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BOTH ANODAL AND CATHODAL TRANSCRANIAL DIRECT CURRENT STIMULATION IMPROVES SEMANTIC PROCESSING

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Abstract—Transcranial direct current stimulation (tDCS) is a common method to modulate cortical activity. Anodal tDCS is usually associated with an enhancement of the stimulated brain area, whereas cathodal tDCS is often described as inhibitory brain stimulation method. Our aim was to investigate whether this canonical assumption derived from the motor system could be transferred to the semantic system. Three groups with 20 healthy subjects each were stimulated at Wernicke's area with either anodal, cathodal or sham tDCS. Subsequently, they performed a simple lexical decision task for a duration of about 25 min. Subjects receiving anodal tDCS revealed faster reaction times (RTs) compared to the sham group, although not reaching statistical significance. Surprisingly, in the cathodal group RTs were decreased significantly. All subjects were faster in the second half of the task, but the tDCS-induced improvement lasted for the entire duration of the task. Error rates were not influenced by tDCS, neither were RTs in a choice reaction time task. Thus, both anodal and cathodal tDCS applied to Wernicke's area improved semantic processing. Recently, a meta-analysis revealed that the canonical anodal excitation and cathodal inhibition assumption is observed rarely in cognitive studies. In particular, an inhibitory effect of cathodal tDCS on cognition is rare. Our findings thus support the speculation, that especially language functions could be somewhat 'immune' to cathodal inhibition. © 2016 The Author(s). Published by Elsevier Ltd on behalf of IBRO. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Key words: cognitive, lexical decision, semantic processing, tDCS, Wernicke's area.

INTRODUCTION

When introduced, anodal transcranial direct current stimulation (tDCS) was shown to increase cortical excitability in the motor system, whereas cathodal tDCS decreases excitability (Nitsche and Paulus, 2000). These effects were confirmed by many studies investigating the motor system (Lang et al., 2004; Furubayashi et al., 2008; Stagg et al., 2009), leading to the canonical assumption "anodal excitation, cathodal inhibition" (AeCi-effect, Jacobson et al., 2012). Although some studies observed comparable modulations applying tDCS to other cortical regions like the visual cortex (Antal et al., 2003), a meta-analysis showed that the AeCi-effect occurred rarely in cognitive studies (Jacobson et al., 2012). In most studies investigating cognitive functions, anodal stimulation indeed improved performance (e.g., Iyer et al., 2005; Floel et al., 2008; Sparing et al., 2008; Kraft et al., 2010), and the expected inhibitory effect of cathodal tDCS was observed in a few investigations (e.g., Rogalewski et al., 2004; Knoch et al., 2008; Berryhill et al., 2010). Nevertheless, some studies showed an improvement of performance following cathodal tDCS (Antal et al., 2004; Dockery et al., 2009; Karim et al., 2010; Weiss and Lavidor, 2012; Pirulli et al., 2014). However, there is evidence that the direction of modulation caused by cathodal tDCS may depend on the task investigated (Weiss and Lavidor, 2012; Nozari et al., 2014). Depending on the level of observation and the complexity of neural circuitry, facilitation or inhibition of behavior might depend on different electrophysiological modifications (cf. Bestmann et al., 2015).

Applying another common brain stimulation method, we showed that 1-Hz repetitive magnetic stimulation (rTMS) as well as continuous theta burst stimulation (cTBS) of Wernicke's area both impaired semantic processing (Brückner et al., 2013). Therefore, the canonical assumption from rTMS motor studies (e.g., Chen et al., 1997; Huang et al., 2005) declaring 1 Hz rTMS and cTBS as "inhibitory" brain stimulation methods, was successfully transferred to a higher cognitive function. In the present study, we aimed to apply tDCS to investigate whether the canonical AeCi-effects known from the motor cortex could also be observed in the semantic system. Using the same lexical decision task as in our former study (Brückner et al., 2013), modulation of semantic processing was examined following anodal, cathodal and sham tDCS. So far, several studies observed modulatory effects applying tDCS to Wernicke's area (Floel et al., 2008; Fiori et al., 2011; Peretz and Lavidor, 2013; Weltman and Lavidor, 2013; Perry and Lupyan, 2014), with very variable findings concerning the direction of the effects. Interestingly, to our knowledge, there is only one study investigating tDCS effects on a simple lexical

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Abbreviations: AeCi, anodal excitatory cathodal inhibitory; CRT, choice reaction time task; cTBS, continuous theta burst stimulation; rmANOVA, repeated-measures analyses of variance; RT, reaction time; rTMS, repetitive transcranial magnetic stimulation; tDCS, transcranial direct current stimulation.

