Brain Stimulation 9 (2016) 372–379

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: www.brainstimjrnl.com

Endogenous Action Selection Processes in Dorsolateral Prefrontal Cortex Contribute to Sense of Agency: A Meta-Analysis of tDCS Studies of 'Intentional Binding'

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ARTICLE INFO

Article history:
Received 2 September 2015
Received in revised form 6 January 2016
Accepted 9 January 2016
Available online 21 January 2016

Keywords:
Sense of agency
Dorsolateral prefrontal cortex
Action selection
Intentional binding
tDCS
Meta-analysis

ABSTRACT

Background: Sense of agency is the experience of being in control of one's own actions and their consequences. The role of frontal cortex in this aspect of action control and awareness remains unclear.
Objective/hypothesis: Given the role of dorsolateral prefrontal cortex (DLPFC) in action selection, we predicted that DLPFC may contribute to sense of agency when participants select between multiple actions.
Methods: We performed a series of experiments by manipulating a range of task parameters related to action selection and action outcomes while participants were exposed to tDCS stimulation of the left DLPFC. We measured the temporal association between a voluntary action and its outcome using the intentional binding effect, as an implicit measure of sense of agency.
Results: Fixed-effect meta-analysis of our primary data showed a trend towards a frontal tDCS, together with considerable heterogeneity between our experiments. Classifying the experiments into subsets of studies, according to whether participants *endogenously* selected between alternative actions or not, explained 71% of this heterogeneity. Anodal stimulation of DLPFC increased the temporal binding of actions towards tones in the subset of studies involving endogenous action selection, but not in the other studies.
Conclusions: DLPFC may contribute to sense of agency when participants selected between multiple actions. This enhanced feeling of control over voluntary actions could be related to the observed therapeutic effects of frontal tDCS in depression.

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Introduction

Performing a voluntary action that produces an intended outcome is accompanied by a characteristic subjective experience, referred to as 'sense of agency'. Sense of agency is a fundamental feature of normal human mental life [1]. Indeed, many neurological and psychiatric disorders involve deficits in sense of agency [2], most notably the positive symptoms of schizophrenia [3].

The neural basis of the sense of agency is poorly understood. Previous neuroimaging studies used explicit agency attribution tasks. Farrer and colleagues found activation of angular gyrus (AG) for reduced or absent sense of agency [4–6] using such paradigms.

However, experiences of agency occur even when no explicit judgement occurs [7]. The perceived temporal interval between a voluntary action and sensory outcome is a potential implicit measure of this experience [8,9]. The perceived times of voluntary actions and their outcomes are attracted toward each other, compared to both involuntary movements, and for sensory events not involving voluntary action [10].

Transcranial direct current stimulation (tDCS) is a form of non-invasive brain stimulation that delivers weak electric current to the brain. It is known to modify the neuronal excitability of the targeted brain region. Notably, anodal stimulation of primary motor cortex increases corticospinal excitability, while cathodal stimulation decreases it [11]. We recently investigated the contributions of parietal and frontal areas to sense of agency [12] by combining tDCS and intentional binding. Anodal stimulation of the left AG reduced intentional binding, in three separate experiments. We suggested that AG may generate experience of agency by monitoring the linkage of actions to outcomes. However, the possible role of frontal cortex is less clear. In one experiment, we found that anodal stimulation of the dorsolateral prefrontal cortex (DLPFC) had a much weaker effect on intentional binding.

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http://dx.doi.org/10.1016/j.brs.2016.01.005

DLPFC has been identified as key area in selection and monitoring of voluntary action [13,14]. Previous studies of intentional binding focused primarily on medial frontal cortex (MFC) [15,16]. The division of labour between these two centres in voluntary action remains unclear, but the DLPFC may be related to selection [17], while the MFC related to the 'urge' or motivation to act [18].

