EJN EUROPEAN JOURNAL OF NEUROSCIENCE

FENS Federation of European Neuroscience Societies

European Journal of Neuroscience, Vol. 42, pp. 1889–1894, 2015 doi:10.1111/ejn.12937

COGNITIVE NEUROSCIENCE

Neural underpinnings of the 'agent brain': new evidence from transcranial direct current stimulation

EJN FEATURED ARTICLE

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Keywords: intentional binding, neural bases, pre-SMA, sense of agency, tDCS, voluntary action

Abstract

Intentional binding (IB) refers to the temporal compression between a voluntary action and its sensory effect, and it is considered an implicit measure of sense of agency (SoA), that is, the capacity to control one's own actions. IB has been thoroughly studied from a behavioural point of view but only few studies have investigated its neural underpinnings, always using the same two paradigms. Although providing evidence that the supplementary motor complex is involved, findings are still too scarce to draw definitive conclusions. The aim of the present study was to establish a causal relationship between the pre-supplementary motor area (pre-SMA), known for its key role in action planning and initiation, and IB by means of transcranial direct current stimulation (tDCS). Participants underwent anodal, cathodal and sham control stimulations during three separate sessions (Experiment I). Subsequently, they underwent the same stimulation protocol (Experiment II) using as control a region potentially involved in the processing of the sensory effects of voluntary action (i.e., the right primary auditory cortex for the auditory effects of action). A significant reduction in IB was found only after stimulation of the pre-SMA, which supports the causal contribution of this prefrontal area in the perceived linkage between action and its effects. As SoA could be disrupted in many psychiatric and neurological diseases, these results have direct clinical relevance as tDCS could be successfully used in this domain in virtue of the promising advantages it offers for rehabilitation.

Introduction

Intentional binding (IB; Haggard *et al.*, 2002) is an example of how voluntary actions are associated with changes in time perception. It consists of a temporal compression between an intentional action and its sensory effect, and represents an indirect measure of sense of agency (SoA), the sense of being the author of one's own actions and sensory consequences (Haggard & Chambon, 2012). Since its discovery, IB has been adopted to study SoA in healthy individuals and in clinical populations (Moore & Obhi, 2012). However, although the underlying cognitive mechanisms have been thoroughly investigated, to our knowledge only three studies have tried to explore its neural underpinnings, using different methods. Kühn *et al.* (2013) and Jo *et al.* (2014) adopted correlational techniques (fMRI and EEG, respectively), while Moore *et al.* (2010a) used theta-burst transcranial magnetic stimulation (TMS). These studies provided evidence that the supplementary motor complex is involved; in particular, the latter research demonstrated that disruption of pre-SMA reduced IB. However, the available evidence is still too scarce for drawing definitive conclusions on its neural bases. This is especially true when considering that the same two well-validated paradigms (i.e., the rotating spot method and the interval paradigm) have been used in the above studies, and both present several weaknesses (Gomes, 2002; Cravo *et al.*, 2011).

The aim of the present research was to collect new evidence on the neural bases of SoA by introducing novel aspects compared to the abovementioned studies. (i) Transcranial direct current stimulation (tDCS: Dayan *et al.*, 2013) was adopted, for the first time in this research field, for its potential use in the clinical practice. Indeed, establishing a causal relationship between the stimulated area and IB by means of tDCS might have direct clinical relevance for the treatment of certain neurological and psychiatric diseases in which SoA is disrupted. tDCS could be therefore a suitable tool for intervening in these domains, enhancing awareness of voluntary action. (ii) A new paradigm (Cavazzana *et al.*, 2014) was used to assess IB, allowing us to further generalise the phenomenon by excluding the possibility that previous results could be somehow dependent on specific features of the few paradigms used to assess it. (iii) The effects of non-invasive brain stimulation on IB have been tested in another sensory modality compared to that tested in the aforementioned study (Moore *et al.*, 2010a), aimed at giving additional evidence on the possible supra-modal nature of the effect. Specifically, unlike the quoted study that used a somatosensory feedback, the sensory effect produced by the voluntary action in our task was a tone, typically adopted in IB studies.

