Cerebral Cortex, March 2021;31: 1569–1581

doi: 10.1093/cercor/bhaa309
Advance Access Publication Date: 2 November 2020
Original Article

ORIGINAL ARTICLE

Enhancing Motor Brain Activity Improves Memory for Action Language: A tDCS Study

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Abstract

The embodied cognition approach to linguistic meaning posits that action language understanding is grounded in sensory–motor systems. However, evidence that the human motor cortex is necessary for action language memory is meager. To address this issue, in two groups of healthy individuals, we perturbed the left primary motor cortex (M1) by means of either anodal or cathodal transcranial direct current stimulation (tDCS), before participants had to memorize lists of manual action and attentional sentences. In each group, participants received sham and active tDCS in two separate sessions. Following anodal tDCS (a-tDCS), participants improved the recall of action sentences compared with sham tDCS. No similar effects were detected following cathodal tDCS (c-tDCS). Both a-tDCS and c-tDCS induced variable changes in motor excitability, as measured by motor-evoked potentials induced by transcranial magnetic stimulation. Remarkably, across groups, action-specific memory improvements were positively predicted by changes in motor excitability. We provide evidence that excitatory modulation of the motor cortex selectively improves performance in a task requiring comprehension and memory of action sentences. These findings indicate that M1 is necessary for accurate processing of linguistic meanings and thus provide causal evidence that high-order cognitive functions are grounded in the human motor system.

Key words: action language, embodied cognition, memory, motor cortex, transcranial direct current stimulation

Introduction

According to the embodied cognition (EC) theories, understanding action language is associated with the activation of perceptual and motor processes, which simulate the referred action. For instance, action words or sentences activate sensory–motor circuits required to produce the action being described (Barsalou et al. 2008; Fischer and Zwaan 2008; Glenberg et al. 2008; García and Ibáñez 2016). A conspicuous number of behavioral (Glenberg and Kaschak 2002; Zwaan and Taylor 2006; de Vega et al. 2013), neuroimaging (Tettamanti et al. 2005; Aziz-Zadeh et al. 2006; Raposo et al. 2009; de Vega et al. 2014), and EEG studies (van Elk et al. 2010; Moreno et al. 2013, 2015) have provided evidence supporting the EC approach to language meaning. In particular, single-pulse transcranial magnetic stimulation (TMS) studies have shown that understanding action-related language modulates motor cortical excitability, as measured by motor-evoked potentials (MEPs) (Oliveri et al. 2004; Buccino et al. 2005; Papeo et al. 2009; Candidi et al. 2010; Scorolli et al. 2012). Taken together, these studies show a consistent involvement of the human motor cortex—that is, a set of frontal brain areas involved in the control of body movements and including the primary motor cortex (M1) and premotor areas—during comprehension of action language and support the view that motor cortex activation reflects motor simulation of linguistic meanings.

It is worth noting that such conclusions are mainly supported by indirect correlational evidence that leaves unsolved the fundamental question of whether the motor cortex is causally essential for understanding action-related sentences or merely reflects such understanding—as contended by critics of EC theories (Mahon and Caramazza 2008; Papeo et al. 2013; Mahon 2015; Leshinskaya and Caramazza 2016). For example, using a perturb-and-measure TMS protocol combining low frequency repetitive TMS (rTMS) and MEPs recording (Avenanti et al. 2007; Avenanti, Annella, et al. 2013a), Papeo et al. (2015) showed that neuromodulation of the posterior middle temporal gyrus (pMTG), a key area involved in verb conceptual processing (e.g., Peelen et al. 2012), impoverished the semantic processing of verbs and disrupted MEPs modulation during comprehension of action language, thus suggesting that action simulation occurring in the motor cortex can reflect downstream processing of temporal areas. Remarkably, however, a few studies have also shown that TMS over M1 affects action language understanding. In their seminal study, Pulvermüller et al. (2005) used online single-pulse TMS over hand and leg representations in M1 to demonstrate a somatotopic-specific quickening of responses in a lexical decision task. On the other hand, Vukovic et al. (2017) administered online rTMS to interfere with M1 activity and found delayed response to action words in a semantic task. Additionally, in two studies (Gerfo et al. 2008; Repetto et al. 2013) offline low-frequency rTMS over M1 delayed response to action-related words during morphological or semantic tasks. These behavioral effects of TMS provide causal evidence supporting EC theories. However, the neural mechanism underlying these effects remains unclear, as none of these studies monitored physiological changes induced by brain stimulation. Moreover, although increasing the excitability of frontal motor areas can lead to long-lasting behavioral gains (e.g., Hashemirad et al. 2016; Avenanti et al. 2018; Fiori et al. 2018) and, importantly, can enhance motor learning (e.g., it ameliorated acquisition and retention of new motor skills or adaptation of previously learned ones; see Nitsche, Schauenburg, et al. 2003b; Reis and Fritsch 2011; López-Alonso et al. 2015; Buch et al. 2017), no prior study has tested whether enhancing M1 would also improve memory of action-related language.

The current study aims to fill these gaps, by investigating the potential facilitatory after-effects of M1 neuromodulation in an action-language memory task. To this end, we used transcranial direct current stimulation (tDCS) to test whether exogenous excitatory manipulation of M1 activity would improve memory performance of items associated with action verbs. Participants were tested in a delayed memory task inspired by recent behavioral studies (e.g., Dutriaux and Gyselinck 2016; Dutriaux et al. 2018; de Vega et al. unpublished data). In these studies, participants' hand posture was manipulated to interfere with motor simulation while participants had to read and memorize linguistic material. In one of these studies, the authors presented lists of manipulable and nonmanipulable objects, and participants were instructed to memorize the items while adopting different hand postures. The authors found that during learning, keeping the hands behind the back rather than having them in front of oneself selectively interfered with the recall of manipulable objects as compared with nonmanipulable objects (Dutriaux and Gyselinck 2016). In another study, the same research group (Dutriaux et al. 2018) tested whether postural interference could also be observed in the context of action-related language. In a learning phase, participants were exposed to object–verb sentences while keeping their hands back or in front. Researchers found that the hands back posture interfered with recall of object nouns (e.g., cup) exclusively when nouns appeared in the context of action verbs (e.g., to take a cup) rather than in the context of attentional verbs (e.g., to see a cup), suggesting that motor simulation has a functional role in language processing. These behavioral findings were replicated in a further electrophysiological (EEG) study that used a similar posture manipulation task (de Vega et al. unpublished data). Additionally, this EEG study revealed a fronto-central beta rhythm desynchronization (index of motor process) while participants read manual action sentences in the hands front posture, but this modulation was suppressed in the hands back posture, suggesting that the latter interferes with motor simulation in the motor cortex.