Here we focused on tDCS of the DLPFC. Given the previous evidence, we predicted that DLPFC may contribute to sense of agency when participants select between multiple actions. We designed several independent experiments to test whether DLPFC tDCS would alter intentional binding in the context of: endogenously selected actions with different outcome identities (Exp. 1), endogenously selected actions converging on the same outcome identity (Exp. 2), rule-based endogenously selected actions with different outcome identities (Exp. 3), endogenously selected actions with different outcome values (Exp. 4), exogenously-instructed actions converging on a single outcome (Exp. 5), and endogenously selected actions with uncertain outcomes (Exp. 6). For purposes of meta-analysis, we also included our previously-published result [11], involving endogenous initiation of a single action, producing a single outcome, in which we refer to as dataset 7.

We predicted that left DLPFC tDCS would modulate intentional binding relative to a sham control condition. The overall aim of the series of experiments was to identify if and how the DLPFC might contribute to agency by investigating a specific experimental condition in each experiment.

Material and methods

Participants

In total 100 healthy volunteers, aged 18–35 years of age, were recruited from the Institute of Cognitive Neuroscience subject data pool for six separate experiments. No other experiment was performed involving these conditions or measures. All participants were right handed, had normal or corrected to normal vision, had no history or family history of seizure, epilepsy or any neurologic or psychiatric disorder and did not have any metallic or electronic object in the head. Participants affirmed that they had not participated in any other brain stimulation experiment in the last 48 h, nor had consumed alcohol in the last 24 h. Experimental design and procedure were approved by the UCL research ethics committee and followed the principles of the Declaration of Helsinki.

Behavioural task

The intentional binding paradigm was used as an implicit measure of sense of agency across our experiments [8]. Briefly, in each experimental session, participants looked at a clock hand rotating on a computer screen (viewing distance: 60 cm). The initial clock position was random. Clock rotation was initiated by participants pressing the return key on a keyboard. Each full rotation lasted 2560 ms. Participants were instructed to look at the centre of the clock and to make time judgement according to the condition. Each condition was presented in a separate and randomised block. Brief instructions were displayed on the screen before each condition. In the two action conditions, participants had to press a key on the keyboard at a time of their own free choice. This key press either produced a tone after 250 ms (*operant action*) or produced no sensory outcome (*baseline action*). The clock hand stopped after 1500–2500 ms (at random), and participants then judged the clock hand position at the time of their key press, entering their response on the keyboard. For the *baseline tone* condition, participants were instructed to look at the clock but not to press any key. While the clock was rotating, a pure tone (based on the experiment) was played over a loudspeaker, 1750–4000 ms (at random) after the onset of the trial. Participants were then asked to judge the clock hand position at the time of the tone. Finally, the *operant tone* condition was similar to the *operant action* condition, with the difference that participants had to judge the clock hand position at the time of the tone and not the key press. All four conditions were done by all participants, except experiments 1 and 6, which only involved action binding, and so tested only baseline action and operant action conditions.

This common basic design was modified according to the specific requirements of each experiment (Table 1; see also supplementary material).

