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Neuromodulation of premotor and posterior parietal cortices for enhancing explicit motor sequence learning in healthy individuals: a randomized, sham-controlled crossover trial

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Abstract:

Background: *Anodal transcranial Direct Current Stimulation (tDCS) has been shown to be effective in improving human motor learning when applied over the contralateral primary motor cortex (M1). However, the stimulation of other cortical areas, such as the posterior parietal (PPC) and premotor (PMC) cortices, may be also beneficial.*

Methods: *The present study (crossover design) investigated the effects of tDCS applied over PPC, PMC, and M1 on the acquisition and retention of a new motor skill, and on the generalization of such learned skill in healthy individuals. During a sequential finger-tapping task (FTT), performed with the non-dominant (left) hand, participants received real or sham anodal tDCS (1.5 mA, 20 min) over PPC, PMC, and the M1 of the right hemisphere. Explicit motor sequence learning was measured online (during the training with tDCS; primary outcome) and 24 hours after tDCS (retention, secondary outcome). A new, untrained, sequence was used to assess generalization effects (secondary outcome).*

Results: *Anodal tDCS of M1 improved both online learning and retention. PMC tDCS facilitated the generalization of the learning effect to the untrained motor sequence. In contrast, neuromodulation of the PPC does not influence motor sequence learning.*

Conclusions: *These findings show that, in addition to M1, higher-order associative cortical regions (PMC and PPC) are involved in explicit online motor sequence learning, retention and generalization playing different roles, as indicated by the differential modulatory effects of anodal tDCS.*

Keywords: *tDCS, motor sequence learning, motor cortex, premotor cortex, parietal cortex.*

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INTRODUCTION

Transcranial Direct Current Stimulation (tDCS) is a well-known non-invasive brain stimulation technique, widely used to modulate brain activity and behavior. Through a pair of electrodes placed over the scalp, a weak (usually 1-2 mA) direct electrical current is delivered to the brain, modulating cortical excitability in a reversible and painless way. Cortical excitability changes are polarity-specific: tDCS depolarizes (anodal stimulation) or hyperpolarizes (cathodal stimulation) neuronal membranes at a subthreshold level, changing the likelihood of neuronal firing. While stimulation of short duration (several seconds or few minutes) is able to induce short-lasting and reversible effects, several minutes of tDCS induce longer lasting effects, which remain stable after the stimulation has ended (Nitsche et al., 2008).

Cortical excitability changes induced by tDCS can drive long-term shifts that rely on rearrangements of neural areas and are also usually accompanied by the strengthening of synaptic plasticity processes, reflecting long-term potentiation (LTP). Since LTP-like processes are thought to represent the physiological basis of learning, it has been hypothesized that tDCS could represent an effective tool to prime, boost or even guide learning via a sort of associative plasticity (Bolognini, Pascual-Leone, & Fregni, 2009). TDCS has been extensively applied to facilitate learning, especially in the motor domain. The prevailing approach involves the stimulation of the primary motor cortex (M1), known to be the final common pathway of movement control. The majority of studies have applied anodal tDCS over M1, using different motor learning paradigms, showing its effectiveness in improving motor learning processes both in healthy individuals and in stroke patients with motor deficits (Buch et al., 2017).

The almost exclusive emphasis on M1 may be due to the easiness of the target, in terms of cortical localization and measurable effects of stimulation. Notwithstanding, other cortical areas, such as the premotor cortex (PMC) and the posterior parietal cortex (PPC), may be also involved at different stages of motor learning, influencing planning, sensorimotor integration and consolidation (Nudo, 2003).

A specific type of motor learning is motor sequence learning, which involves executing a sequence effortlessly, through repeated practice, as a unit (Dahms et al., 2020). As a multilevel process, motor sequence learning involves different, though related, mechanisms: processes driving improvements during practice (online learning), and processes driving stabilization over time or improvement between sessions (retention) (Robertson & Cohen, 2006). In addition, learning is expected to be specific to the trained task, with little to no improvements in untrained new tasks. A distributed network of cortical and subcortical brain circuits is involved in motor sequence learning. This includes M1, different frontal areas (PMC, supplementary motor area and prefrontal cortex), PPC, the basal ganglia and the cerebellum.