In the current study, like in the aforementioned studies (i.e., Dutriaux et al. 2018; de Vega et al. unpublished data), we tested performance on a delayed memory test: participants were initially presented with a set of sentences composed of object nouns presented in the context of either action or attentional verbs (learning phase); then, in the testing phase, we evaluated participants' ability to recall object nouns that were associated with action or attentional verbs, using a cued recall procedure. However, rather than testing the interferential effects of hand posture, we exogenously enhanced the motor cortex with tDCS and asked whether this manipulation improved memory performance with action sentences rather than with attention sentences. We targeted M1 using a classical bicephalic montage with a reference electrode over the supraorbital area, as modeling and neuroimaging studies indicate that this is best suited to modulate frontal motor areas (Datta et al. 2009; Jang et al. 2009; Stagg et al. 2009; Polanía, Paulus, et al. 2011a; Polanía, Nitsche, et al. 2011b; Opitz et al. 2015; Ho et al. 2016). We administered two different types of tDCS protocols over M1. In the experimental group, we administered anodal tDCS (a-tDCS), as classical studies have shown that anodal currents can enhance motor excitability (Nitsche and Paulus 2000, 2001; Nitsche, Nitsche, et al. 2003a; Stagg and Nitsche 2011; Stagg et al. 2018) and such increase can be associated with behavioral gains (e.g., Convento et al. 2014; Orban de Xivry and Shadmehr 2014; Hashemirad et al. 2016; Alix-Fages et al. 2019). We stimulated M1 for 20 min using 2 mA a-tDCS, as this protocol consistently increases motor excitability for up to 60 min (Batsikadze et al. 2013; Jamil et al. 2017). In different sessions, participants were tested following active a-tDCS and sham tDCS, which served as a baseline control session. We reasoned that if motor simulations occurring in the motor cortex while learning action sentences are functionally relevant, enhancing M1 activity through a-tDCS would selectively improve memory retrieval for action sentences in the a-tDCS relative to the sham session, providing new evidence of a functional link between the motor system and "higher-order" cognitive functions such as comprehension and memory.

Additionally, to test polarity-dependent effects of tDCS, in a further group of participants, we administered 2 mA cathodal tDCS (c-tDCS). While we expected that 2 mA a-tDCS would increase motor excitability and improve memory performance for action language, we had no similar expectation for the contrast group submitted to 2 mA c-tDCS. Although classical studies suggest that cathodal currents over M1 tend to inhibit the excitability of the motor cortex, it is now established that tDCS effects are not linear and vary across individuals; in particular, c-tDCS at an intensity of 2 mA has been associated with an inconsistent pattern of results in different studies (e.g., Batsikadze et al. 2013; Wiethoff et al. 2014; Jamil et al. 2017). Yet, we selected this c-tDCS protocol to provide an adequate contrast to the anodal stimulation and rule out unspecific effects of brain stimulation. Therefore, we expected to find a facilitation following a-tDCS, with larger MEPs after a-tDCS relative to prestimulation level and MEPs following c-tDCS. We expected that c-tDCS should induce variable results among the participants, with approximately half showing trends for increased motor excitability and half showing trends for decreased motor excitability (Wiethoff et al. 2014), resulting in statistically null physiological and behavioral effects at the group level.

To monitor the physiological effect of a-tDCS and c-tDCS, MEPs to single-pulse TMS over the left M1 were recorded in each session before and after tDCS administration, allowing us to evaluate the interindividual variability previously reported (Kaup and Zwaan 2003; López-Alonso et al. 2014; Wiethoff et al. 2014; Chew et al. 2015; Strube et al. 2015; Ammann et al. 2017) and, most importantly, to test whether physiological changes in motor excitability following tDCS predict behavioral changes in memory performance. We hypothesized that improved performance occurring after a-tDCS would be associated with an increment of motor excitability. However, because c-tDCS is expected to induce variable physiological effects, we also tested whether increased motor excitability (irrespective of whether this was achieved via a-tDCS or c-tDCS) predicted larger action-specific behavioral improvements.

In sum, this neuromodulation study has several novelties in the field of embodied semantics: 1) it used for the first time a long-term dependent measure, rather than online neurophysiological measures, like MEPs, or online behavioral measures, like reaction times or reading times. This is relevant, because purely online effects reported elsewhere are compatible with a momentary neural resonance without further cognitive consequences, whereas a modulation of a delayed memory task indicates that the embodied representations have functional impact beyond the language encoding moment; 2) it provided a robust baseline condition, as the same participants performed the task in two sessions, after active tDCS and after sham tDCS, rather than using a less reliable between-participants contrast with a sham group; 3) it tested in the same participants how neuromodulation induced changes both in M1 corticospinal excitability and in the recall of action language and explored the association between both measures, suggesting a functional link between motor physiology and memory performance.

Materials and Methods

Participants

Fifty healthy undergraduate students participated in this study. The sample size was determined through a power analysis conducted using G∗Power 3 software (Faul et al. 2007), with power $(1-\beta)=0.95$ and $\alpha=0.05$. We expected a low-medium effect size ($f=0.15$) and high correlation between measures ($r>0.6$; de Vega et al. unpublished data). The analysis yielded required sample sizes of 25 participants per group. We thus decided to test 50 participants who were randomly assigned to two stimulation groups: 25 participants (6 men, mean age ± SD: 20.3 years ±3.3) were assigned to the a-tDCS group and 25 participants (1 man, mean age ± SD: 19.6 years ±1.3) were assigned to the c-tDCS group. All participants were right-handed, had Spanish as their mother tongue, and did not report any neurological disease, visual problems, or medicine intake. All students gave informed consent and received course credit for volunteering. The Research Ethics Committee of the University of La Laguna approved this study, and the experiment was conducted according to the principles expressed in the Declaration of Helsinki.

