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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

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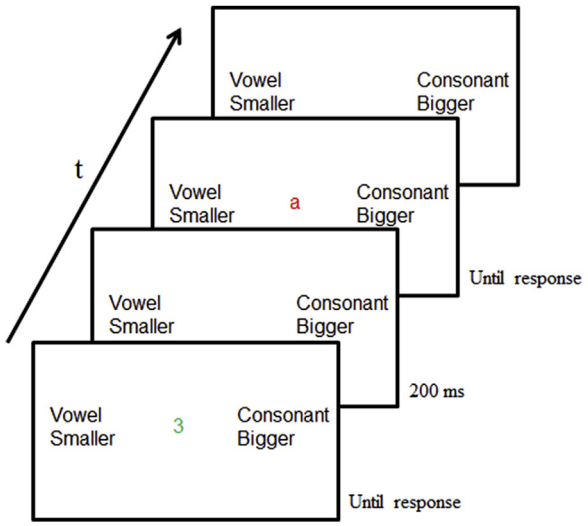

Fig. 1. Two trials of the TSL [5]. The actual background was black. The stimuli were digits or letters presented in green or red. Left and right from the stimuli there were the instructional reminders. The instructional reminders indicated compatible response mapping. The correct response for "3" green would be pressing keyboard button "1" with the left index finger. The correct response for "a" red would be pressing keyboard button "5" with the right index finger. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

E-Prime version 1.2 (Psychology Software Tools, Pittsburgh, PA). Fig. 2 illustrates the experimental procedure.

At the end of the second session, participants were informed that there was a repeating sequence composed by task types and response mappings. They were asked whether they noticed any sequence. Then, they were requested to guess a sequence on a sheet of paper showing a series of eight boxes. Each box represented the screen. They had to write either a digit or a letter, indicating in this way the task type, in green or in red, indicating in this way the response mapping. The number of consecutive reproduced sequence elements was calculated as a measure of explicit knowledge.

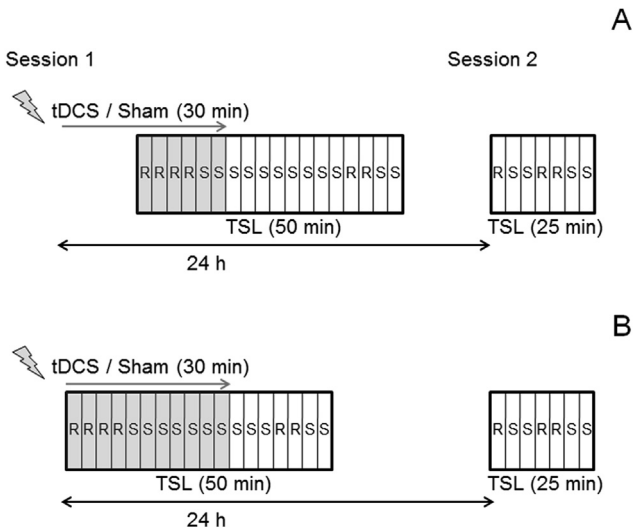

Fig. 2. Procedures used in Experiment 1 (A) and Experiment 2 (B). "R" equals random, "S" equals sequenced blocks. The blocks colored in grey mark ongoing tDCS.

2.4. Data analysis

The first trial of each block, trials in which errors were made, trials after an error, and trials with RTs below 100 ms were excluded. For Session 1, the increase of RTs in pseudorandom blocks 15 and 16 was indicative of sequence-specific learning. For Session 2, the increase of RTs in pseudorandom blocks 4 and 5 was indicative of sequence-specific learning. For Session 1 and 2 the analysis of switch costs was restricted to blocks 13–18 and blocks 2–7, respectively. The RTs of the four possible trial-to-trial relations (i.e., task: repeated vs. switched, and response mapping: repeated vs. switched) were compared between each other. Disruption scores of Session 1 were calculated as RTs difference between the mean of pseudorandom blocks 15 and 16 and the mean of the surrounding sequenced blocks 13, 14, 17, and 18. Disruption scores of Session 2 were calculated as RTs difference between the mean of pseudorandom blocks 4 and 5 and the mean of the surrounding sequenced blocks 2, 3, 6, and 7. For evaluating tDCS effects with time passing by disruption scores of Session 1 and 2 were compared. For all statistical analysis an alpha value of 0.05 was used. Effect sizes are indicated in partial η^2.

