ending of stimulation (Nitsche et al., 2008). Current ramping has not only been found to reduce the subjective feelings experienced by participants but also to make the difference between active and sham tDCS unidentifiable, thus allowing for a sham-tDCS mode (Schlaug & Renga, 2008), which is conducive to placebo-controlled studies.

Conclusions

Given its positive outcomes in studies relevant to treating depression and stroke and improving memory and attention, along with its easy portability, relatively low monetary cost compared to other brain stimulation techniques, and low potential for harmful side effects, tDCS holds promise for eventual use by a variety of rehabilitation professionals. Practitioners, such as rehabilitation counselors, OTs, physical therapists (PTs), recreational therapists, vocational evaluators, rehabilitation psychologists, neuropsychologists, medical providers, and other rehabilitation professionals, may find tDCS to be a viable augment to or replacement for traditional treatments when the treatment becomes approved for clinical use outside of research. Rehabilitation professionals already familiar with the emergent treatment modality of tDCS may be in a better position to knowledgeably consider tDCS as a low-cost, safe, and effective option. It is, therefore, our hope and anticipation that this paper will serve to provide useful information about and spark dialog among rehabilitation professionals on tDCS as an emerging treatment for a variety of disorders and problems treated in a range of rehabilitation settings.

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