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A single session of prefrontal cortex transcranial direct current stimulation does not modulate implicit task sequence learning and consolidation

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ABSTRACT

Background: Transcranial direct current stimulation (tDCS) is assumed to affect cortical excitability and dependent on the specific stimulation conditions either to increase or decrease learning.
Objective: The purpose of this study was to modulate implicit *task* sequence learning with tDCS.
Methods: As cortico-striatal loops are critically involved in implicit task sequence learning, tDCS was applied above the dorsolateral prefrontal cortex (DLPFC). In Experiment 1, anodal, cathodal, or sham tDCS was applied before the start of the sequence learning task. In Experiment 2, stimulation was applied during the sequence learning task. Consolidation of learning was assessed after 24 h.
Results: The results of both experiments showed that implicit task sequence learning occurred consistently but it was not modulated by different tDCS conditions. Similarly, consolidation measured after a 24 h-interval including sleep was also not affected by stimulation.
Conclusions: These results indicate that a single session of DLPFC tDCS is not sufficient to modulate implicit task sequence learning. This study adds to the accumulating evidence that tDCS may not be as effective as originally thought.

1. Introduction

Recently, transcranial direct current stimulation (tDCS) has been established as a promising tool for boosting learning by applying weak electrical currents on participants' scalp [1]. Here we test the impact of tDCS on implicit task sequence learning. Although there are several studies that have addressed the impact of tDCS on sequence learning, this is the first study that addresses its impact on *implicit task sequence learning*.

Implicit sequence learning is the incidental acquisition of a succession of events. It results in knowledge difficult to express, or implicit [2]. Classically, implicit sequence learning is tested with the serial reaction time task (SRTT). In the SRTT participants press one of four key responses when a visual cue appears on a corresponding location on a screen. Unbeknownst to them, the visual cues locations follow a sequenced order. Because for each visual cue there is a corresponding response button, the SRTT involves correlated streams of perceptual and motor sequences [3]. To disentangle these two streams the *task sequence learning paradigm* (TSL) was developed [3,4,5,cf.6]. In the present study we used a TSL paradigm in which digits or letters are presented in green or in red. When a digit appears participants have to decide if it is smaller or bigger than five, when a letter appears they have to decide if it is a vowel or a consonant. When the digit or the letter is green, participants have to follow screen indicators for which a left key response is used for vowels and digits smaller than five, and a right key response is used for consonants and digits bigger than five. When the letter or the digit is red, participants have to do the opposite than the screen indicators. Unbeknownst to participants, the order of tasks (digit vs. letter task) and the order of response mappings (compatible vs. incompatible response mapping relative to the screen indicators) follow a sequence with the same length. Reaction times (RTs) decrease with practice and, when the sequenced order is switched to random, RTs increase. This increase indicates sequence-specific learning that is to say participants learnt a specific sequence. After the TSL, participants are not able or they partially recall the sequence. Notably, sequence-specific learning in

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the TSL does not involve a stimulus sequence or a motor response sequence. Thus it represents learning of more abstract sequence information based on higher order cognitive processes [5,7].

At the neural level, the networks connecting the frontal lobes to the basal ganglia, namely the fronto-striatal loops, seem crucial for implicit sequence learning [8–13]. Similarly, for the TSL patients suffering from Parkinson's disease, and patients with dorsolateral prefrontal cortex (DLPFC) lesions do not show sequence-specific learning in the TSL [7]. In the present study, we used a TSL paradigm that required participants to switch between the digit and the letter tasks, and between compatible and incompatible response mappings relative to the screen indicators. As task switching comes at costs, that is RTs are higher in trials in which the task or the response mapping are switched compared to trials in which they are repeated, these costs are taken as a control parameter to asses DLPFC modulation by tDCS [5,6]. In fact the ability to switch between tasks depends on the DLPFC [14–17].

The aim of the present study was to modulate sequence-specific learning in the TSL by applying tDCS over the DLPFC. Participants received anodal or cathodal tDCS above the left or the right DLPFC. After 15 min of tDCS, participants started the TSL. To evaluate the impact of tDCS on consolidation, learning was assessed again after a 24 h-interval including a night sleep. As there are good reasons for the involvement of both hemispheres in TSL, each hemisphere was stimulated. In particular, left DLPFC tDCS may modulate sequence-specific learning because left hemisphere tDCS has been shown to modulate memory tasks [18,19]; right DLPFC tDCS may modulate sequence-specific learning in the TSL [20,21] because the right hemisphere is involved in integrating different types of information. Additionally, we also tested whether tDCS modulated switch costs.