In the present study, tDCS was firstly applied to healthy participants' pre-SMA. Secondly, in the same sample it was applied to a

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Received 20 December 2014, revised 27 April 2015, accepted 28 April 2015

control region involved in processing action-auditory effects, i.e., the right primary auditory cortex (PAC). In view of the findings provided by the previous TMS study, we expected stimulation-dependent alteration of IB only when tDCS was applied over the pre-supplementary motor area (pre-SMA), with no contribution by the PAC.

Experiment I: tDCS over pre-SMA

Materials and methods

Participants

Fifteen right-handed healthy participants (mean ± SD, 22.9 ± 1.9 years; four males), who met the inclusion criteria for participating in brain stimulation studies, gave their written informed consent to take part in the experiment, which was performed in accordance with the principles of the Declaration of Helsinki and adopted the safety procedures of non-invasive brain stimulation. The study was approved by the ethical committee of the University of Padua.

Materials and procedure

IB was assessed using a new paradigm (Cavazzana *et al.*, 2014). Participants were asked to observe a stream of unpredictable consonants at the centre of a screen in order to detect the letter displayed when a given event of interest (i.e., either a voluntary action or a sound) occurred. Each letter was presented separately and lasted for 150 ms, without time gaps in between. At the end of each trial, a set of response options, consisting of five letters including the target (i.e., the letter that was on the screen at the actual appearance of the event of interest) was presented. Participants had to choose the correct consonant using the keyboard with their left hand.

The experiment consisted of two baseline conditions (BCs) and two experimental conditions (ECs), for a total of four conditions. In the BCs only one event (i.e., either voluntary action or tone) occurred per condition. The participants had to detect which consonant was on the screen when (i) they made a free voluntary key-press with their right index finger or (ii) they heard an auditory stimulus (1 kHz, 100-ms duration) presented through headphones. For the ECs, two events occurred per condition: the voluntary action was always followed, after a 250-ms fixed interval, by the auditory stimulus. The participants had to detect which consonant was displayed when (iii) they made a free voluntary action that produced the tone and (iv) they heard the tone caused by their voluntary action. Twenty-five trials per condition were administered, for a total of 100 trials. The first three trials of each condition were discarded to allow for familiarisation and were not included in the analysis. Participants performed all the conditions (BCs and ECs) in a different, random order over a single session. Condition order was randomised anew for each session. Stimulation was delivered before the task.

Participants underwent three stimulation sessions (sham-placebo stimulation and two active stimulations), separated by at least 24 h. The ordering for the stimulation conditions was counterbalanced across participants.

To rule out alternative accounts of tDCS effects, a self-report questionnaire measuring mood and arousal was administered at both the beginning and the end of the experiment.

tDCS

tDCS was delivered through a battery-driven current stimulator (BrainStim; EMS Medical, Bologna, Italy), using a pair of surface saline-soaked sponge electrodes. The active electrode (4 × 4 cm) was placed over pre-SMA, which was localised with the EEG 10–20 system, with the centre of the tDCS electrode placed over the site of Fz (Hsu *et al.*, 2011). The reference electrode (10 × 10 cm) was placed over the deltoid muscle of the right arm to exclude the confounding effects of the reference electrode. A constant current of 1.5 mA was applied for 20 min (including fade-in and fade-out times of 30 s each) in both the active stimulation conditions. In the sham condition, a 1.5-mA current was applied for 20 s at the beginning and end of the stimulation period. Testing sessions took place at the same time of the day to minimise circadian effects.

Data analyses

For each trial, we first calculated a judgment error (JE), that is, the difference between the actual time of occurrence of the judged event and the perceived time of its occurrence. A negative JE was interpreted as anticipatory awareness of events (the participants perceived the event occurring before it really did), while a positive JE was interpreted as delayed awareness (the participants perceived the event occurring after it really did). For each of the four conditions (i.e., baseline voluntary action, baseline tone, experimental voluntary action, experimental tone), a mean JE (mJE) was obtained. As the numerical value of the mJE in a single condition is generally not informative and is difficult to interpret, the differences between the mJE of an identical physical event in two different contexts (the BCs and ECs) were calculated by subtracting the mJE of each event in the BC from the mJE of the same event in the EC (i.e., the perceptual shift). For example, the shift of the action towards the tone (i.e., action binding) was calculated by subtracting the mJE of the voluntary action in the BC from the mJE of the voluntary action in the EC, whereas the shift of the tone towards the action (i.e., effect binding) was found by subtracting the mJE of the tone in the BC from the mJE of the same tone in the EC. Finally, we also computed an overall binding measure (Haggard *et al.*, 2003) by combining the first (i.e., action binding) and the second (i.e., effect binding) events. Specifically, the overall binding was calculated as follows: [250 ms − (action binding − effect binding)]. The obtained value represents the perceived linkage between an action and an effect, and provides an implicit measure of SoA, smaller values of overall binding indicating stronger IB.