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decision task (Weltman and Lavidor, 2013). However, in their study bilateral stimulation was applied to Wernicke's area and its right homolog, making it difficult to interpret the result in terms of polarity dependency of unilateral modulation. In our study, the effects of anodal and cathodal stimulation of Wernicke's area only were investigated, enabling a better comparison with our former study applying unilateral rTMS (Brückner et al., 2013). Due to the contradictory results of previous studies investigating tDCS effects on cognitive tasks, it is difficult to make clear predictions concerning the results of the present study. Since our lexical decision task has been shown to be suitable to detect modulations of Wernicke's area caused by brain stimulation methods before (Brückner et al., 2013), we expected to observe clear modulations with tDCS as well. In our former study, the canonical assumption of the effects of several inhibitory rTMS protocols from the motor system was successfully transferred to the semantic system. The present study aimed to investigate whether the same conclusion for tDCS can be drawn. However, previous findings suggest that observing an improvement following anodal tDCS is more likely than an impairment following cathodal tDCS.

In this study, we observed faster reaction times (RTs) following both anodal and cathodal tDCS in a lexical decision task. This finding supports the notion of Jacobson et al. (2012), that AeCi-effects of tDCS are not common in cognitive domains, and that in particular in language tasks cathodal tDCS does not evolve inhibitory effects.

EXPERIMENTAL PROCEDURES

Subjects

A total of 66 healthy subjects were recruited for the study. Six subjects had to be excluded, two because they were left-handed and four due to technical problems during the measurement. The remaining 60 subjects (30 male, mean age 22.7 ± 2.8 years) all were right-handed according to a modified version of the Edinburgh scale (Oldfield, 1971) and native German speakers. Subjects had no metallic implants, no prior history of any neurological or psychiatric disorders, alcoholism or drug abuse. All were free of any medication except contraceptives at the time of the experiment. Subjects gave written informed consent and were paid for participation. The study followed the Declaration of Helsinki and was approved by the Ethics Committee of the University of Ulm.

tDCS

Subjects were divided into three groups with 20 subjects each, receiving either anodal (10 male, mean age 21.5 ± 1.9 years), cathodal (10 male, mean age 23.7 ± 3.2 years) or sham stimulation (10 male, mean age 22.9 ± 2.7 years). TDCS was delivered by a battery-driven direct current stimulator (DC-STIMULATOR, NeuroConn GmbH, Ilmenau, Germany) through a pair of 7 × 5-cm saline-soaked surface sponge electrodes. The NaCl solution concentration was 15 mM since lower concentrations are more likely to be perceived as comfortable during stimulation (Dundas et al., 2007). For anodal (cathodal) stimulation, the anode (cathode) was placed over CP5 according to the international EEG 10–10 system (left posterior temporal cortex, Wernicke's area). The reference electrode was placed on the left shoulder (extra-cephalic reference). For active stimulation, tDCS was applied for 15 min at 1 mA with a ramping period of 15 s (fade-in/fade-out). In the sham group, stimulation lasted 30 s with either anodal or cathodal polarity. To control for general attention and to standardize cognitive activity, subjects had to perform an acoustic oddball task during stimulation. Two minutes after tDCS subjects started to perform the lexical decision task.

Lexical decision task

The lexical decision task was almost identical to that used in our former study (Brückner et al., 2013). It was realized using Presentation (V 18.1 Neurobehavioral Systems, San Francisco, CA, USA). For details regarding the lexical decision task, see Brückner et al. (2013). In brief, 100 German words and 100 pseudowords (in four blocks with 50 presentations each) were presented randomized on a computer screen. The words were all nouns with comparable length (mean six letters). They were controlled for frequency, familiarity, and visual and functional associations. Subjects had to decide whether the stimulus is a real word or not. Prior to tDCS, subjects performed a practice run with 16 trials. Stimuli of the practice run were not included in the main task. Additionally, at the beginning of each block, five stimuli of the practice set were presented to keep subjects familiar with the task. These first five stimuli of each block were discarded afterward. In addition, after the second as well as after the fourth block, a short motor control task was performed.

Motor control task

Since the electrodes and thus the stimulated cortex area is quite large (7 × 5 cm), we controlled for motor cortex modulations using a choice reaction time task (CRT) two times prior to tDCS as well as in the middle and at the end of the lexical decision task. Each trial started with a fixation cross (0.5 s). After a blank period (0.3–1.5 s), an arrow was presented in the middle of the screen, pointing either to the right or to the left. Subjects had to determine the direction of the arrow as quickly as possible by pressing one of two buttons. One run of the motor control task consisted of 30 trials.

Data analysis

Mean RTs of the correct responses were calculated for words and pseudowords of each subject separately. RTs slower or faster than two standard deviations of the mean were defined as outliers and excluded from the analysis (for each subject and stimulus type separately, 4.67% of the data set). For the motor control task, the same exclusion procedure was applied. RTs and error rates were analyzed regarding normal distribution for the three groups separately and analyzed by means of repeated-measures analyses of variance (rmANOVAs).