Given these premises, it is likely that, beyond M1, the electrical stimulation of other cortical areas, such as PMC and PPC, may also influence motor sequence learning. To the best of our knowledge, no study has so far performed a direct comparison of tDCS effects on explicit motor sequence learning, with the stimulation being applied over different cortical areas, while the need of a better understanding of tDCS effects on the generalization of learning has been recently acknowledged. We address this issue in healthy individuals, exploring the modulatory effects of a single application of tDCS delivered to PPC and PMC, as well as M1 in different sessions (crossover design), on motor sequence learning, which was measured with the finger-tapping task (FTT).

MATERIALS AND METHODS

Participants

Thirty-three healthy individuals (Mean age=23.5 years, Standard Deviation, SD=± 2.3; 30 females), took part in this study. Participants were mostly undergraduate students, recruited through advertisements in printed and digital media published at the University of Milano-Bicocca and in the neighborhood. Individuals were included according to the following criteria: i) No history or clinical evidence of diseases, including psychiatric or neurological disorders; ii) No history of dependence and/or substance abuse; iii) No use of medications affecting the central nervous system; iv) No contraindication to non-invasive brain stimulation (Rossi et al., 2009); v) right-handedness, as assessed through the Edinburgh Handedness Inventory (Oldfield, 1971). All participants gave their written informed consent to participate in the study, which was carried out according to the guidelines of the Declaration of Helsinki and approved by the Ethical Committee of the University of Milano-Bicocca.

Study design

A randomized, sham-controlled, crossover trial was performed. By using a crossover design, each participant received anodal tDCS to M1, PPC and PMC, as well as a sham stimulation (to which both the participant and the experimenter were blinded), so that each served as his/her own control. Hence, all the participants underwent 4 different tDCS sessions, separated by a wash-out period of 24 hours, in order to minimize carry-over effects (Monte-Silva et al., 2013). The order of the tDCS sessions was randomized across participants. The random allocation sequence was achieved with a computer generating the randomization list.

Finger Tapping Task

A sequential finger-tapping task (FTT) (Zimerman et al., 2012) was executed: during each session, participants were trained to perform a sequential digit pressing of a

fixed 9-element sequence (e.g., 2-4-3-1-2-1-3-4-2) on a 4-button keyboard using their non-dominant left hand. The number sequence was displayed over a computer screen with each number representing a finger of the left hand: little (1), ring (2), middle (3), and index finger (4). The E-Prime software (version 2.0 Psychology Software Tools) was used to present the to-be-learnt digit sequences, recording participants' responses. Participants were instructed to perform the FTT, by using their left hand, as accurately and rapidly as possible. Participants received instructions not to correct their response in case of error, rather to continue the task with no pause (e.g., Tecchio et al., 2010). After each button press, an asterisk mark appeared below each number of the digit sequence, independently of the correctness of the pressed button. The task required to reproduce the entire 9-element sequence correctly; consequently, the performed sequence was incorrect if it contained even a single wrong press. No feedback regarding accuracy was provided. From the FTT, two variables were extracted to assess motor learning: (i) the number of correct sequences reproduced in a block of practice and (ii) the number of total sequences performed in the same block. These two variables were then used to assess our primary outcome: online learning (performance improvements during the task), as well secondary outcomes: retention (performance improvements in the trained sequence after 24 hours) and generalization (performance improvements during the execution of a new, different, sequence comparable to the trained sequence) (Censor et al., 2012).