Linguistic Material

Two sets of 120 Spanish sentences with the format "verb + article -+ noun" were used. A total of 30 manual action verbs, 30 attentional verbs (Supplementary Table 1), and 120 nouns referring to manipulable objects were used to construct the sets. Within each set of sentences, each verb appeared twice associated with two different objects. The objects were not repeated within each set; however, the sentences in the two sets differed in the combination of nouns and verbs in such a way that if a given noun appeared with a manual verb in set 1 (e.g., *colgar un bastón*/to hang a cane), it was associated with an attentional verb in set 2 (e.g., *observar un bastón*/to observe a cane) and vice versa (Supplementary Table 2). Values of frequency and length of each verb were downloaded from the EsPal database, a web-accessible repository containing a comprehensive set of properties of Spanish words (Duchon et al. 2013). Manual and attentional verbs did not differ in frequency (mean ± SD: manual action = 23.83 ± 54.91; attentional = 56.84 ± 93.87; $t_{58}=-1.66$, $P=0.10$) or length (manual action = 6.67 ± 1.37; attentional = 7.27 ± 1.87; $t_{58}=-1.41$, $P=0.16$). In an additional normative study, 30 university students, who did not participate in the subsequent experiment, were asked to judge on a 7-point Likert scale the familiarity and concreteness of the verbs. The familiarity was similar for the two types of verbs (manual action = 6.24 ± 0.52; attentional = 5.97 ± 0.76; $t_{58}=1.55$, $P=0.13$), while, as expected, the manual action verbs were judged as more concrete than the attentional verbs (manual action = 5.72 ± 0.51; attentional = 4.28 ± 0.63; $t_{58}=9.77$, $P<0.001$), reflecting the intended semantic differences between the 2 types of verbs. The noun frequency and length values were 29.70 ± 195.20 and 6.35 ± 1.73, respectively. To assess whether the manual action sentences and the attentional sentences were semantically comparable, we utilized the search engine "Google" to check the number of co-occurrences of the verb–object pair for each sentences, by using quotation marks (Page et al. 1999; Griffiths et al. 2007; Sha 2010). For both sets, the co-occurrence values of the manual action sentences did not differ from the values of the attentional sentences (set 1: manual action = 31 762 ± 55 992, attentional = 78 917 ± 343 442; $t_{118}=-1.05$, $P=0.30$; set 2: manual action = 88 682 ± 310 006, attentional = 115 036 ± 409 065; $t_{118}=-.40$, $P=0.69$).

Transcranial Direct Current Stimulation

The tDCS was delivered by a battery-driven constant direct current stimulator (NeuroConn DC-STIMULATOR) and applied through a pair of saline-soaked surface sponge electrodes. The motor cortex electrode (5 × 7 cm) was fixed over the area representing the right first dorsal interosseous (FDI) muscle as identified by means of the TMS protocol described later, and the reference electrode (7 × 10 cm) was placed over the contralateral orbit, above the right eyebrow. In the active stimulation, the current was ramped up for 20 s, followed by 20 min of 2 mA, then ramped down for 20 s. Participants were blind to the specific tDCS manipulation. For the sham stimulation, the electrode montage was the same and the electrodes were also attached for 20 min; however, the stimulation lasted for 30 s (fade in/out 20 s). This procedure ensures that the participants experienced the sensations initially associated with the onset of stimulation (mild local tingling), without inducing any effective modulation of cortical excitability. Also, this procedure ensured successful blinding of participants in previous research (Gandiga et al. 2006; Loo et al. 2010, 2012; Ambrus et al. 2012; Làdavas et al. 2015; Paracampo et al. 2018; but see O'Connell et al. 2012).

As mentioned above (see Introduction), while these parameters for a-tDCS elicit a facilitation on motor excitability lasting for more than 60 min (Batsikadze et al. 2013; Jamil et al. 2017), c-tDCS at 2 mA for 20 min can produce more inconstant after-effects (Batsikadze et al. 2013; Wiethoff et al. 2014; Jamil et al. 2017). To monitor tDCS current-induced after-affects, we assessed M1 corticospinal excitability using TMS.

TMS and Electromyography Recording

To detect current-driven changes of motor excitability, we recorded MEPs by stimulating the hand representation in the left M1 with single-pulse TMS. MEPs were induced using a Magstim 200 magnetic stimulator (Magstim, Whiteland) and a figure-of-eight magnetic coil (70 mm outer diameter; peak magnetic field 2.2 Tesla). The coil was held tangentially to the skull, with the handle pointing backward and laterally at 45° from the midline, resulting in a posterior–anterior direction of current flow in the brain. Surface electromyography (EMG) was recorded from the right FDI with Ag-AgCl electrodes in a belly-tendon montage with ground electrode on the wrist, using Topas (Schwarzer) EMG system. The signals were amplified and filtered with a time constant of 10 ms and a low-pass filter of 2.5 kHz. The motor area for the right hand was defined as the point where stimulation consistently evoked the largest MEPs in the right FDI. To record MEPs, TMS intensity was set at 120% of the resting motor threshold, which was defined as the lowest intensity of output that evoked five small responses (~50 μV) in the relaxed FDI muscle in a series of 10 stimuli (Rossini et al. 2015). The motor threshold means for participants of the anodal and cathodal groups were 37.0% ± 5.4 and 40.1% ± 5.6 of the maximum stimulator output. Participants were instructed to maintain their right hand relaxed, and the absence of involuntary contractions was continuously verified throughout the entire experiment.

Procedure

The study involved a 2 Stimulation group (a-tDCS, c-tDCS) × 2 Sessions (active, sham) × 2 Type of sentences (action, attentional) experimental design. The Stimulation group was a between-participants factor, whereas the Session and the Type of sentences were manipulated within-participants.

Participants were randomly assigned to the a-tDCS or c-tDCS group. All participants were tested in two separate sessions. In the active session, they performed the memory task immediately after 20 min of active tDCS over M1; in the sham session, they performed the task following sham stimulation. The order of the sessions was counterbalanced across participants, and the 2 sessions were separated by at least 3 days.

To explore whether the behavioral results were associated with changes in motor excitability due to tDCS, MEPs induced by single-pulse TMS were recorded in three moments during the experimental sessions. First, a set of 25 baseline MEPs were collected before the active or sham tDCS was applied (baseline); second, immediately after tDCS and before the memory task (T0), another set of 25 MEPs were taken; finally, after performing the memory task (lasting about 25 min), a final set of MEPs was collected (T25) (Fig. 1A).

The memory task included 12 experimental blocks, split into 6 blocks for each session. Each block was characterized by a learning phase, followed by a 45-s distractive task and a cue recall phase. The learning phase started with a filler sentence added at the beginning of each block to avoid the recall primacy effect, then 5 manual action and 5 attentional sentences were presented in a random order, and the participants were asked to memorize them and informed that they would receive a posterior memory test. The sentences were presented word-by-word (see Fig. 1B), with a short intertrial interval (2 s), to minimize mental repetition of the sentence just read. Following the learning phase, a 45-s distractive task was introduced to avoid the recency effect of memory, consisting of several trials, in which a target lower-case letter was presented beside a group of nine upper-case letters and the participants had to identify whether the target letter appeared in the group of the upper-case letters. Finally, in the recall phase, the verbs contained in the previous sentences were visually presented, and the participants had to recall orally the object associated with the verb (see Fig. 1C). The answers were recorded and subsequently analyzed.

Data Analysis

Three-way mixed factors ANOVAs by participants, with Group (a-tDCS and c-tDCS) as between-participants factor and Session (active and sham) and Type of sentences (action and attentional) as within-participants factors, were performed for memory accuracy, calculated as the percentage of words correctly recalled. The post hoc comparison was performed using the Newman–Keuls test. Partial eta^2 ($\eta_p{}^2$) was computed as a measure of effect size for the main effects and interactions, whereas repeated measures Cohen's *d* was computed for post hoc comparisons (Cohen 1992).