2.5. Results

2.5.1. Session 1

To investigate whether tDCS modulated sequence-specific learning a mixed three factorial analysis of variance (ANOVA) was conducted, with blocks (mean RT of pseudorandom blocks 15 and 16 vs. mean RT of sequenced blocks 13, 14, 17, and 18) as within subject factor, and with hemisphere (left DLPFC vs. right DLPFC) and stimulation type (anodal vs. cathodal vs. sham) as between subjects factors. The ANOVA showed a significant main effect of block $F(1, 92) = 83.75$, $p < 0.001$, $\eta^2 = 0.47$, and no other significant main effect or interaction ($ps > 0.07$), indicating that in all conditions RTs increased when the sequence order was changed to pseudorandom. These results are depicted in Fig. 3.

To investigate tDCS effects on switch costs a mixed four factorial ANOVA was conducted, with task (repeated vs. switched) and response mapping (repeated vs. switched) as within subject factors and hemisphere (left DLPFC vs. right DLPFC) and stimulation type (anodal vs. cathodal vs. sham) as between subjects factor. The ANOVA showed a main effect of task $F(1, 92) = 71.98$, $p < 0.001$, $\eta^2 = 0.43$ and a main effect of response mapping $F(1, 92) = 195.95$, $p < 0.001$, $\eta^2 = 0.68$, indicating that when the task or the response mapping were switched there was an increase in RTs. Furthermore, the interaction task x response mapping was significant $F(1, 92) = 46.39$, $p < 0.001$, $\eta^2 = 0.33$, indicating that the RT difference between trials in which the task was switched and trials in which the task was repeated was bigger when the response mapping was repeated compared to when it was switched. Importantly, there was no main effect or interaction with the between subjects factors hemisphere and stimulation type ($ps > 0.16$) indicating similar switch costs in all conditions (i.e., task switch costs = 141, $SE = 16$, response mapping switch costs = 213, $SE = 15$) (see Supplementary Material Fig. S1 for full descriptives).

2.5.2. Session 2

For Session 2, the mixed three factorial ANOVA for investigating tDCS effects on sequence-specific learning showed a significant main effect of block $F(1, 92) = 87.47$, $p < 0.001$, $\eta^2 = 0.48$, and no other significant main effect or interaction ($ps > 0.21$), indicating that across all conditions RTs increased when the sequenced order was changed to pseudorandom. These results are depicted in Fig. 3.

The mixed four factorial ANOVA on switch costs showed the same results of Session 1. Hence, a significant main effect of task F