Transcranial Direct Current Stimulation

TDCS was delivered by a battery-driven, constant current stimulator (BrainStim, EMS, Bologna, Italy, http://brainstim.it/), using two electrodes (5 x 5 cm), covered by saline-soaked sponges. Direct electric current was applied with an intensity of 1.5 mA for 20 min (fade-in/fade-out phases=8 sec), following current safety data (Antal et al., 2017). In a crossover design, active tDCS was applied over 3 different cortical areas of the right hemisphere located by using the 10/20 electroencephalography system: (i) PPC: the anode was placed over P4; (ii) PMC: the anode was placed over F4, and (iii) M1: the anode was placed over C4. In all cases, the reference electrode (cathode) was placed over the contralateral (left) supraorbital area. In the sham condition, tDCS montage was the same of the real conditions (i.e., anode over right P4 or F4 or C4 and the reference electrode over the left supraorbital area). During sham tDCS, the same parameters of the active stimulation were used, but the stimulator was turned off after 30 sec. This ensures participants an itching sensation at the beginning of tDCS, while no effective stimulation was delivered, thus allowing a successful blinding for real vs sham stimulation (Gandiga et al., 2006). The target area for the placebo stimulation was randomly defined. Therefore, participants were blinded to the real/sham intervention delivered and somewhat blinded even respect to the area (it is difficult for a subject to distinguish whether the anode is placed over M1 or PMC). The experimenter had to know over which area tDCS had to be applied, but he/she was blind with respect to the stimulation delivered. Indeed, the real/sham modes of the tDCS device were activated through the use of codes, set and then saved by the principal investigator (N.B.), who did not participate in data collection. This method has been shown to be reliable for keeping both the experimenter and the participant blinded to sham and real tDCS (e.g., Bolognini et al., 2013).

Experimental procedure

Participants underwent 4 training sessions during which, concomitant to the FTT, real or sham anodal tDCS was delivered over the right cortex: (i) PPC; (ii) PMC; (iii) M1; (iv) Sham tDCS, randomly applied over the right PPC, PMC or M1.

The presence of adverse effects related to the stimulation was monitored with an ad-hoc questionnaire administered at the end of every tDCS session (Brunoni et al., 2011).

Participants performed the FTT in sessions comprised by 2 phases: (i) training and (ii) post-training. During the training phase, participants were instructed to repeatedly perform a given target sequence for 5 blocks of 3 min each, with 2 min of break between them (Zimerman et al., 2012) while receiving tDCS. At the post-training phase, participants were presented with a new (different) sequence in a single block lasting 3 min. Such sequence was comparable in terms of complexity with the trained one (Zimerman et al., 2012). Overall, the FTT lasted 25 min. Twenty-four hours after the end of tDCS (FU24), that is, immediately before the beginning of the next session, participants underwent a retention test: they were asked again to perform the target, trained sequence, for a single block of 3 min.

Statistical analyses

Statistical analyses were performed using Statistica for Windows, release 10 (StatSoft). Significance was set at alpha=.05; main effects and interactions were further explored by means of Newman-Keuls correction. Normality of all data was assessed by the Shapiro-Wilk test. Then, since data did not violate normality (p>.05), repeated measures Analyses of Variance (rm-ANOVAs) were used to analyze tDCS effects on learning.

Primary outcome

To assess tDCS effects on online learning, both the number of the correct sequences reproduced and the number of total sequences performed (regardless of their correctness, i.e. correct plus incorrect) were analyzed via a rm-ANOVA with tDCS (Sham, PPC, PMC and M1) and Blocks (B1, B2, B3, B4, B5) as within-subjects factors.

Secondary outcomes

In order to assess tDCS effects on retention, the correct and the total number of sequences performed were both analyzed via a rm-ANOVA with tDCS and Time (B5 - last block of learning, and FU24 - retention test after 24 hours) as main factors. To assess tDCS effects on generalization, both the correct and the total number of sequences performed were analyzed via a rm-ANOVA with tDCS as within-subjects factor.