To corroborate the effectiveness of our manipulation, we further conducted an item analysis. Item accuracy was computed as the percentage of participants who correctly remembered each item. Since the data were not normally distributed (as shown by the Lilliefors test), they were analyzed with nonparametric Friedman ANOVAs. Two ANOVAs were carried out separately for the 2 Type of sentences (action and attentional), with Condition (a-tDCS-active, a-tDCS-sham, c-tDCS-active, c-tDCS-sham) as within-item factors. Post hoc comparisons within factors were conducted with the Bonferroni-corrected Wilcoxon matched pairs.

MEPs were measured in mV and computed as the median of peak-to-peak amplitude for the three 25-MEPs sets obtained before and after tDCS for each session. MEPs contaminated by magnetic artifacts or preceding EMG activations were excluded from analysis (2%). For each session and group, we normalized the MEPs recorded after tDCS, averaging them at T0 and T25, resulting in values representing either increased (>1.0) or decreased (<1.0) motor excitability induced by tDCS. The normalized MEPs were entered into a two-way mixed factors ANOVA with Group (a-tDCS, c-tDCS) as between-subjects factor and Session (active, sham) as within-subjects factor.

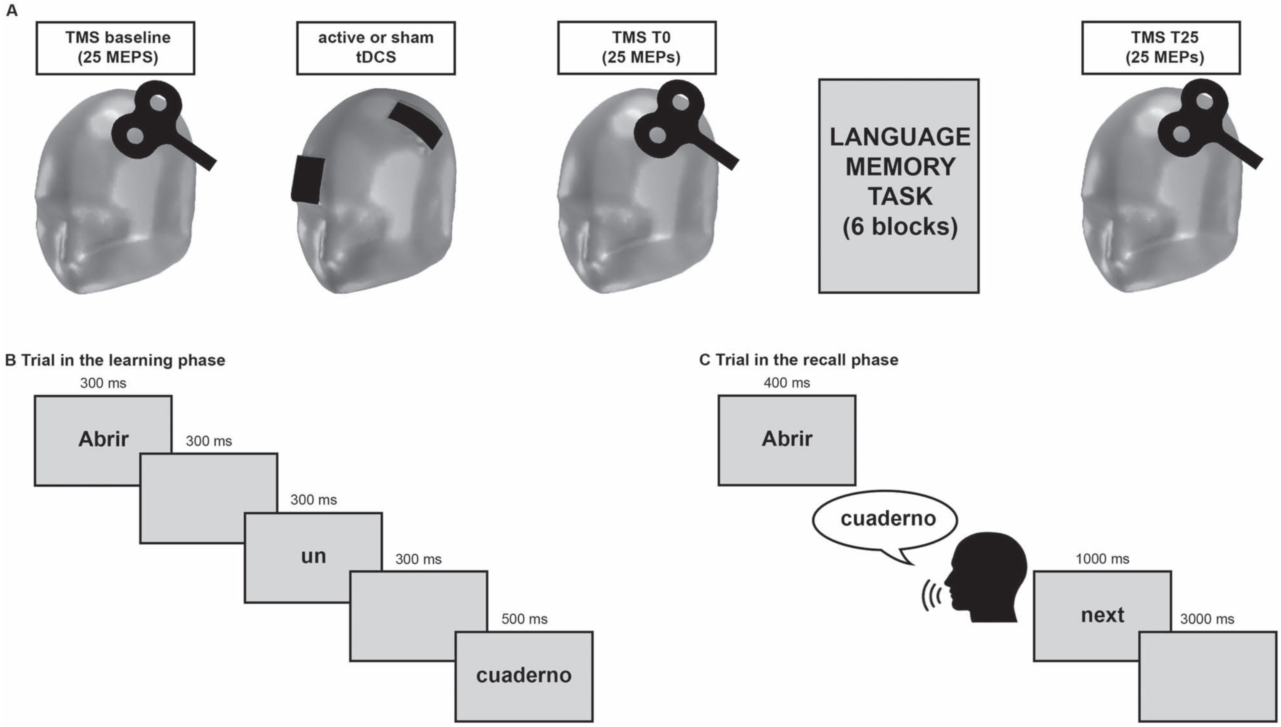

Figure 1. Structure of experimental procedure. (A) Schematic representation of behavioral and neurophysiological sessions. (B) Example of a trial in the learning phase (translation: to open/a/notebook). (C) Example of a trial in the recall phase.

To directly test whether the effect of tDCS on behavioral performance was predicted by tDCS-induced physiological changes, regression analyses were performed. To this end, an index of change in motor excitability was computed as the difference between normalized MEPs in the active versus sham tDCS session, and this index was entered as a continuous predictor in the regression model. In a similar way, an index of action-specific change in recall accuracy was entered as a dependent variable in the model. The index was calculated as follows. To assess action specificity, we subtracted accuracy values in the attentional sentences (serving as control condition) from accuracy values in the action sentences (experimental condition) separately for each session. Then, to assess the effect of tDCS, the two contrasts were combined in a differential index of the active versus sham tDCS sessions. In a further regression model, we additionally entered the categorical predictor Group, to test whether similar relationships between physiological and behavioral data were observed in the two groups. To calculate Cohen's effect size (f^2) of regression, we used the formula $f^2 = R^2/(1 - R^2)$ (Cohen 1992).

Results

Behavioral Results

The Group × Session × Type of sentences ANOVA performed on memory accuracy indicated a strong main effect of the Type of sentences ($F_{1,48} = 40.56$, $P < 0.001$, $\eta_p{}^2 = 0.458$). Manual action sentences were better remembered (mean accuracy ± SD: 35% ± 17) relative to attentional sentences (28% ± 16). More importantly, the expected triple Group × Session × Type of sentences interaction was also significant ($F_{1,48} = 5.03$, $P = 0.03$, $\eta_p{}^2 = 0.095$; Table 1).

To further explore such interaction, we performed separate Session × Type of sentences ANOVAs in the a-tDCS and c-tDCS groups, separately. The ANOVA performed in the a-tDCS group maintained the significant main effect of Type of sentences ($F_{1,24} = 12.52$, $P < 0.001$, $\eta_p{}^2 = 0.34$), indicating an advantage of manual action sentences (mean accuracy ± SD: 33% ± 16) relative to attentional sentences (27% ± 14, $P < 0.001$). Most importantly, the interaction Session × Type of sentences was also significant ($F_{1,24} = 4.34$, $P = 0.048$, $\eta_p{}^2 = 0.15$). Such interaction indicates that active a-tDCS improved memory for action sentences (35% ± 18) relative to sham a-tDCS (31% ± 16; $P = 0.048$, Cohen's $d = 0.23$), whereas no difference was found between sham and active a-tDCS for the attentional sentences (sham: 28% ± 14; active: 26% ± 17; $P = 0.40$).