Results

Table 1 summarises the mJEs, perceptual shifts (i.e., action binding and effect binding) and overall binding for sham, anodal and cathodal stimulations.

A one-way repeated-measures ANOVA was calculated in order to study the effects of three tDCS stimulations (sham, anodal, cathodal) on the overall binding. Results showed a significant effect ($F_{2,28} = 5.8$, $\eta^2_p = 0.3$, $P = 0.008$). *Post hoc* analyses with Bonferroni correction for multiple comparisons revealed significant differences between the effects of sham tDCS and anodal tDCS ($P = 0.02$) and between sham tDCS and cathodal tDCS ($P = 0.04$). Both anodal and cathodal stimulations reduced (i.e., higher values) the overall binding with compared to sham condition, and did not significantly differ from each other (P = n.s.; Fig. 1a and b).

Further analyses explored the perceptual shifts (i.e., action binding and effect binding) using a 3 (‘stimulation’: sham, anodal, cathodal) × 2 (‘event judged’: either the action or the tone) repeated-measures ANOVA. No main effect of stimulation was found ($F_{2,28} = 2.9$, $\eta^2_p = 0.18$, $P = 0.07$), whereas the effect of the event judged was

TABLE 1. mJEs, perceptual shifts and overall binding for sham, anodal and cathodal stimulations (Experiment 1: tDCS over pre-SMA)

Stimulation	Event judged	mJE (ms)	Mean shift (ms)	Overall binding (ms)
BCs				
Sham	Voluntary action	21.8 ± 52.9		
	Tone	23.2 ± 32.1		
Anodal	Voluntary action	18.2 ± 56.0		
	Tone	24.1 ± 33.6		
Cathodal	Voluntary Action	33.6 ± 46.8		
	Tone	32.7 ± 32.7		
ECs				
Sham	Voluntary Action	95.5 ± 62.9	73.6 ± 48.8	125.0 ± 78.9
	Tone	−28.2 ± 55.9	−51.4 ± 47.2	
Anodal	Voluntary Action	39.6 ± 41.3	21.4 ± 51.6	181.8 ± 56.7
	Tone	−22.7 ± 47.9	−46.8 ± 40.3	
Cathodal	Voluntary Action	61.4 ± 57.9	27.7 ± 47.8	188.2 ± 68.3
	Tone	−1.4 ± 22.6	−34 ± 33.6	

'Experiment' consisted of voluntary action followed by a fixed 250-ms interval and then the tone. Values are mean ± SD.

significant ($F_{1,14} = 41.3$, $\eta^2_p = 0.7$, $P < 0.001$). More relevant, a significant interaction emerged ($F_{2,28} = 5.8$, $\eta^2_p = 0.3$, $P = 0.008$). We thus conducted a *post hoc* analysis applying Bonferroni correction for multiple comparisons, in order to examine it in more detail. The *post hoc* analysis revealed that type of stimulation influenced only the shift of the action towards the tone (i.e., action binding): in particular, sham stimulation was significantly different from anodal ($P = 0.007$) and cathodal ($P = 0.014$) stimulations (Fig. 1b). No difference was found between anodal and cathodal stimulations (P = n.s.) which both showed a reduced action binding compared to sham stimulation.

Analyses of the self-report questionnaire measuring mood and arousal revealed no significant differences in any of the items as a function of stimulation conditions. With regard to the self-report questionnaire assessing the sensations experienced during the stimulation, sham and active protocols were found to be indiscernible.

Experiment II: tDCS over right primary auditory cortex

Materials and methods

Participants

Participants were the same as in Experiment I.

Materials, procedure and data analyses

All the materials, the procedure and data analyses were the same of those used and applied in Experiment I. Experiment II was run 1 month after Experiment I.

tDCS

In this experiment, all stimulation parameters were the same as in Experiment I, except for the placement of the active electrode (4 × 4 cm). This was placed over the right PAC, localised with the EEG 10–20 system and placed 1 cm inferior to the midpoint of C4 and T4 (Mathys *et al.*, 2010; Tang & Hammond, 2013).