RESULTS

Primary outcome: online learning

Correct sequences reproduced

The rm-ANOVA showed a main effect of *tDCS* [$F_{(3,96)}$=3.8, p=.01, η^2_p=.10]: the number of correct reproduced sequences during the 5 blocks of training was higher under M1 stimulation (Mean number of correct sequences=38, Standard Deviation=±10.22) as compared to all other tDCS conditions, except for PMC (36±8.21, p=.06): Sham (35.3±8.39, p=.04) and PPC (34.4±8.21, p<.01). As compared to sham tDCS, neither PMC nor PPC stimulations improved online performance (p=.55 and .45, respectively; see **Figure 1A**). The main effect of Blocks [$F_{(4,12)}$=8.6, p<.001, η^2_p=.20] showed the typical learning effect: the number of correct sequences in Blocks 1 (34.6±8.21) and 2 (35.4±8.04) was significantly lower than that in Blocks 4 (36.8±7.87, p=.01) and 5 (37±7.75, p<.01). The rate of correct sequences reproduced in Block 3 (36.2±7.58) was higher than that in Block 1 (p<.01), but not different from Blocks 2 (p=.09), 4 (p=.24), and 5 (p=.2). The *tDCS X Blocks* interaction [$F_{(12,38)}$=1.5, p=.13, η^2_p=.04] was not significant.

Total (correct plus incorrect) sequences performed

The rm-ANOVA revealed a significant *tDCS* X *Blocks* interaction [$F_{(12,38)}$=1.8, p=.04, η^2_p=.05], as well as a main effect of *Blocks* [$F_{(4,12)}$=37.7, p<.001, η^2_p=.54], while no significant effect of the main factor *tDCS* was found [$F_{(3,96)}$=2.2, p=.09, η^2_p=.06]. As shown in **Figure 1B**, the total number of sequences performed during M1 stimulation was higher than in other conditions starting from the first block of practice (B1=42.8±11.08); the M1-induced improvement was evident also in Blocks 2 (B2=44.6±10.86, p=.03), 3 (B3=45±10.51), 4

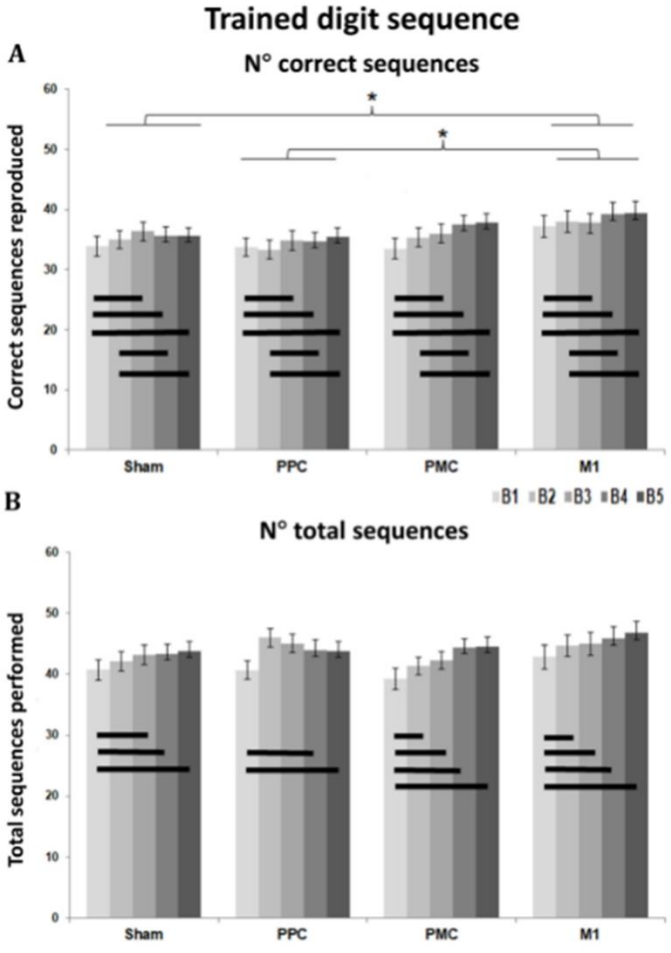

Figure 1. *Online learning effects.* Number of correct sequences reproduced (A) and number of total sequences performed (B) of the trained digit sequence during the 5 blocks of learning; B1=block 1, B2=block 2, B3=block 3, B4=block 4, B5=block 5. Bold lines= within-group differences; *= between-group differences; p<.05. Error bars= SE.