The ANOVA conducted on the c-tDCS group also revealed a significant main effect of Type of sentences ($F_{1,24} = 29.94$, $P < 0.001$, $\eta_p{}^2 = 0.56$; action sentences: 38% ± 15 vs. attentional sentences: 29% ± 15), whereas neither the session nor the interaction produced significant effects (all $P > 0.30$), confirming that only active a-tDCS of M1 improved memory performance and that this was selective for action sentences (Fig. 2).

The item analysis carried out with Friedman ANOVA on action sentences was significant ($\chi^2 = 9.16$, $P = 0.03$). The Bonferroni-corrected Wilcoxon tests performed in the a-tDCS group showed that the action sentence items were better remembered in the active session compared with the sham session (9% ± 6 vs. 8% ± 6; $P = 0.05$), whereas the same comparison was not significant in the c-tDCS Group (10% ± 6

Table 1 Percentage of object recall for each session of the a-tDCS and c-tDCS groups (mean ± SD)

	a-tDCS group		c-tDCS group	
	Sham	Active	Sham	Active
Action sentences	31% ± 16	35% ± 18	38% ± 14	38% ± 18
Attentional sentences	28% ± 14	26% ± 17	28% ± 15	30% ± 19

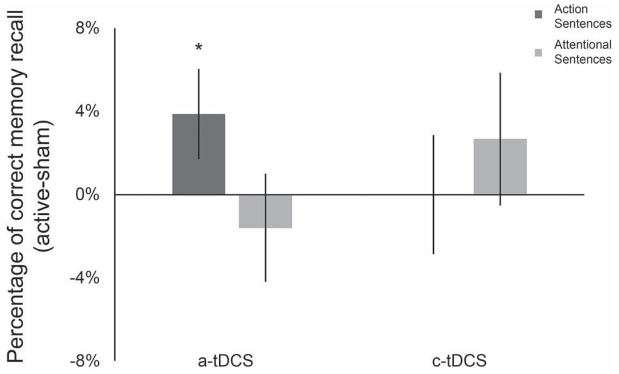

Figure 2. Differential means percentage of recalled items between active and sham sessions, as a function of stimulation group and type of sentences. Error bars indicate standard error of the mean (SEM). *$P < 0.05$.

vs. 9% ± 6; $P = 0.40$), confirming the result revealed by the main ANOVA by participants on memory accuracy. As expected, the Friedman ANOVA by items with attentional sentences was not significant ($\chi^2 = 3.67$, $P = 0.30$).

MEP Results

The Group × Session ANOVA on normalized MEPs did not reach statistical significance (all $F < 2.14$, all $P > 0.15$; Fig. 3A). Yet, we directly tested the prediction that a-tDCS would increase motor excitability by using a one-sample *t*-test against 1. We found that normalized MEPs following active a-tDCS were marginally greater than 1 ($t_{24} = 1.46$, $P = 0.078$), suggesting a weak increase in motor excitability induced by a-tDCS (mean MEP amplitude ± SD: 1.10 ± 0.36). Indeed, the effect of a-tDCS was variable across participants (Fig. 3B), with 18 showing increased MEP amplitudes and 7 showing decreased MEP amplitudes. On the other hand, one-sample *t*-tests showed a nonsignificant reduction in MEP amplitudes following c-tDCS (0.95 ± 0.15; $P = 0.32$): the effects of c-tDCS were quite variable across participants (Fig. 3C) with 13 of them showing reduced MEPs and 12 showing increased MEPs. A planed comparison showed that MEPs following a-tDCS were larger than MEPs following c-tDCS ($P = 0.04$). No consistent modulations were observed following sham tDCS in either group (~1.00, all $P > 0.95$).

In a further analysis, we tested whether individual variations in motor excitability induced by tDCS predicted changes in performance across the 2 groups. To this end, we first entered the memory accuracy index as a dependent variable and the normalized MEP index (normalized MEPs following active tDCS minus normalized MEPs following sham tDCS) as a continuous predictor in a regression model. The model was significant ($R^2 = 0.08$, $F_{1,48} = 4.43$, $P = 0.04$; $f^2 = 0.09$), and it improved after the removal of two outliers with standard residual greater than 2 SD ($R^2 = 0.11$, $F_{1,46} = 5.84$, $P = 0.02$; $f^2 = 0.13$; Fig. 4). Interestingly, the model showed a positive relationship ($\beta = 0.34$, $P = 0.02$), indicating that larger normalized MEP index values (i.e., larger increase in motor excitability induced by tDCS) predicted increased memory performance with action language across the two groups.

Then, we asked whether the highlighted relationship was different in the 2 groups. We therefore entered Group as a further (categorical) predictor in the previous model and tested for any possible interaction between the 2 predictors. The whole model was significant ($R^2 = 0.21$, $F_{3,44} = 4.00$, $P = 0.01$; $f^2 = 0.27$; Fig. 4) and showed that the best predictor of memory performance was the predictor Group ($\beta = 0.30$, $P = 0.032$; Fig. 4B), thus confirming the results of the main ANOVA, with larger action-specific improvements in the a-tDCS as compared with the c-tDCS group. Remarkably, the model also showed the significance of the predictor normalized MEP index ($\beta = 0.28$, $P = 0.047$; Fig. 4A), but no interaction between the 2 predictors ($\beta = 0.10$, $P = 0.44$), indicating that similar positive relationships between changes in M1 excitability and action-specific memory improvements were observed in the experimental and control groups, although only the former showed consistent improvements at the group level.

Discussion

The present study investigated the functional role of the motor system in memory for action-related sentences. In two different groups, we applied offline a-tDCS or c-tDCS over the participants' left M1 before they performed a language memory task, which consisted of memorizing sentences with manual action and attentional verbs. Compared with sham stimulation, a-tDCS improved the recall of sentences with manual action verbs but did not affect the recall of attentional sentences. No similar effects were observed following c-tDCS. As expected, a-tDCS tended to increase the amplitude of MEPs, although this effect was weak and only marginally significant. On the other hand, c-tDCS induced highly variable physiological effects, but no net change in motor excitability. Although only a-tDCS significantly improved action language performance at the group level, in both groups, participants who showed larger increase in motor excitability following active tDCS tended to show larger action-specific memory improvements, as shown by a regression analysis. These findings highlight a clear relationship between changes in the excitability of the motor cortex and action-specific memory performance.