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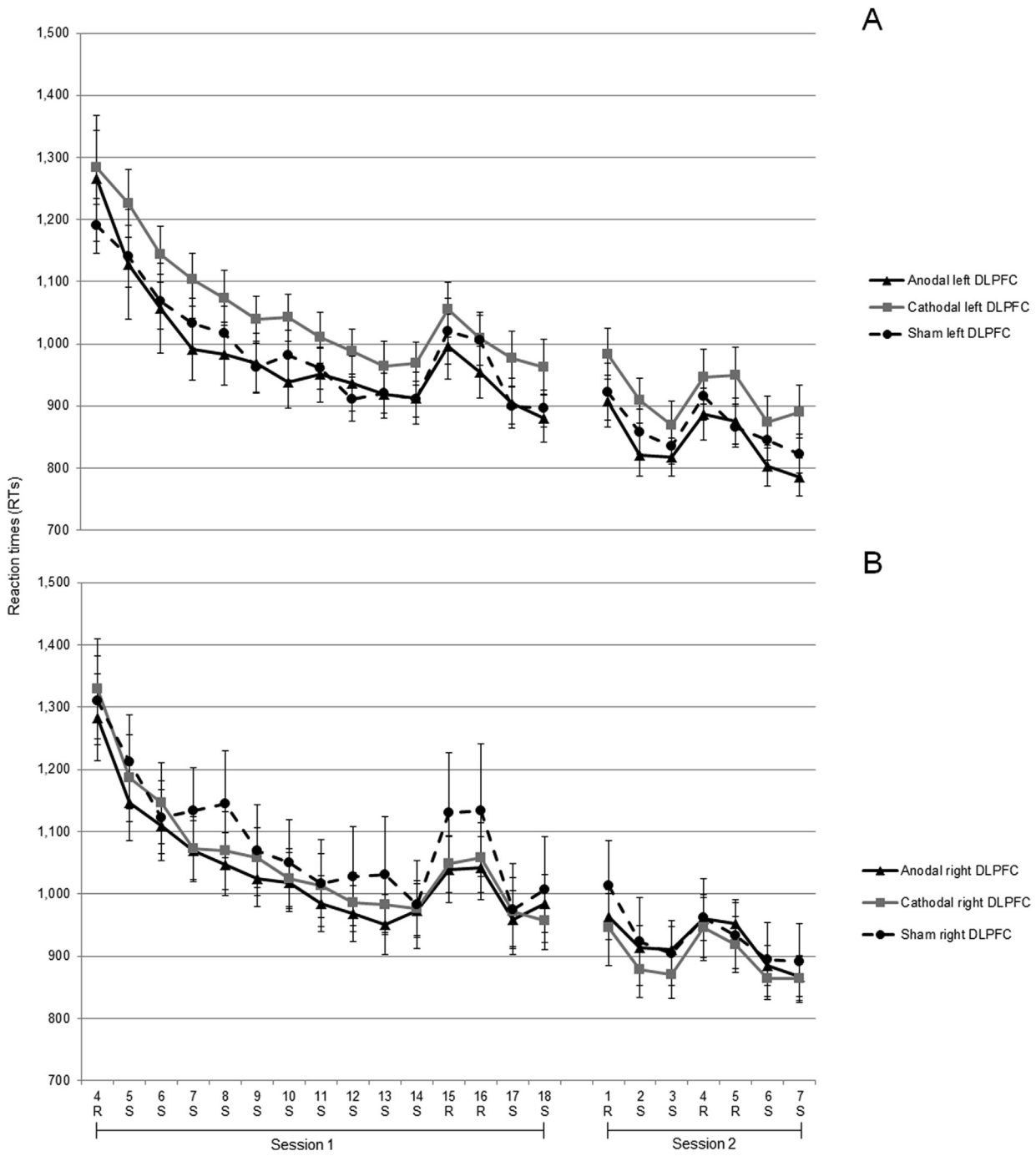

Fig. 3. RT trajectories across blocks for Experiment 1 (stimulation before onset of TSL). Separately for left hemisphere tDCS (A) and right hemisphere tDCS (B), respectively. "R" equals random, "S" equals sequenced block. Bars represent standard errors.

(1, 92) = 61.54, $p < 0.001$, $\eta^2 = 0.40$, a main effect of response mapping $F(1, 92) = 163.98$, $p < 0.001$, $\eta^2 = 0.64$, a task x response mapping interaction $F(1, 92) = 33.55$, $p < 0.001$, $\eta^2 = 0.26$, and no other main effect or interaction ($ps > 0.12$), indicating similar switch costs in all conditions (i.e., task switch costs = 85, $SE = 11$, response mapping switch costs = 163, $SE = 12$).

2.5.3. Session 1 vs. session 2

To investigate tDCS effects across sessions, a mixed three factorial ANOVA was conducted, with the disruption scores of the two sessions as within subject factor, and with hemisphere (left DLPFC vs. right DLPFC) and stimulation type (anodal vs. cathodal vs. sham) as between subjects factor. The ANOVA showed a significant main effect of disruption scores $F(1, 92) = 8.93$, $p < 0.05$, $\eta^2 = 0.08$, and a significant disruption scores x stimulation type interaction $F(2, 92) = 4.97$, $p < 0.05$, $\eta^2 = 0.09$, no other main effect or interaction was significant ($ps > 0.25$). Further analyses for each stimulation type showed a significant main effect of disruption scores for sham stimulation type $F(1, 30) = 11.31$, $p < 0.05$, $\eta^2 = 0.27$, but not for anodal stimulation type $F(1, 32) = 0.12$, $p = 0.73$, $\eta^2 = 0.00$, and not for cathodal stimulation type $F(1, 30) = 0.44$, $p = 0.51$, $\eta^2 = 0.01$, indicating that in the sham conditions the disruption scores decreased across sessions. These results are depicted in Fig. 4.