Results

Table 2 summarises the mJEs, perceptual shifts (i.e., action binding and effect binding) and overall binding for sham, anodal and cathodal stimulations.

A one-way repeated-measures ANOVA was calculated in order to study the effects of three tDCS stimulations (sham, anodal, cathodal) on the overall binding. Results showed no significant differences of tDCS stimulations ($F_{2,28} = 0.3$, $\eta^2_p = 0.022$, $P = 0.7$).

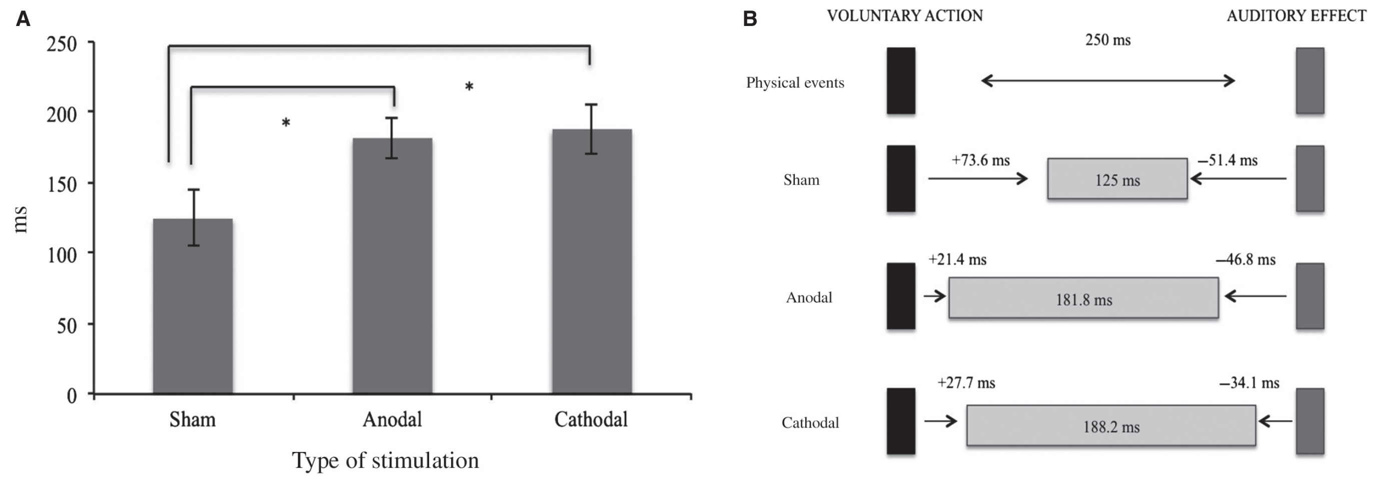

FIG. 1. (A) Effects of three tDCS stimulations (sham, anodal and cathodal) on the overall binding (i.e. the perceived linkage between the action and its effect). Error bars represent SEM; *$P < 0.05$ for the difference in overall binding between stimulations. Sham stimulation, which differed from both anodal and cathodal, reduced the overall binding. (B) Schematic and illustrative illustration of the data. Physical events represent the experimental conditions in which the voluntary action was followed by a fixed 250-ms interval and then its auditory effect. Lower rows indicate the perceptual shifts (i.e. action binding and effect binding) and overall binding when sham, anodal and cathodal stimulations were applied. Sham significantly differed from both anodal and cathodal stimulations in both overall binding (125 ms) and action binding (73.64 ms).

TABLE 2. mJEs, perceptual shifts and overall binding for sham, anodal and cathodal stimulations (Experiment 2: tDCS over primary auditory cortex)

Stimulation	Event judged	mJE (ms)	Mean shift (ms)	Overall binding (ms)
BCs				
Sham	Voluntary action	27.7 ± 60.0		
	Tone	29.1 ± 40.0		
Anodal	Voluntary action	53.6 ± 54.6		
	Tone	60.9 ± 50.8		
Cathodal	Voluntary Action	44.1 ± 63.9		
	Tone	42.7 ± 31.2		
ECs				
Sham	Voluntary Action	66.4 ± 81.1	38.6 ± 59.4	169.1 ± 92.6
	Tone	−13.2 ± 53.2	−42.3 ± 45.9	
Anodal	Voluntary Action	64.4 ± 61.4	10.7 ± 47.9	187.9 ± 82.7
	Tone	9.6 ± 47.4	−51.4 ± 56.9	
Cathodal	Voluntary Action	66.4 ± 57.1	22.3 ± 42.2	175.0 ± 66.6
	Tone	−10.0 ± 58.9	−52.7 ± 54.1	

‘Experiment’ consisted of voluntary action followed by a fixed 250-ms interval and then the tone. Values are mean ± SD.