The present study provides strong evidence of a causal link between the motor system and memory for action language. It demonstrates for the first time that an excitatory modulation of the motor cortex improves performance in the comprehension and later recall of action language. Previous research has shown that a-tDCS over M1 can transiently enhance a variety of motor functions including control of manual dexterity, endurance, and

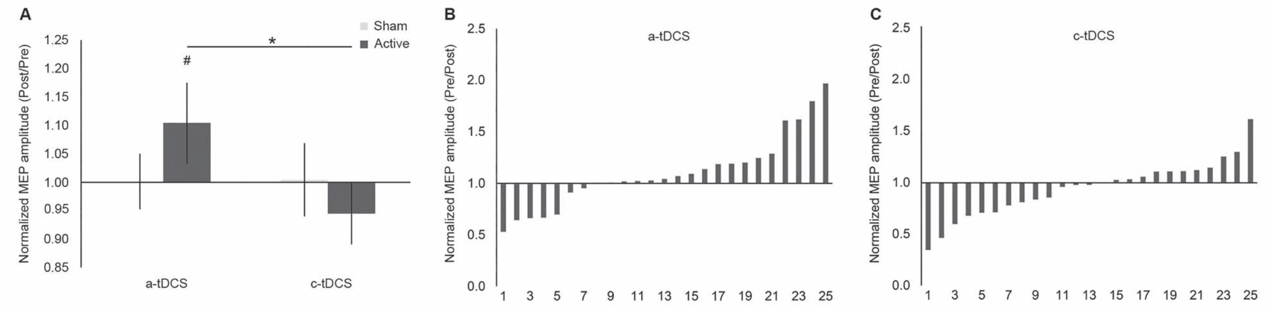

Figure 3. Changes in MEPs following tDCS. (*A*) Effect of Group and Session on normalized MEP amplitudes. MEPs following active a-tDCS tended to marginally increase relative to baseline levels. Error bars indicate SEM. $^{*}P < 0.05$, $^{\#}P = 0.078$. (*B*) Individual normalized MEP amplitude values following active a-tDCS. (*C*) Individual normalized MEP amplitude values following active c-tDCS.

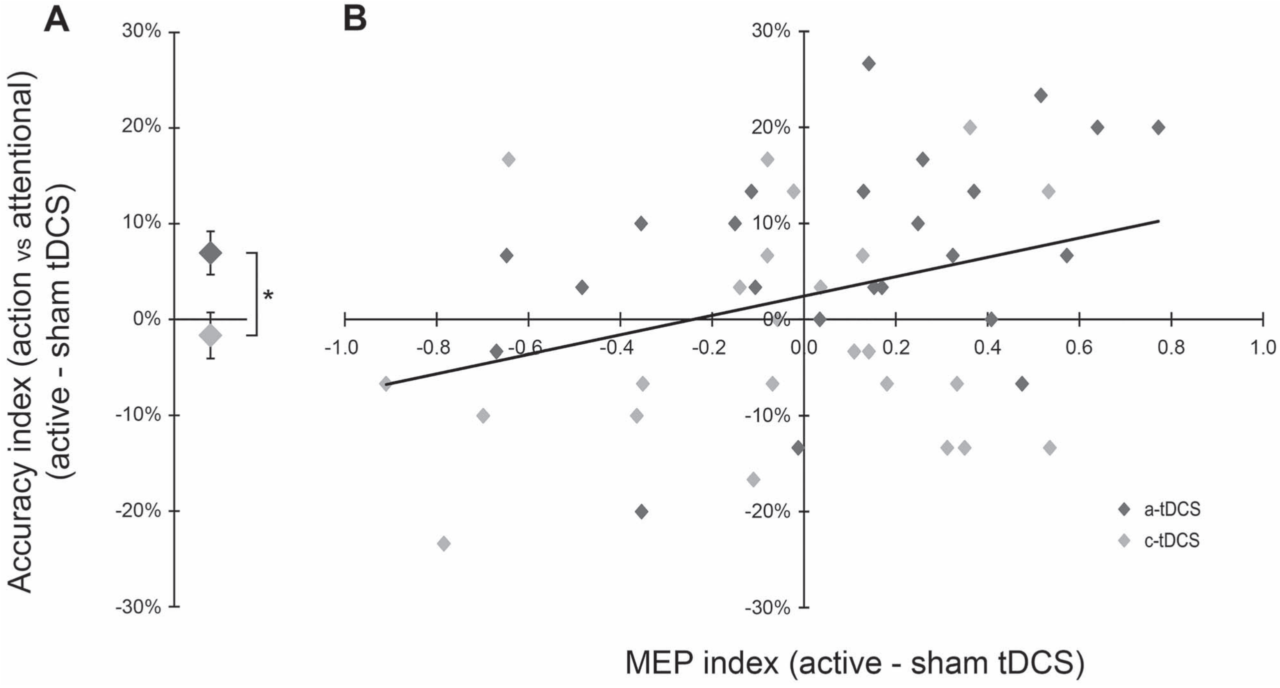

Figure 4. Results of the regression model. (*A*) Effect of the predictor Group. (*B*) Scatter plot of the relationship between normalized MEPs index and the differential accuracy index across groups.

maximal force production (Orban de Xivry and Shadmehr 2014; Alix-Fages et al. 2019). Remarkably, a-tDCS improved learning of a variety of motor tasks (Buch et al. 2017) and, in particular, it improved performance in a serial reaction time task, which offers a well-established measure of implicit motor learning (Nitsche, Schauenburg, et al. 2003b; López-Alonso et al. 2015; see Reis and Fritsch 2011 for a review). Additionally, in a recent study, Buchwald et al. (2019) reported preliminary evidence that a-tDCS also improves motor learning in the speech domain. In the present research, however, we observed facilitatory effects of neuromodulation in an entirely different cognitive domain tapping on the processing of linguistic meaning. In spite of that, the mechanism underlying these effects could be similar, that is, a-tDCS applied on M1 improves motor learning and selectively enhances memory of action-related sentences, possibly because the motor cortex is causally engaged during both motor learning and action language comprehension and memory.

Importantly, our study complements and extends some recent TMS studies that have supported a functional relevance of the motor system in language comprehension. These studies have mainly reported delayed response to action language following online rTMS interference (Vukovic et al. 2017) or offline rTMS protocols that are supposed to inhibit motor excitability (Gerfo et al. 2008; Kuipers et al. 2013; Repetto et al. 2013). However, some obvious differences between our study and prior work must be noted. First, we investigated performance on a task requiring understanding and memorizing short noun–verb sentences, whereas previous studies used tasks requiring (online) morphological, lexical, or semantic operations in response to action words. Second, here performance was improved by excitatory tDCS neuromodulations, rather than reduced by interferential or supposedly inhibitory TMS. Critically, rather than assuming a net physiological effect of brain stimulation, we directly monitored tDCS-induced changes in the excitability of the motor cortex and explored their relationship with changes in performance. Our study expands previous work by showing, for the first time, a linear relationship between tDCS-induced action-specific memory improvements and changes in motor excitability.