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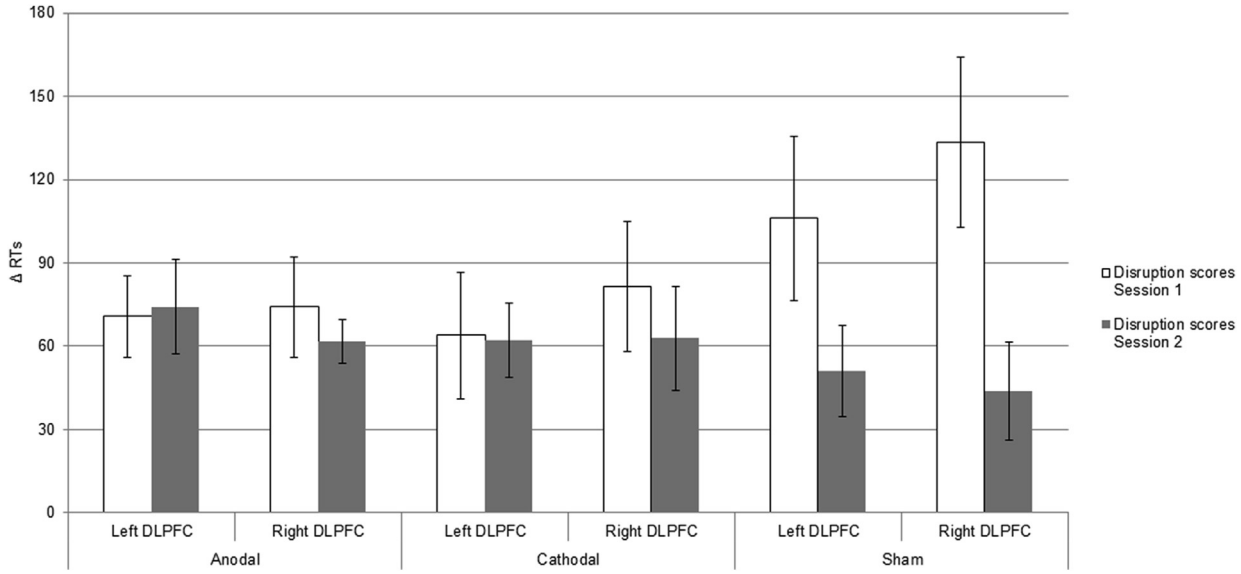

Fig. 4. Sequence learning scores for Experiment 1, separately for Session 1 and Session 2, and each experimental condition respectively. Bars represent standard errors.

2.5.4. Explicit knowledge

The mean number of correctly recalled items of the sequence was 2.9 ($SD = 1.4$), 2.8 ($SD = 1.4$), 2.9 ($SD = 0.9$), 3.6 ($SD = 1.4$), 3.1 ($SD = 2$), 2.9 ($SD = 1.2$), for anodal left DLPFC, anodal right DLPFC, cathodal left DLPFC, cathodal right DLPFC, sham left DLPFC, and sham right DLPFC, respectively. Participants that recalled more than four items were suspected of having explicit knowledge of the sequence. In total, 11 participants recalled more than four items (i.e., seven recalled five, two recalled six, and two recalled seven items).

To investigate whether explicit knowledge affected sequence-specific learning, the disruption scores were calculated separately for the 11 participants and the remaining participants. For Session 1, the disruption score of the participants with potential explicit knowledge was 89 ms ($SE = 33$), and for the rest the disruption score was 87 ms ($SE = 10$). As revealed by an independent-samples t-test, the disruption scores of the two groups did not differ ($p = 0.96$). Furthermore, the disruption score of the remaining participants was significantly different from zero t (86) = 8.63, $p < 0.001$, indicating sequence-specific learning for participants who had little or no explicit knowledge. For Session 2, the disruption score of the participants with potential explicit knowledge was 55 ms ($SE = 22$), and for the rest the disruption score was 59 ms ($SE = 6$). As revealed by an independent-samples t-test the disruption scores of the two groups did not differ ($p = 0.83$). Furthermore, the disruption score of the remaining participants was significantly different from zero t (86) = 9.22, $p < 0.001$, indicating sequence-specific learning for participants who had little or no explicit knowledge.