Further analyses explored the perceptual shifts (i.e., action binding and effect binding) using a 3 (stimulation: sham, anodal, cathodal) × 2 (event judged: either the first or the second) repeated-measures ANOVA. No main effect of stimulation was found ($F_{2,28}$ = 1,7, η^2_p = 0.1, P = 0.2), whereas the effect of the event judged was significant ($F_{1,14}$ = 21.9, η^2_p = 0.6, P < 0.001). The interaction did not emerge as significant ($F_{2,28}$ = 0.3, η^2_p = 0.02, P = 0.7).

Also for Experiment II analyses of the self-report questionnaires measuring mood and arousal and the sensations experienced during the stimulation revealed no significant differences as a function of stimulation conditions.

General discussion

For the first time in this research field, tDCS was adopted to gain insights into the neural underpinnings of SoA, using IB as implicit measure. Pre-SMA has been selected as a potential region involved in this phenomenon. The reason behind this choice is linked to the fact that the experience of agency is strictly related to executive functions, given that it requires (i) a plan to perform a goal-directed action and (ii) the identification of the consequences of our behaviour in the external world, while avoiding and inhibiting erroneous and maladaptive behaviours. In this sense, the involvement of pre-SMA becomes crucial, based on its relevant contribution to the executive functioning. This area is indeed considered to belong to the pre-frontal cortex and not to the motor cortex (Picard & Strick, 2001; Akkal *et al.*, 2007; Nachev *et al.*, 2007). Indeed, differently from the SMA proper, the pre-SMA has extensive connections with pre-frontal regions and is associated with the higher cognitive aspects of tasks (e.g., action planning and initiation). In addition to the previous findings obtained using TMS (Moore *et al.*, 2010a), a very recent study conducted by Wolpe *et al.* (2014) also highlighted the importance of this area for the process under investigation. The authors, using IB as an implicit marker of agency in patients with corticobasal syndrome, have underlined that patterns of functional connectivity between the pre-SMA and the prefrontal cortex in resting conditions seem to change according to IB effects, suggesting that a medial frontal–prefrontal network is necessary for awareness and control of voluntary action. Pre-SMA has therefore been selected in the present study as the target area of stimulation to further verify its causal involvement in the complex phenomenon of SoA.

Subsequently, PAC was also modulated, as a control area, given its key role in the processing of the auditory stimuli (Pickles, 2012), which here represent the effects of voluntary actions.

As we expected, results showed a significant reduction in IB only after stimulating pre-SMA. In detail, sham stimulation significantly differed from anodal and cathodal stimulations, which both tended to reduce IB producing an inhibitory effect. Perceptual shifts were also analysed separately (action binding vs. effect binding) as they seemed to be mediated by different underlying mechanisms (Wolpe *et al.*, 2013). Only action binding (i.e., the shift of the action towards its auditory effect) was significantly reduced. Also in this case, sham stimulation differed from anodal and cathodal stimulations, which both tend to inhibit the shift of the action towards its effect.