To what extent does this study contribute to clarifying the current debate on embodied-disembodied meaning (e.g., de Vega et al. 2008)? The "disembodied" theories of linguistic meaning accept the overwhelming evidence that sensory–motor brain networks are activated during the comprehension of action language, but they doubt that these activations reflect a necessary aspect of meaning or play any functional role (e.g., Mahon and Caramazza 2008; Chatterjee 2010; Papeo et al. 2013; Mahon 2015). For instance, Mahon and Caramazza (2008) consider that the observed embodied effects are due to "cascade" spreading activation between the conceptual system to the sensory and motor systems but that ultimately the proper representation of meaning is amodal or disembodied. Moreover, they claim that most evidence of embodied meaning comes from correlational measures, such as the BOLD signal activity, and corresponds to short-lived "reverberations" of sensory–motor regions, which are irrelevant for lexico-conceptual processing. Our results speak against these claims. Our data are not merely correlational, because they demonstrated a causal link between the human motor cortex and the ability to memorize action sentences. Also, the embodied effects were not short-lived, because they extended to a delayed memory task.

We propose that a-tDCS—and, potentially, other protocols that could increase the excitability of the motor cortex, see below—improves performance in our task by enhancing the simulation of motor actions, which occurs while encoding action sentences (i.e., during the learning phase of the task). The selective enhancement simulation of action sentences caused by a-tDCS would result in stronger memory traces of the same sentences. However, we do not rule out that increased motor excitability may have also favored action simulation during the testing phase of our cued recall procedure. In keeping with our findings, recent behavioral studies using a similar task (Dutriaux and Gyselinck 2016; Dutriaux et al. 2018) reported memory impairment for images and words denoting manipulable objects when participants assumed a posture that would potentially interfere with action simulation (hand behind the back). Taken together, these findings support the EC proposal that a high-level cognitive process, such as action language, is grounded in the sensory–motor system (Glenberg and Kaschak 2002; Fischer and Zwaan 2008; Glenberg et al. 2008). In other words, to understand words or sentences referring to actions, the simulation of the corresponding actions in the motor system contributes at least in part to comprehension and memory.

We have empirically demonstrated that the motor cortex is causally associated with memory of action-related meaning. Clearly, other neural structures might be additionally involved in processing linguistic meaning (e.g., in control monitoring, inhibition, semantic processing, etc.), either because of cascade spread activation or because they play some functional role. Interestingly, Kemmerer et al. (2012) performed a large-scale neuropsychological study on 226 brain-damaged patients and reported that low performance in tasks requiring to process action language was most consistently associated with lesions occurring in left frontal areas (i.e., in the inferior frontal gyrus/anterior insula, ventral premotor cortex, and M1). Poor performance was also associated with lesion of the left parietal (ventral postcentral and supramarginal gyri) and temporal areas (pMTG). Hence, because brain stimulation can exert its influence not only locally but also over interconnected brain regions (Valchev et al. 2015, 2016; Polanía et al. 2018; Zanon et al. 2018), it is possible that our a-tDCS protocol could have modulated not only M1 activity but also the activity of other sectors of the motor cortex overlapping with those documented by Kemmerer and colleagues, and these regions could thus participate in the observed memory improvement (see the excellent review of Papeo et al. 2013 for a critical discussion on the issue). Regarding the last statement, modeling and neuroimaging studies support that M1 and other premotor areas are primarily modulated by tDCS. Computational modeling for a-tDCS with a 7 × 5 cm electrode (the same size as in the present study), placed on the left M1, shows that the most stimulated brain regions are anterior to the targeted M1, that is, in the premotor cortex (Datta et al. 2009; Opitz et al. 2015; Ho et al. 2016). In keeping, functional magnetic resonance imaging (fMRI) measurements recorded, while participants performed a motor task after receiving a-tDCS over M1, showed an increase in the activity of M1 and premotor areas (Jang et al. 2009; Stagg et al. 2009). These motor regions are also more functionally coupled after a-tDCS over M1, as suggested by resting-state fMRI (Polanía, Paulus, et al. 2011a) and EEG (Polanía, Nitsche, et al. 2011b).

The current results are compatible with hybrid proposals of semantic processing such as the Hub and Spoke theory (e.g., Lambon Ralph 2014). According to this theory, processing words activates highly distributed multimodal networks (spokes), including the motor system, as well as a transmodal semantic network (the hub) typically located in the bilateral anterior temporal lobes (ATL), which are responsible for integrative semantic processing. The functional role of the semantic hub has been supported by neuropsychological studies with semantic dementia patients, who suffer atrophy of the ATL and manifest dramatic impairment in semantic tasks (Hodges and Patterson, 2007). Also, applying inhibitory stimulation (1-Hz rTMS) over ATL in neurotypical individuals induces difficulties in processing semantic information (Pobric et al. 2007, 2010). However, this approach leaves open the possibility that spokes such as the motor system can be part of the semantic machinery involved in linguistic meaning. Additional research will be needed to know how the motor cortex and ATL interact. In any case, whether the activation of the motor system precedes the activity of the ATL (García et al. 2019) or flows downstream from the ATL (Mahon and Caramazza 2008), the issue of the functionality of the motor cortex requires empirical demonstrations beyond that of pure speculation. This study provides just such a demonstration.

Interestingly, Papeo et al. (2015) reported that the activation of the motor cortex by action verbs is functionally dependent on the activity of the left pMTG, a region involved in the conceptual distinction between verbs and nouns. Papeo et al. (2015) applied inhibitory stimulation (1-Hz rTMS) over the pMTG and observed selective impairment in the semantic processing of verbs and, more relevant here, the elimination of the motor cortex modulation generally associated with action verbs. Again, our proposal is compatible with the above results. Even if the activation of pMTG precedes (and modulates) the activation of the motor cortex during processing of action language, this does not necessarily relegate the latter activation to the category of a simple epiphenomenon. That being the case, exogenous manipulation of M1 should not affect performance in our task.

Thus, because we found that a-tDCS over M1 enhanced the recall of action language, we conclude that the motor system provides signals that are functionally relevant to performing our task. The current study clearly reinforces the idea that, at some stage, the motor system can play a crucial role in memory for action-related language.

A semantic theory of linguistic meaning should be able to accommodate the current evidence or accept that at least in some cases embodied representations are causally involved in the recall of action language. Note that our embodiment approach is not reductionist; namely, we do not imply that semantic representations are purely motor in action language. That is, having demonstrated the causal role of the motor system in action language does not preclude that other networks (semantic, visual, executive control) could also cooperate to produce meaning or memorize it. Yet, our results also indicate that a purely semantic reductionist approach (proposing that meaning exclusively relies on amodal activity in the temporal cortex and cascading activations to sensory–motor networks are epiphenomenal) does not work either.