2.6. Discussion

The aim of Experiment 1 was to modulate sequence-specific learning in the TSL by using DLPFC tDCS. Additionally, tDCS was also expected to modulate switch costs. The results showed that sequence-specific learning was present in all conditions in both sessions. By comparing the two sessions, results showed that sequence-specific learning either decreased or stayed the same across sessions. Although in the first session the sham conditions showed more sequence-specific learning than anodal and cathodal conditions, the results did not reach statistical significance. Moreover, in both sessions the switch costs were similar across conditions. Hence, anodal and cathodal tDCS above the right and left DLPFC modulated neither sequence-specific learning nor switch costs.

One possible explanation for the absence of tDCS effects is that the DLPFC is not critically involved in the TSL. This explanation is unlikely because both neuroimaging and patients studies evidenced the DLPFC role for implicit sequence learning [7,11,25]. Additionally, several previous results evidenced the DLPFC role for task switching which is embedded in the TSL [14–17,26].

Another explanation for the null effects of Experiment 1 is that tDCS applied *before the start* of the TSL did not influence performance. Several previous studies suggest that tDCS delivered during a task can enhance learning [[27–32], see Ref. [33] for a biological model]. Hence, in Experiment 2 we used the same method as in Experiment 1, except that tDCS was applied during the TSL. Because in Experiment 1 there was no effect of stimulated hemisphere, in Experiment 2 we tested only one sham condition.

3. Experiment 2

3.1. Method

3.1.1. Participants and design

Eighty-two right handed participants were assigned to one of the experimental conditions. Participants were blind to the experimental conditions. None of them reported psychiatric or neurologic history. Two 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 80 participants: 15 for anodal left DLPFC, 16 for anodal right DLPFC, 16 for cathodal left DLPFC, 17 for cathodal right DLPFC, and 16 for sham (53 woman, 27 man, mean age 25, $SD = 9$). Stimulation type (anodal left DLPFC vs. anodal right DLPFC vs. cathodal left DLPFC vs. cathodal right DLPFC vs. sham) was manipulated between subjects, and block was manipulated within subject, resulting in a mixed design.

3.2. Material and procedure

The material and procedure used in Experiment 2 were the same as in Experiment 1 except that tDCS started with the onset of the TSL (see Fig. 2).

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3.3. Results

3.3.1. Session 1

To investigate whether tDCS modulated sequence-specific learning a mixed two factorial ANOVA was conducted, with blocks (mean RT of pseudorandom blocks 15 and 16 vs. mean RT of sequenced blocks 13, 14, 17, and 18) as within subject factor, and stimulation type (anodal left DLPFC vs. anodal right DLPFC vs. cathodal left DLPFC vs. cathodal right DLPFC vs. sham) as between subjects factor. The ANOVA showed a significant main effect of block $F(1, 75) = 60.93$, $p < 0.001$, $\eta^2 = 0.45$, and no other significant main effect or interaction ($ps > 0.29$), indicating that in all conditions RTs increased when the sequence was changed to pseudorandom. These results are depicted in Fig. 5 Session 1.

To investigate tDCS effects on switch costs a mixed three factorial ANOVA was conducted with task (repeated vs. switched) and response mapping (repeated vs. switched) as within subject factors and stimulation type (anodal left DLPFC vs. anodal right DLPFC vs. cathodal left DLPFC vs. cathodal right DLPFC vs. sham) as between subjects factor. The ANOVA showed a main effect of task $F(1, 75) = 89.92$, $p < 0.001$, $\eta^2 = 0.54$, and a main effect of response mapping $F(1, 75) = 213.32$, $p < 0.001$, $\eta^2 = 0.74$, indicating that when the task or the response mapping were switched there was an increase in RTs. Moreover, the interaction task x response mapping was significant $F(1, 75) = 11.32$, $p < 0.01$, $\eta^2 = 0.13$, indicating that the RTs difference between trials in which the task was switched and trials in which the task was repeated was bigger when the response mapping was repeated compared to when it was switched. Importantly, there was no main effect or interaction with the factor stimulation type ($ps > 0.31$) indicating similar switch costs in all conditions (i.e., task switch costs = 124, $SE = 13$, response mapping switch costs = 232, $SE = 16$) (see Supplementary Material Fig. S2 for full descriptives).

