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Research report

Transcranial direct current stimulation over multiple days improves learning and maintenance of a novel vocabulary

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ABSTRACT

Introduction: Recently, growing interest emerged in the enhancement of human potential by means of non-invasive brain stimulation. In particular, anodal transcranial direct current stimulation (atDCS) has been shown to exert beneficial effects on motor and higher cognitive functions. However, the majority of transcranial direct current stimulation (tDCS) studies have assessed effects of single stimulation sessions that are mediated by transient neural modulation. Studies assessing the impact of multiple stimulation sessions on learning that may induce long-lasting behavioural and neural changes are scarce and have not yet been accomplished in the language domain in healthy individuals.

Method: The present study probed the potential of atDCS to enhance language learning over multiple days by employing an explicit word learning paradigm. Forty healthy young participants were randomized to learning with either simultaneous atDCS or sham stimulation ($N = 20$/group; comparable regarding demographic variables and neurocognitive status). All participants acquired a novel vocabulary (familiar and novel object picture – non-word pairs) over five consecutive days. Two memory tasks (free recall; forced choice recognition tasks) were administered immediately after each training session. A one week follow-up tested the maintenance of learning success.

Results: Linear mixed effects model analysis revealed superior learning during atDCS compared to sham stimulation for both familiar and novel objects. atDCS yielded a steeper learning curve and significantly more pronounced learning at the end of the training during the recall task. During the recognition task, the atDCS group reached ceiling levels earlier and overall learning success was greater. For both tasks, beneficial atDCS effects were maintained during the follow-up assessment.

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Conclusions: The present study provides direct evidence that atDCS administered during multiple learning sessions facilitates language learning and that effects are maintained over time. This study contributes important novel information about the extent of stimulation effects in the healthy brain, thereby highlighting the potential of atDCS to enhance language recovery after stroke.

1. Introduction

Neuroplasticity refers to dynamic structural and functional central nervous system reorganization due to internal or external demands and is recognized as the main physiological basis for adaptive behavioural changes (Pascual-Leone, Amedi, Fregni, & Merabet, 2005). Recently, growing interest emerged in the enhancement of neuroplasticity by means of non-invasive brain stimulation techniques like transcranial direct current stimulation (tDCS; Floel & Cohen (2010)) to improve human performance and learning. During tDCS, weak electrical currents are applied to the scalp to modulate excitability of underlying neural populations (Nitsche et al., 2003). The most consistent beneficial effects on motor and cognitive functions have been reported for anodal stimulation (anodal transcranial direct current stimulation – atDCS; Kuo & Nitsche (2012)) that facilitates firing of task-specific neuronal populations. Moreover, due to its excellent safety profile and effective placebo ("sham") stimulation option (Gandiga, Hummel, & Cohen, 2006), atDCS has become increasingly popular in research and clinical settings (Flöel, 2012; Kuo & Nitsche, 2012).

In the language domain, a number of studies have demonstrated that atDCS administered to left perisylvian cortices improves word-retrieval and lexical processing when administered prior to or during task performance (Cattaneo, Pisoni, & Papagno, 2011; Flöel, 2012; Meinzer et al., 2012; Meinzer, Lindenberg, Antonenko, Flaisch, & Flöel, 2013; Peretz & Lavidor, 2013; Sparing, Dafotakis, Meister, Thirugnanasambandam, & Fink, 2008). In addition, atDCS has also improved vocabulary (Fiori et al., 2011; Flöel, Rösser, Michka, Knecht, & Breitenstein, 2008) and artificial grammar learning (de Vries et al., 2010). In the latter studies, training was accomplished across several blocks during a single stimulation session and superior learning immediately after the training was reported for anodal compared to sham or inhibitory cathodal tDCS. Those short-term effects can be explained by transient modulation of resting-membrane potentials that outlast the stimulation only for short periods of time (Nitsche et al, 2003). As a result, immediate beneficial effects on language functions may not be maintained over time (Flöel et al., 2008).

However, with regard to potential clinical applications, stimulation protocols that induce long-lasting behavioural modifications are of utmost importance. Indeed, long-lasting modifications are feasible with tDCS, since repeated stimulation sessions result in modification of post-synaptic connections similar to long-term potentiation which is critical for learning and neuroplasticity (Stagg & Nitsche, 2011). However, such studies have not yet been accomplished in the language domain in healthy individuals and so far, only few studies assessed the impact of repeated atDCS sessions on learning in other domains. For example, two recent studies demonstrated faster and better motor skill learning after a one week training period with atDCS compared to training alone (Reis et al., 2009; Zimerman et al., 2013). Superior training outcome was maintained for up to three months (Reis et al., 2009). For higher cognitive functions, Cohen Kadosh, Soskic, Iuculano, Kanai, and Walsh (2010) demonstrated enhanced numerical learning after six days of training with atDCS compared to sham or inhibitory cathodal tDCS and gains were maintained for six months. Another recent study, however, failed to demonstrate maintenance of immediate atDCS effects on cognitive functions after 10 days of computer assisted training (Martin et al., 2013). This study highlights the pressing need to further explore the extent of potential beneficial effects of repeated atDCS sessions in healthy subjects.

Based on the above studies in healthy individuals and also previous studies in stroke patients showing that the combination of atDCS and motor therapy resulted in enhanced outcome compared to treatment alone (for review see Reis & Fritsch, 2011), it has been suggested that atDCS may be valuable as an adjunct treatment for post-stroke language disorders (aphasia, Holland & Crinion, 2012). Indeed, overall beneficial effects of atDCS (compared to sham or cathodal tDCS) have been demonstrated in preliminary pilot trials (Baker, Rorden, & Fridriksson, 2010; Fiori et al., 2011; Flöel et al., 2011). However, these previous studies also yielded highly variable stimulation effects in individual patients, possibly due to the unknown relationship between language system reorganization after stroke and the stimulation site (for further discussion see Flöel, 2012, 2013; Meinzer, Harnish, Conway, & Crosson, 2011). This emphasizes the urgent need for proof-of-principle studies in healthy participants, to explore the extent of tDCS-effects on language learning under highly controlled experimental conditions. Indeed, it has been suggested that studies of new word learning in healthy participants can be informative regarding how to optimize language re-learning in stroke patients (Basso, Marangolo, Piras, & Galluzzi, 2001). Therefore, the present study employed an explicit new word learning paradigm (Whiting, Chenery, Chalk, Darnell, & Copland, 2007; Whiting, Chenery, Chalk, Darnell, & Copland, 2008) scheduled over five consecutive days either with concurrent atDCS or sham stimulation. By examining learning of new names associated with both familiar and unfamiliar objects (Laine & Salmelin, 2010), we also examined the linguistic specificity of atDCS effects on learning. In addition, long-term effects of the stimulation were assessed during a one week follow-up period. Based on previous studies in other domains (Cohen Kadosh et al., 2010;

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