Unlike many previous findings in the motor domain, showing that cortical excitability is increased by anodal and decreased by cathodal stimulation, we did not find polarity-dependent effects in behavioural measures, as both anodal and cathodal stimulations had an inhibitory effect on IB. Although this result could seem surprising at first sight (especially as regards the lack of facilitation for the anodal stimulation), the same inhibitory effect of both anode and cathode has been reported in other studies (Marshall *et al.*, 2005; Stagg *et al.*, 2011; Westgeest *et al.*, 2014; Zmigrod *et al.*, 2014), which differed in many aspects from ours, thus making it difficult to detect the reasons behind the lack of effects dependent on stimulation polarity. To test the hypothesis that longer durations of stimulation can somehow change the expected opposite anodal-excitation and cathodal-inhibition effects, we performed additive analyses, similar to those described in the Materials and Methods section, on data split into two halves (i.e., relative to the initial vs. final parts of task performance). These new analyses did not confirm the above hypothesis as no significant difference between the two halves of the data was found (for this reason we did not report them in the Materials and Methods section). In this regard, we are incline to think that, beyond the importance of each single stimulation parameter in shaping stimulation-induced behavioural effects, these effects can emerge by complex interactions between a given combination of stimulation parameters, the targeted cognitive functions and the experimental tasks used to test these functions. However, the result pattern we found confirms that the dichotomy between ‘anodal excitation’ and ‘cathodal-inhibition’ in the cognitive domain is far from being considered unquestionable (for a review, see Jacobson *et al.*, 2012), and that the reliability of polarity-dependent effects of stimulation, on both neural and behavioural levels, deserves to be investigated in more depth in future studies. That being said, the similarity between the effects of anodal and cathodal stimulation does not modify the meaning of the findings obtained by the present study, clearly indicating that the pre-SMA is likely to play a key role in the processing of IB. The pre-SMA seems therefore to give a crucial contribution to our feelings of being agents of our own actions. Indeed, inhibition of this area leads to a ‘weakening’ of IB, which may be interpreted as a decreased sense of control or agency. Moreover, our data support the view of distinct mechanisms underlying action and effect binding (Wolpe *et al.*, 2013). Perturbation of pre-SMA indeed alters only action binding, maintaining unchanged the effect binding: this peculiarity seems to keep participants more focused on their voluntary actions, ignoring however the produced sensory effect. Being more focused on the voluntary action itself, without considering the produced effects, suggests that SoA might be decreased. The present data could also be discussed in light of the theories underlying the IB process, which demonstrated that action binding, unlike effect binding, is supported by a 'cue integration theory' (Wolpe *et al.*, 2013). In detail, estimation of time of action depends on an integration of two separate cues: the action and the sensory effect. The final estimate is then a weighted average, where the weight given to each cue depends on its reliability. In the absence of a sensory effect the perception of an action relies more on internal volitional signals, reducing therefore the action binding. On the other hand, unreliable information about the action event would lead to an over-reliance on its sensory effect and therefore increased binding of action. In our specific case, we found a reduced action binding even if its effect was present. It could be possible that participants, who tended to concentrate only on their voluntary actions, behaved as if no sensory effect existed, reducing the shift of the action towards the effect. Effect binding, on the other hand, seems to depend on a more general association process, namely the "pre-activation mechanism" (Waszak *et al.*, 2012). According to this, the neural representation of a predicted sensory event is activated prior to its occurrence: when the sensory event occurs, the perceptual threshold is reached faster than when there is no pre-activation.

The present study adds several novelties to the study of SoA, using IB as implicit measures. This is the first study attempting to elucidate its neural bases by using tDCS. Two previous studies, using different neuroimaging methodologies (fMRI: Kühn *et al.*, 2013; EEG: Jo *et al.*, 2014), have investigated neural correlates and brain dynamics characterising IB, suggesting that the SMC could be a key brain region involved in this phenomenon. However, despite having put the bases for an initial understanding of the neural correlates of IB, these techniques do not enable a clear and definite comprehension of the role of SMC in the IB because they can only provide information correlative in nature. To our knowledge, only one study tried to provide evidence for a causal involvement of the pre-SMA to the IB, adopting TMS (Moore *et al.*, 2010a). Using somatosensory feedback, Moore *et al.* (2010a) targeted two areas thought to be involved in the cognitive aspects of internal movement generation and the sensory feedback: the pre-SMA and the sensorimotor area (SMHA), respectively. They found that TMS over the pre-SMA significantly reduced IB whereas no evidence was found for the involvement of SMHA in the phenomenon.

We decided to use tDCS for reasons relevant for both experimental research and clinical applications. As regard the first aspect, unlike neuroimaging methods this technique is able to demonstrate a causal link between a given stimulated area and a given behavioural effect (hypothesised to be mediated by that area). In addition, by using tDCS it is easier to conduct placebo stimulation-controlled studies as sham stimulation initially produces sensations similar to those produced by real stimulation without inducing changes in cortical excitability, a condition which is difficult to achieve with TMS because of methodological problems. As regards the clinical side, tDCS can be successfully used in this domain by virtue of the promising advantages it offers for the rehabilitation (e.g., more easily tolerated by participants, less expensive and potentially portable), especially when compared with other neurostimulation tools (Nitsche *et al.*, 2008).