3.3.2. Session 2

For Session 2, the mixed two factorial ANOVA for investigating tDCS effects on sequence-specific learning showed a significant main effect of block $F(1, 75) = 104.65$, $p < 0.001$, $\eta^2 = 0.58$, and no other significant main effect or interaction ($ps > 0.18$), indicating that across all conditions when the sequenced order was changed to pseudorandom RTs increased. These results are depicted in Fig. 5 Session 2.

The mixed four factorial ANOVA on switch costs showed a similar result as in Session 1. There was a main effect of task $F(1, 75) = 49.42$, $p < 0.001$, $\eta^2 = 0.39$, a main effect of response mapping $F(1, 75) = 198.02$, $p < 0.001$, $\eta^2 = 0.72$, an interaction task x response mapping $F(1, 75) = 27.61$, $p < 0.001$, $\eta^2 = 0.27$, and no other significant main effect or interaction ($ps > 0.18$), indicating similar switch costs across all conditions (i.e., task switch costs = 82, $SE = 11$, response mapping switch costs = 180, $SE = 13$).

3.3.3. Session 1 vs. session 2

To investigate tDCS effects across sessions, a mixed two factorial ANOVA with the disruption scores of the two sessions as within subject factor, and stimulation type (anodal left DLPFC vs. anodal right DLPFC vs. cathodal left DLPFC vs. cathodal right DLPFC vs. sham) as between subjects factor was conducted. The ANOVA revealed no significant result ($ps > 0.18$), indicating that in all conditions disruption scores did not change across sessions. These results are depicted in Fig. 6.