Previous studies focused on online embodiment effects, such as how inhibiting M1 affects online comprehension of action language (Gerfo et al. 2008; Kuipers et al. 2013; Repetto et al. 2013; Vukovic et al. 2017) or, alternatively, how comprehension of action language modulates online motor excitability (Oliveri et al. 2004; Buccino et al. 2005; Hauk et al. 2008; Papeo et al. 2009; Scorolli et al. 2012). By contrast, here we were particularly interested in testing long-term effects of embodied processes beyond the online effects of comprehension on motor excitability. Consequently, we demonstrated that exciting M1 improved action language recall, but we did not directly test whether comprehension was also improved. It is quite likely, however, that the impact of a-tDCS improved both comprehension and memory. First, the sentence-reading phase was under the influence of a-tDCS as much as the retrieval phase; second, the two processes are functionally related: understanding seems necessary for a cued-memory task like the one used here, which cannot be easily accomplished with shallow processing of language. Concerning the possible use of offline memory strategies by the participants (e.g., mental rehearsal, mental imagery), it was minimized by the presence of a distractive task between the learning and the retrieval phase. However, given the fact that we did not explore the chronometry of motor activations during comprehension, we cannot rule out that certain strategic activities can be carried out immediately after comprehension and, if so, they also were improved by excitatory stimulation of M1.

Although behavioral outcomes of brain stimulation are fundamental to inferring causal links between brain structure and functions, they cannot explain the neural mechanism underlying the functional improvement (Silvanto and Pascual-Leone, 2012; Avenanti, Candidi, et al. 2013b; Valchev et al. 2015, 2016; Polanía et al. 2018). To provide insights on this matter, we monitored the motor excitability using MEPs and tested whether the neurophysiological changes induced by tDCS predict task performance. As expected, we found that the majority of participants in the experimental group showed increased MEP amplitudes after a-tDCS, whereas participants in the control group showed more variable MEP change following c-tDCS and no net physiological change. We leveraged MEP variability in the 2 groups to explore the relationship between physiological and behavioral changes. We highlighted a clear relationship between the 2, suggesting that relative increase and decrease of motor cortex excitability could impact on action-specific memory performance. Regression analysis showed 2 additive effects, with the best predictor of memory performance being the factor Group (larger behavioral improvement following a-tDCS than following c-tDCS) and the second predictor being the normalized MEP index (larger behavioral improvement associated with increased motor excitability across groups), thus confirming and expanding the results of the main ANOVA. No interaction between these 2 predictors, suggesting a similar relationship between physiological and behavioral changes in both the experimental and the control groups.

Thus, two sources of variability appear to affect behavioral data in our study. Overall, a-tDCS appears better suited than c-tDCS for optimizing memory of action sentences, as shown by the effect of group. However, the additive linear relationship between neurophysiological and behavioral data supports the hypothesis that both protocols could affect performance also depending on their effectiveness in driving changes in motor excitability, with larger excitatory modulations associated with relative action-specific improvements and larger motor inhibition associated with relative action-specific impairments. This hypothesis is also in line with the observation that low-frequency rTMS over M1—a supposedly "inhibitory" TMS protocol (e.g., Chen et al. 1997)—decreased action language performance in morphological and semantic tasks (Gerfo et al. 2008; Repetto et al. 2013). These findings suggest that increased and decreased motor cortex excitability reflects a mechanism for enhancing and hindering action simulation that, in turn, could be responsible for the change in performance with action language comprehension and recall in previous research (Gerfo et al. 2008; Repetto et al. 2013) and the present work.

We observed no effect of c-tDCS at the group level, showing that the after-effects of a-tDCS are polarity specific. Is the absence of c-tDCS effect on recall a methodological artifact? Perhaps, the c-tDCS was inefficient because the participants' overall performance in the memory task was quite poor, causing a floor effect. Yet, this interpretation is unlikely, since previous studies with materials and procedures similar to those employed here reported impaired recall due to a disruptive posture of the hands during learning in spite of the low memory performance in the baseline condition (Dutriaux et al. 2018; de Vega et al. unpublished data). A better explanation comes from the neurophysiological measure recorded here. In line with the variability reported in previous studies (e.g., Wiethoff et al. 2014; Jamil et al. 2017), c-tDCS at 2 mA showed a variable pattern of change in motor excitability. Such physiological variability may explain the absence of a clear behavioral effect of c-tDCS. While in the present research c-tDCS parameters were selected as a control for the main experimental manipulation (a-tDCS), future studies could investigate a potential interference effect of c-tDCS, using a more reliable inhibitory protocol (e.g., 1 mA) in a language memory task like the current one.

This research has clear translational implications. There is evidence that patients with motor disorders (e.g., Cardona et al. 2013; Kargieman et al. 2014; García et al. 2017), especially those with Parkinson's disease (Herrera and Cuetos 2012; Melloni et al. 2015; Abrevaya et al. 2017; Birba et al. 2017; García and Ibáñez 2018), have a selective impairment in the processing of action-related language. Here, we reported that a-tDCS applied over M1 in healthy participants selectively improved their performance in an action-related language task. This opens the possibility of applying a-tDCS or other excitatory brain stimulation protocols to help Parkinson's patients to overcome their specific language deficits.

In conclusion, our study demonstrates that a-tDCS administrated over the left M1 improves the recall of manual action sentences but not of attentional sentences. This improvement appears specific to a-tDCS, as it was not shown following c-tDCS. However, both protocols induced variable physiological changes, and action-specific memory improvements were not only predicted by the stimulation protocol (larger improvements following a-tDCS than following c-tDCS) but also by the induced physiological changes, with greater excitatory modulations of the motor cortex associated with larger behavioral improvements and relative inhibitory modulations associated with reduced action language performance. These findings provide causal evidence that the motor system is essential for efficient memory of action language.

Supplementary Material

Supplementary material can be found at *Cerebral Cortex* online.

Notes

Conflict of Interest: None declared.

Funding

Ministerio de Ciencia, Innovación y Universidades (grants PSI2015-66277-R and RTI2018-098730-B-I00 to M.D.V.; the Research Training Predoctoral grant BES-2016-078438 to F.V.); European Regional Development Funds; Bial foundation (grant 347/18 to A.A.); Fondazione del Monte di Bologna e Ravenna (grant 339bis/2017 to A.A.); Cogito foundation (grants R-117/13 and 14-139-R to A.A.); Ministero Istruzione Università e Ricerca (grant 2017N7WCLP to A.A.).

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