2. Experiment 1

2.1. Method

2.1.1. Participants and design

One hundred and three right-handed participants were assigned to one of the six experimental conditions. Participants were blind to the experimental conditions. None of them reported psychiatric or neurologic disorders. One participant trained in different sequences in Session 1 and 2 and was excluded. Also, four participants that had accuracy below 80% in blocks in which the sequence was embedded (i.e., blocks 5–12) were excluded. The final sample consisted of 98 participants: 17 for anodal left DLPFC, 17 for anodal right DLPFC, 16 for cathodal left DLPFC, 16 for cathodal right DLPFC, 16 for sham left DLPFC, and 16 for sham right DLPFC (76 women, 22 men, mean age 25, $SD = 5$). The experimental design was a mixed design, with stimulated hemisphere (left DLPFC vs. right DLPFC) and stimulation type (anodal vs. cathodal vs. sham) manipulated between subjects and block manipulated within subjects. Participants gave written informed consent before the start of the experiment. The study was approved by the Ethical Committee of the Canton Bern.

2.2. Material

The TSL paradigm was adopted from Weiermann et al. [5]. The stimuli were the digits 1, 2, 3, 4, 6, 7, 8, and 9, and the letters a, e, i, u, c, n, r, and s, which were presented on the center of a black screen in 32-point Arial font, either in red or green color.

For tDCS, a DC stimulator plus (neuroConn, Ilmenau, Germany) connected to two squared 35 cm^2 rubber electrodes was used. They were inserted into sponges soaked with saline solution to decrease impedance. The sponges were attached to the participants scalp by two rubber straps.

The stimulation protocol was adopted from Ohn et al. [22] who demonstrated tDCS effects of DLPFC stimulation for up to 30 min duration on a working memory task [22]. The active electrode was placed above the left or the right DLPFC, positions F3 and F4 of the 10–20 electroencephalography (EEG) system [DaSilva et al., [23]]. The return electrode was placed on the contralateral supraorbital region relative to the active electrode. Constant current was delivered at 1 mA for 30 min. For the sham conditions, current was delivered only for 30 s, a procedure that does not influence the neural membranes and, from the experience of a participant, is undistinguishable from real tDCS [24]. At the beginning of tDCS all participants reported skin itching under the electrodes but no other adverse effect.

2.3. Procedure

Participants were tested individually in two sessions separated by 24 h. In Session 1, they received tDCS stimulation. tDCS ended during the TSL and electrodes were kept in place until the end of the session. Fifteen minutes after the start of tDCS, written instructions of the TSL were given. Participants were informed that they would conduct a reaction time task in which they had to make digit decisions or letter decisions. The stimuli determined the task type, a digit signaled digit task and a letter signaled letter task. The digit task consisted of deciding whether a digit was smaller (1, 2, 3, 4) or bigger (6, 7, 8, 9) than five. The letter task consisted of deciding whether a letter was a vowel (a, e, i, u) or a consonant (c, n, r, s). Stimulus color determined the response mapping. Green indicated a compatible response mapping requiring pressing the “1” key with the left index finger for digits smaller than five and for vowels, and pressing the “5” key with the right index finger for digits bigger than five and for consonants. Incompatible response mapping required the opposite key mapping, that is, “1” for digits bigger than five and for consonants and “5” for digits smaller than five and vowels, respectively. As a reminder, the compatible response mapping was indicated on the screen throughout the experiment (in white color and in 26-point Arial font on the left and the right of the stimuli). Fig. 1 depicts two subsequent trials of the task. Participants were told that we were interested in how well they would do in such a complex task. They were asked to respond as quickly and accurately as possible, but were not informed about the presence of a repeating sequence. For each participant, a sequence was drawn from a pool of sixteen sequences of task-response mapping combinations each of which consisted of the four possible trial-to-trial relations (task: repeated vs. switched, and response mapping: repeated vs. switched; cf. Weiermann et al., 2010).

Session 1 consisted of 18 blocks. Blocks 1–4 were practice blocks in which a pseudorandom order of task-response mapping combinations was presented. In blocks 5–14 an eight-element sequence of task types and response mappings was embedded (i.e., sequenced blocks). In blocks 15 and 16 the sequenced order was switched to pseudorandom. In blocks 17 and 18 the sequence was re-established. In each sequenced block the sequence was repeated 13 times. Each block consisted of 104 trials. On each trial, a digit or a letter in green or red was presented on the center of the screen. The trial ended when the participant pressed one of the two response buttons (i.e., keyboard button “1” or keyboard button “5”) with the left or right index finger. The inter-stimulus interval was 200 ms (ms). To prevent fatigue there was a short break between blocks.

Session 2 was composed by seven blocks. A practice block was followed by two sequenced blocks, two pseudorandom blocks, and another two sequenced blocks. The whole procedure was run using