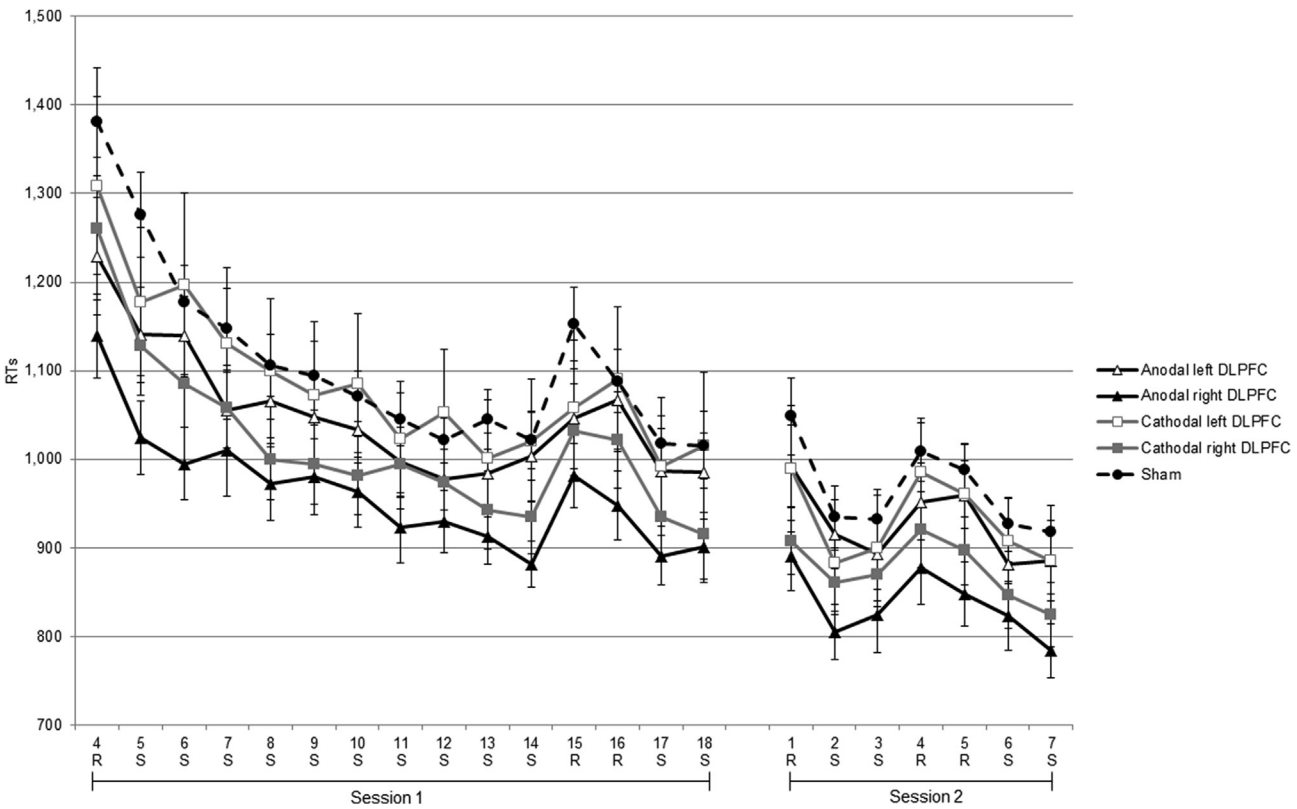

Fig. 5. RT trajectories across block for Experiment 2 (stimulation during TSL). Separately for each stimulation type. "R" equals random, "S" equals sequenced block. Bars represent standard errors.

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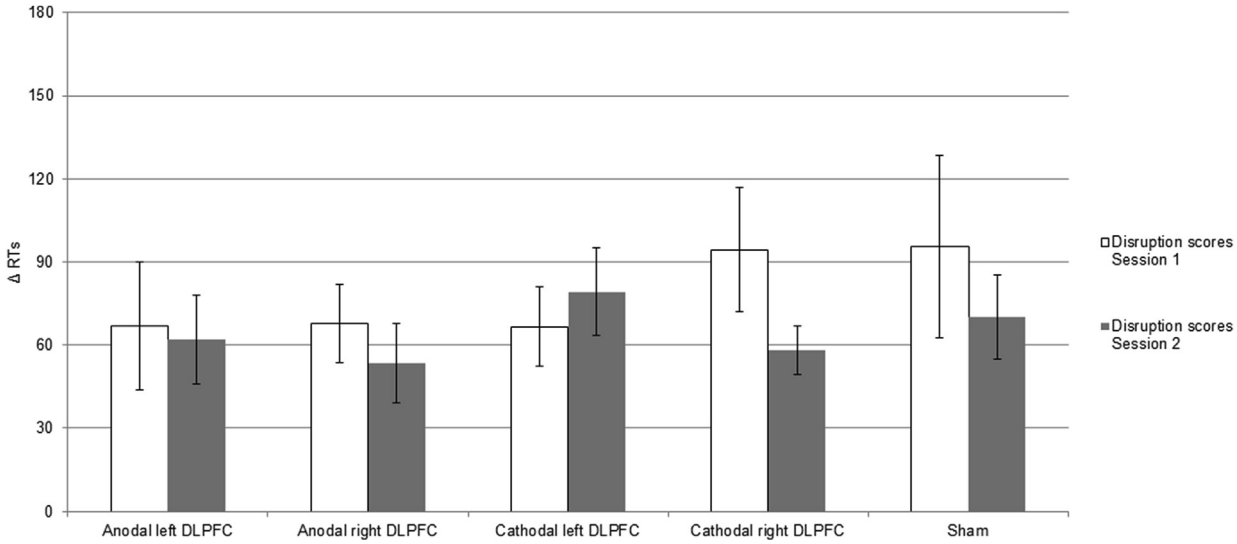

Fig. 6. Sequence learning scores for Experiment 2, separately for Session 1 and Session 2, and each experimental condition respectively. Bars represent standard errors.