Using tDCS we were able not only to replicate, but also to extend, the results obtained by Moore *et al.* (2010a). As the authors previously found, we showed that modulation of pre-SMA reduces IB, with no direct contribution of the area which processes the effects of the action (the PAC in our study and the SMHA in Moore *et al.*, 2010a). The confirmation of these results has relevant consequences on both methodological and theoretical sides. As regards the methodological implications, we were able to corroborate previous findings on IB with a different brain stimulation technique, which is usually described as having a lower spatial resolution than TMS. Similar results obtained with tDCS allow enlargement of the domain of application of the technique itself, which has already also been shown to be a fruitful tool for experimental research in different domains (Penolazzi *et al.*, 2010, 2013, 2014; Foerster *et al.*, 2013; Leow *et al.*, 2014). As regards the theoretical implications, we extended the findings of Moore *et al.* (2010a) in many ways. (i) By adopting a new paradigm we successfully confirmed that pre-SMA contributes to IB (Cavazzana *et al.*, 2014). The replication of the result, by using another paradigm in place of the established method, allows the validation of IB as a strong and reliable phenomenon, thus excluding the possibility that previous results could be somehow strictly dependent on the paradigm *per se*. (ii) In our study the action effects were presented in the auditory modality, unlike in Moore *et al.* (2010a), who investigated the somatosensory modality. Therefore, although we did not directly test the two modalities through the same task, our results probably suggest that the effects of non-invasive brain stimulation on IB can be extended to another sensory domain (i.e., the auditory one). (iii) The present findings enlarge the model proposed by Moore *et al.* (2010a). In that study the authors showed a reduction in effect binding whereas in the present research a behavioural decrement in the action binding was found. This is mainly in line with the fact that the pre-SMA is more involved in awareness and control of voluntary action, supporting action binding and its 'cue integration theory'. (iv) We did not find a contribution of the area implicated in the processing of the sensory effect produced by the action. This result is line with that of Moore *et al.* (2010a); however, as we found it in another sensory modality, it supports the supra-modality power of IB, which is present independently of the type of the sensory feedback. It seems that the perception of the sensory effects in IB does not take place in the specific areas engaged in their processing (i.e., PAC and SMHA). Future studies should try to further verify this hypothesis, stimulating, for example, the whole SMC (both pre-SMA and SMA proper), which isa crucial station for the integration of the incoming sensory information, due to the fact that it indirectly receives sensory afferences from the primary sensory areas (Narayana *et al.*, 2012).

Summing up, overcoming a correlational approach, the present study supports a causal contribution of pre-SMA in the functional genesis of SoA, using tDCS. However, we cannot rule out the possibility that tDCS could also have affected neighbouring regions, anatomically and functionally linked to pre-SMA, and future studies, combining tDCS and neuroimaging techniques, will provide additional critical insights on this issue.

Our findings may have a strong relevance not only for scientists investigating motor, cognitive and neural mechanisms, but also for clinicians working with patients who present an altered awareness of action. For instance, exploring SoA in Parkinson's disease (Moore *et al.*, 2010b) and schizophrenia (Haggard *et al.*, 2003), IB was found to be significantly stronger in patients than in controls. According to these findings, patients would tend to hyper-associate their actions and outcomes and to over-attribute the consequences of their movements to themselves. Based on our findings, showing that the active stimulation over pre-SMA reduced the temporal compression between actions and their effects (i.e., larger values of IB), tDCS might be, therefore, very useful in reducing this tendency in the above pathologies. In other words, tDCS might represent a novel therapeutic tool for those psychiatric and neurological pathologies in which the SoA is disrupted.

Acknowledgments

This study was partially supported by a grant from the Bial Foundation (84/12 to P.S.B). The authors declare no competing financial interests.

Abbreviations

BC, baseline condition; EC, experimental condition; IB, intentional binding; JE, judgment error; mJE, mean JE; PAC, primary auditory cortex; pre-SMA, pre-supplementary motor area; SMC, supplementary motor cortex; SoA, sense of agency; tDCS, transcranial direct current stimulation; TMS, transcranial magnetic stimulation.

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