(B4=45.8±11.08), and 5 (B5=46.7±9.99) (p<.01 for comparisons of B3, B4 and B5). During PMC stimulation, the total number of performed sequences significantly increased in Block 2 (B2=41.3±9.25) and was even greater in the following blocks (B3=42.2±8.90; B4=44.4±8.5; B5=44.6±8.39) (p<.01 for comparisons of B2, B3, B4 and B5), as compared to Block 1 (39.3±9.94). During PPC modulation, the increase took place later, starting from Block 4 (B4=42.8±9.24; B5=43.8±8.78) (p<.01 for comparisons of B4 and B5), as compared to the first block of practice (B1=40.7±9.01). Importantly, during sham tDCS, an increase of the total sequences performed was found in Block 3 (43.1±9.76), 4 (43.3±8.79), and 5 (43.8±9.02) (p<.01 for comparisons of B3, B4 and B5), as compared to Block 1 (B1=40.7, SD=±9.53). Block 2 (B2=42.1, SD=±9.47) did not differ from Block 1 (p=.12), as Block 3 did not differ from Block 4 (p=.8) and 5 (p=.7).

Secondary outcome: retention

Correct sequences reproduced

As shown in **Figure 2A**, the rm-ANOVA revealed a main effect of *tDCS* [$F_{(3,96)}$=4.7, p<.01, η^2_p=.12], showing better performance after M1 stimulation (40.7±10.11) as compared to sham (37.9±8.1, p=.03) and PPC (37±7.98, p<.01) tDCS. On the other hand, while PMC stimulation (39.8±1.39) did not differ from M1 (p=.38) and sham (p=.09) stimulations, PMC tDCS improved performance as compared to PPC tDCS (p=.04). The main effect of Time [$F_{(1,32)}$=28, p<.001, η^2_p=.5] showed a further improvement of correct sequence reproduction after 24 hours (FU24=40.6±8.1 vs. B5=37±7.75, p<.01). The *tDCS* X *Time* interaction [$F_{(3,96)}$=.7, p=.5, η^2_p=.02] was not significant.

Total (correct plus incorrect) sequences performed

The main effect of *tDCS* [$F_{(3,96)}$=3.8, p=.01, η^2_p=.10] showed a better performance after M1 tDCS (47.5±10.22), as compared to PMC (45.5±8.1, p=.048), PPC (44.5±8.39, p=.02), and sham (44.7±8.79, p=.01) stimulations (see **Figure 2B**). The main effect of *Time* [$F_{(1,32)}$=11.5, p<.001, η^2_p=.3] showed a further improvement after 24 hours (FU24=46.4±8.56), as compared to the last block of practice (B5=44.7±8.1, p<.001). The interaction *tDCS* X *Time* [$F_{(3,96)}$=.06, p=.98, η^2_p<.001] was not significant.

Secondary outcome: generalization

Correct sequences reproduced

As shown in **Figure 3A**, the main effect of tDCS [$F_{(3,93)}$=22.2, p<.01, η^2_p=.40] showed that PMC