3.3.4. Explicit knowledge

The mean number of correctly recalled items of the sequence was 2.3 ($SD = 1.5$), 2.7 ($SD = 1.7$), 2.8 ($SD = 1.5$), 3 ($SD = 1$), and 3.3 ($SD = 1.4$) for anodal left DLPFC, anodal right DLPFC, cathodal left DLPFC, cathodal right DLPFC, and sham respectively. Participants that recalled more than four items were suspected of having explicit knowledge of the sequence. In total, nine participants recalled more than four items (i.e., seven recalled five and two six items).

To investigate whether explicit knowledge affected sequence-specific learning, the disruption scores were calculated separately for the nine participants and the remaining participants. For Session 1, the disruption score of the participants with potential explicit knowledge was 113 ms ($SE = 37$), and for the rest the disruption score was 74 ms ($SE = 10$). As revealed by an independent-samples t-test, the disruption scores of the two groups did not differ ($p = 0.24$). Furthermore, the disruption score of the remaining participants was significantly different from zero $t(70) = 7.38$, $p < 0.001$, indicating sequence-specific learning for participants who had little or no explicit knowledge. For Session 2, the disruption score of the participants with potential explicit knowledge was 77 ms ($SE = 15$), and for the rest the disruption score was 63 ms ($SE = 6$). As revealed by an independent-samples t-test the disruption scores of the two groups did not differ ($p = 0.63$). Furthermore, the disruption score of the remaining participants was significantly different from zero $t(70) = 9.33$, $p < 0.001$, indicating sequence-specific learning for participants who had little or no explicit knowledge.

3.4. Discussion

The aim of Experiment 2 was to modulate sequence-specific learning in the TSL by applying DLPFC tDCS during the TSL. Also, tDCS was expected to modulate switch costs. The results showed that sequence-specific learning was present in all conditions in both sessions. By comparing the two sessions, results showed that sequence-specific learning was maintained across sessions. However, tDCS on the DLPFC applied during the TSL did not modulate sequence-specific learning. Similarly, tDCS did not modulate switch costs.

4. General discussion

The aim of the study was to modulate implicit task sequence learning with DLPFC tDCS. Previous results showed that patients with lesioned DLPFC do not show sequence-specific learning in the TSL [7]. Based on these results, we expected tDCS above the left and right DLPFC to modulate sequence-specific learning. We did not find significant tDCS modulation on TSL. Nevertheless, our results are important: They show that sequence-specific learning was present in both experiments across all conditions. Hence, implicit task sequence learning can be reliably measured with the TSL paradigm. There was no change in the degree of learning across sessions. This is consistent with previous results showing that, with the SRTT, consolidation of sequence-specific learning is robust across time [34].

There are several possibilities why tDCS did not modulate learning. A first possibility is that the DLPFC is not involved in implicit task sequence learning. However, both patients and neuroimaging evidences speak clearly against it [7,11,12,25].

A second possibility is that the DLPFC was not appropriately stimulated. As tDCS of the DLPFC did not influence task switching, an ability supported by the DLPFC, this second possibility is more likely. For example, decreasing the distance between the anode and the cathode increases the current quantity that passes through the scalp without reaching neurons [35], hence the null results obtained here could have been provoked by the proximity of the electrodes. This supposition could be tested by placing one electrode on the DLPFC, and the other one on the contralateral side of the body ["unilateral monopolar" electrode setting, cf. 36]. Computational modeling showed that the electric field produced by the active electrode is localized more rostral and medial than the actual position of the active electrode [37–40]. For future studies a way to overcome this limitation is using tDCS protocols or stimulation technologies with higher spatial resolution, such as "high definition" tDCS, "concentric electrodes" tDCS, or transcranial magnetic stimulation (TMS) [41–45]. Finally, it has been shown that tDCS at 2 mA is more effective on cortical excitability than tDCS at 1 mA [[46], but see Ref. [47]].

A third possibility is that tDCS is too weak to modulate the TSL. This possibility is likely since recent results showed that tDCS effects on cortical excitability are not as robust as originally thought

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[32,48–54]. Particularly, a single session of tDCS may not be sufficient to influence RTs performance, attention, and memory abilities [55,56]. In conclusion, the results shown here add to this literature by showing that a single session of tDCS above the DLPFC does not modulate the TSL.

Disclosure statement

No potential conflicts of interest were reported from the authors.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.brs.2017.01.001.

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