tDCS procedure

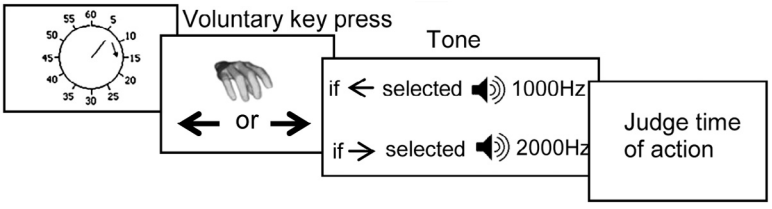
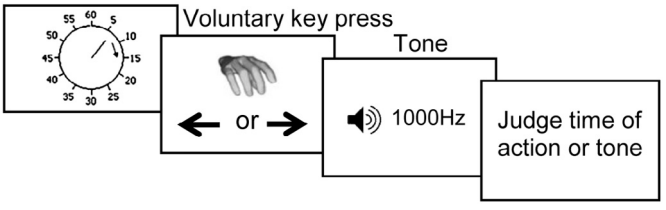
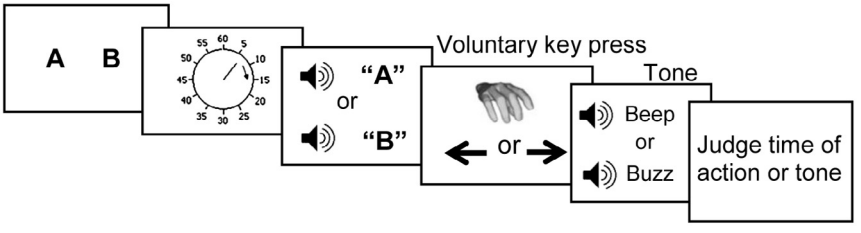
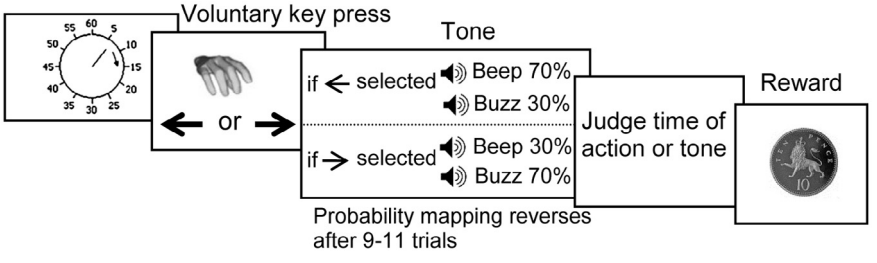
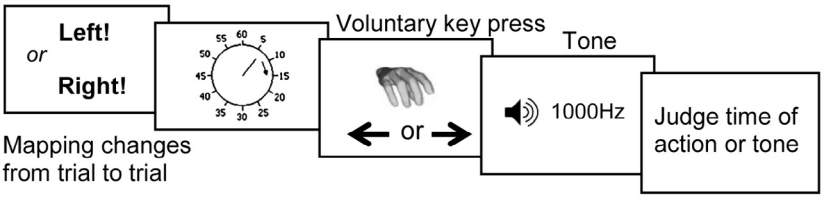
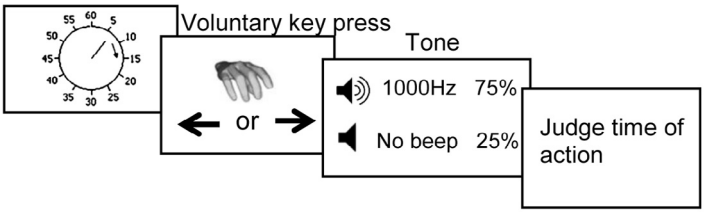
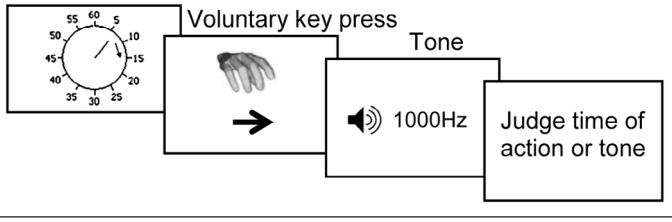
Direct current stimulation was delivered by StarStim noninvasive wireless neurostimulator (Neuroelectrics, Barcelona, Spain). Circular rubber electrodes (25 cm^2) were covered in saline-soaked sponges, installed in a neoprene cap, and connected to a Neuroelectrics Instrument Controller (NIC v1.2). Current strength was set at 1 mA in all experiments, generating a current density of .04 mA/cm^2 at the scalp surface. A common tDCS montage was used for all six experiments. For anodal stimulation of the left DLPFC, anodal electrode was placed on F3 (according to the 10/20 international EEG electrode placement) and cathodal electrode on right supraorbital area. This arrangement was reversed for the cathodal stimulation of left DLPFC. For sham stimulation the anode or cathode were randomly placed at F3.