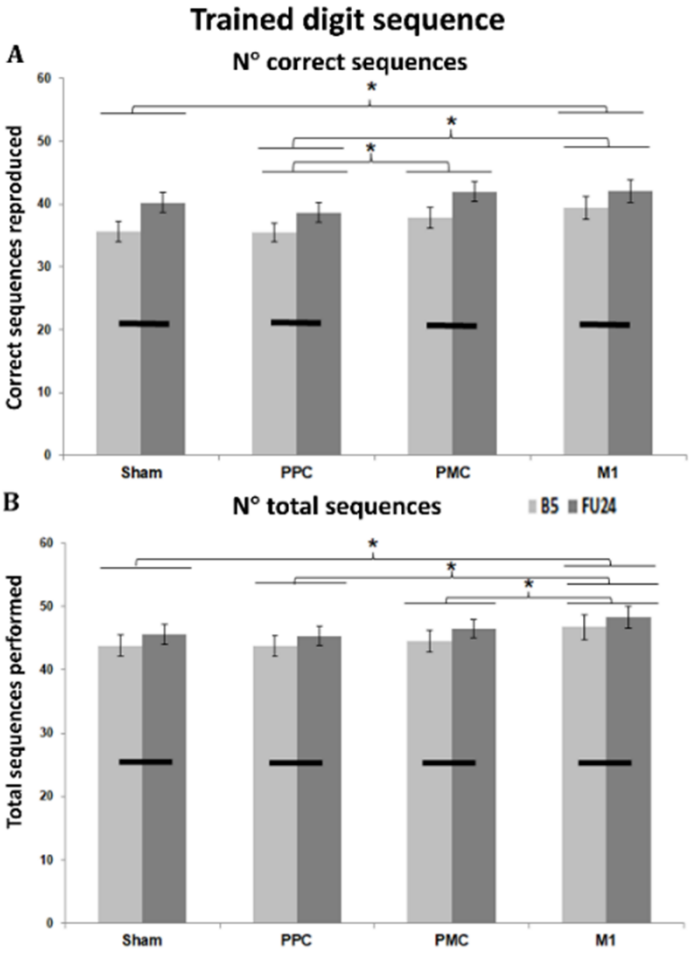

Figure 2. *Retention effects.* Number of correct sequences reproduces (A) and number of total sequences performed (B) of the trained digit sequence in the last block of training *vs.* 24 hours after; B5= block 5, FU24= follow-up 24 hours after the end of the training. Bold lines= within-group differences; *= between-group differences; p< .05. Error bars= SE.

stimulation improved the reproduction of the new, untrained, digit sequence (37.3±10.30) as compared to all other conditions (p<.01): Sham (28±9.31), PPC (28.3±8.89), and M1 (30.2±9.75). Sham tDCS did not differ from M1 (p=.24) nor PPC (p=.79) stimulations.

Total (correct plus incorrect) sequences performed

The significant effect of tDCS [$F_{(3,93)}$=9.6, p<.01, η^2_p=.20] showed the facilitatory effect of PMC tDCS (43.6±9.89), which induced a larger generalization effect as compared to all other conditions (p<.01): M1 (40±10.45), PPC (37.7±8.84), and Sham (37.4±8.14). Sham tDCS did not differ from M1 (p=.11) nor PPC (p=.85) stimulations (see **Figure 3B**).

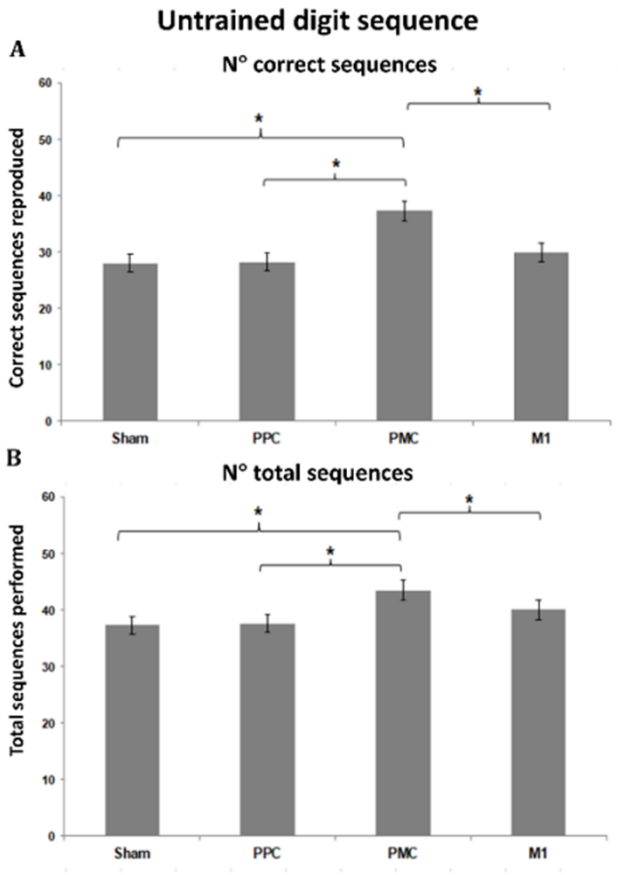

Figure 3. *Generalization effects.* Number of correct sequences reproduced (A), and number of total sequences performed (B) for the untrained digit sequence in the post-training phase. *= between-group differences; p< .05. Error bars= SE.

DISCUSSION

The present study assessed the effects of anodal tDCS over different fronto-parietal areas (PPC, PMC and M1) on motor sequence learning (FTT), across various components of the learning process: the online acquisition of a new skill, its retention and the generalization to a not-trained activity. Overall, our results feature elements of confirmation and novelty: they provide evidence that anodal M1 tDCS facilitates both online learning and retention, and also demonstrated that anodal PMC tDCS promotes generalization, while PPC tDCS does not influence motor sequence learning.

With respect to M1 stimulation, our results support current evidence. Considering the correct number of reproduced sequences, it confirmed M1 as a key area of the motor network to be stimulated with tDCS to increase both online motor sequence learning and retention. Moreover, M1 stimulation facilitates the performance from the very beginning of the practice also in terms of total sequences performed.

As for retention, M1 tDCS can further enhance off-line motor sequence learning. In fact, both the rate of the correct sequences reproduced and the total number of sequences performed increased 24 hours after M1 stimulation, at least with respect to sham and PPC tDCS. It is known that excitatory M1 stimulation facilitates motor learning, as assessed through various tasks (e.g., Reis et al., 2009; Stagg et al., 2011). While the underlying neural mechanisms are still under investigation, such effect seems related to long-term potentiation LTP mechanisms and the functioning of N-methyl-D-glutamate (NMDA) receptors. Particularly, since M1 is rich of dopaminergic terminals, an excitatory stimulation would boost LTP processes. Indeed, it has been shown that blocking dopaminergic activity in M1 hampers LTP and, consequently, reduces learning (Molina-Luna et al., 2009).

With respect to PMC stimulation, we found intriguing results. While M1 tDCS facilitates online motor sequence learning compared to sham and PPC tDCS, PMC stimulation is placed somehow in between: learning effects (correct reproduced sequence) driven by PMC stimulation are similar to those elicited by M1 tDCS, although they are not different from the performance under sham condition. In terms of total sequences performed, PMC neuromodulation facilitates the performance from the very beginning of the practice, as M1 tDCS does. The efficacy of PMC stimulation could be related to the role of this area in early learning stages of a motor sequence task (Steele & Penhune, 2010). Although PMC is bilaterally recruited during the early stages of skill learning, there is a more prominent activation of the PMC in the right hemisphere (Deiber et al., 1997), which likely reflects the spatial processing necessary for motor acquisition. Indeed, an increased cognitive information processing is expected during the early learning stage, as individuals associate sensory cues with correct motor commands (Kantak et al., 2012). Hence, increasing the activity of the right PMC during motor sequence learning likely facilitates the establishment of novel visuo-motor association, with the effect of a widespread motor behavior facilitation (more reproduced sequences), but this occurs before the storage of the acquisition of a new visuomotor skill, which needs the recruitment of left PMC to allow the establishment of the learning effect, for improving motor accuracy (Halsband & Lange, 2006). As for retention, the right

PMC tDCS has similar effects to those induced by M1 tDCS when the ability to correctly reproduce a digit sequence is considered. However, PMC stimulation has larger effect than M1 when the global performance, regardless of its accuracy, is considered.

The main novel finding of our study is represented by the effects on a new, untrained, motor sequence, which is selectively facilitated by PMC stimulation. Current literature shows that the integration of sensory information into motor commands are assignments of PMC, which is also involved in movement selection and retention (Gremel & Costa, 2013). A long-term practice results in a faster, effortless and accurate performance primarily because movements are planned in a motor-center coordinate system, rather than a vision-center one as in earlier learning stages (Marinelli et al., 2017). Successful consolidation processes include memory association and translocation, which means that recently acquired information are integrated with past experiences, while an anatomical reorganization of memory representation occurs. Here, we may speculate that PMC tDCS can reinforce the memory trace of the learned digit sequence, allowing an effective movement translocation, resulting in the ability to recognize the new activity "pattern" and successfully perform it.

Finally, PPC tDCS has no effect on motor sequence learning by itself; rather, it seems even detrimental, delaying practice-induced improvements, at least in terms of the total amount of sequences reproduced, regardless of their correctness. In fact, as compared to sham tDCS, during the PPC stimulation, the performance improvement emerges only at the end of training (Block 4), while it appears sooner without tDCS (Block 3 during sham tDCS) and it is even anticipated during M1 and PMC tDCS (Block 2). In addition, also the retention of the learnt digit sequence, in terms of both correct and overall performance, was significantly lower in the PPC condition, as compared to M1 and PMC stimulations. A possible speculation may be that the anodal (excitatory) tDCS applied over the right PPC could interfere with movement planning and learning by causing an indirect interhemispheric inhibition of the left PPC.

Limitations

A main limitation of the present study, given its pilot nature, is the small size of the sample. Studies involving larger samples of participants, with higher statistical power, are mandatory to confirm and extend the present evidence. A possible source of potential bias is that the experiment was not blind to the target area; however, the experimenter who applied the stimulation was not the same who performed the analysis, and FTT were computed and extracted by a software, therefore, we believe, lowering the risk of such bias.

Secondly, we compared many conditions, running multiple comparisons, due to the adoption of a crossover design and the need to evaluate the effects over different time-points, with the risk of increasing type one error.

Finally, it should be noted that this study was carried out in our Department of Psychology; therefore, the sample is mainly composed by female (30 out of 33) young adults (mean age= 23.5 years). It follows that both gender and age of our experimental group could represent potential sample biases that may hinder external validity of our findings. With respect to gender, to the best of our knowledge, there is no evidence in the literature regarding substantial gender-related difference in motor sequence learning, but they could be in relation to tDCS effects (Thomas et al., 2019). As for age, an intriguing review (Voelcker-Rehage, 2008) pointed out how the decline in motor learning due to age is task-specific, with a comparable learning of younger and older adults in low-complexity tasks. On the other hand, an age-related variability in tDCS effects has been acknowledged (Li et al., 2015). Since age and gender could limit the generalizability of our results, this should prompt future investigation to seek to explore putative intriguing interactions between age, gender and neuromodulation effects on motor sequence learning.

A final note of caution is needed with respect to the neuromodulation of PMC; tDCS has low spatial focality, hence it is highly probable that the delivery of tDCS over PMC may have also affected the functioning of neighboring cortical areas, in particular the Dorsolateral Prefrontal Cortex.

CONCLUSIONS

In conclusion, results of the present exploratory study confirm the efficacy of M1 tDCS on motor sequence learning, with beneficial effects emerging during the training phase and in the long-term. On the other hand, M1 tDCS, as well as PPC tDCS, does not affect the generalization of the learned skill to a new untrained sequence. PMC tDCS has similar effects as M1 tDCS on online learning and retention, but it also has a larger facilitatory effect on the generalization of learning. PPC tDCS, instead, does not influence motor sequence learning. Therefore, we found an interesting dissociation between M1 and PMC effects: while M1

plays a main role in promoting online learning and retention, PMC is recruited at a later stage for allowing the generalization to untrained movements.

These suggestive findings may have some important clinical implications: tDCS protocols targeting different cortical areas could be used to promote specific components of motor learning during upper-limb, post-stroke rehabilitation (Bolognini et al., 2009). The expectation is that different areas may be targeted to drive specific effects on hand motor recovery, depending on the damaged function/neural pathway (Plow et al., 2015). For instance, with respect to our findings, PMC could represent a potential candidate to facilitate the transfer of a tDCS rehabilitation targeting M1 on daily living. On the other hand, PPC may represent a more promising target, whenever higher order levels of motor programming and execution are affected (Bolognini et al., 2015), rather than low-level learning processes as found here. In this perspective, assessing the therapeutic effects of premotor and parietal stimulations could pave the way to offer more rehabilitation alternatives for the treatment of post-stroke patients with hemiparesis.

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Conflict of Interest

None.

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