For experiments 2–5, all participants underwent anode and sham stimulation in separate sessions. An additional session of cathodal stimulation was added to experiments 1 and 6 (Table 1). The order of the sessions was randomised and counterbalanced across participants. To minimise any potential carry-over effect, there was at least 48 hr gap between each stimulation session [19]. Stimulation in each session lasted 25 minutes, including 30 s to ramp-up and down the stimulating current. For the sham condition, electrical current was only applied during the first and last 30 s of the stimulation, so as to induce the same cutaneous sensation as real stimulation, and thus blind the participants as to stimulation condition. During the first 5 minutes of stimulation, participants sat relaxed with eyes closed. This delay was designed to allow potential neuro-modulatory effects to build up [20]. Next, participants began the behavioural task while stimulation continued. All participants finished the behavioural task within around 20 min, coincident with the end of stimulation. In case participants finished the task prior to the end of stimulation, they were asked to remain seated until the end of the stimulation. In case the task outlasted the stimulation, they continued to perform the task without further stimulation. The task period never exceeded the stimulation period by more than 2 min. No adverse effect of stimulation was reported by the participants other than mild tingling sensation.

Data analysis

For each condition a judgement error was calculated as the difference between judged and actual clock time. The averaged judgement error across trials was then calculated for each condition. 'Action binding' was defined as the difference between the mean judgement error in the operant action and the baseline action conditions. A positive value represents perceptual shift of the action towards its outcome. 'Tone binding' was defined as the difference between the judgement error in operant tone and baseline tone conditions. A negative value of tone binding represents the perceptual shift of outcome towards its action.

Table 1
Experimental designs, tDCS montage and dependent variables of experiments 1–6 and dataset 7.

Experiment	Design	tDCS montage conditions	Dependent variables
Exp. 1 *Endogenously selected actions* *Different outcome identities*		Anode Cathode Sham	Action binding
Exp. 2 *Endogenously selected actions* *Same outcome identity*		Anode Sham	Action binding Tone binding
Exp. 3 *Rule-based endogenously selected actions* *Different outcome identities*		Anode Sham	Action binding Tone binding
Exp. 4 *Endogenously selected actions* *Different outcome values*		Anode Sham	Action binding Tone binding
Exp. 5 *Exogenously selected actions* *Same outcome identity*		Anode Sham	Action binding Tone binding
Exp. 6 *Endogenously selected actions* *Uncertain outcomes*		Anode Cathode Sham	Action binding
Dataset 7 *Fixed action* *Fixed outcome*		Anode Sham	Action binding Tone binding

One-way repeated measure ANOVA and paired-samples t-test were used for comparisons within each experiment (anode and/or cathode vs. sham).

We used two statistical methods to investigate commonality across experiments. First, we performed meta-analyses using both fixed effects and random effects models [21]. The analysis followed the steps described by Lipsey and Wilson [22] and made use of freely-available software for plotting [23]. Effect sizes were calculated using Cohen's d_{av}, with Hedges' correction for sample size biases (Hedges's g_{av}) [24]. This measure is recommended for within-subjects designs, because of its ready compatibility with other more familiar between-subject effect size measures, and because alternative effect size measures such as g_{rm} can be overconservative when observations are highly correlated across conditions [24]. To investigate the heterogeneity between our experiments, we both calculated the Cochran's Q test statistic, and we also quantified degree of inconsistency using the established I^2 measure [25].

Finally, we also pooled data across experiments and used a mixed design ANOVA with the within subject factor of stimulation and the between subject fixed-effect factor of experiment.

Results

The overall picture emerging from individual experiments is complex, with some experiments producing a significant result, and others not. The individual results are presented in supplementary material and are summarised in Table 2. The experiments were not direct replications, since the behavioural paradigms and stimulation conditions included varied between experiments. However, anodal and sham stimulation of the left DLPFC were common conditions, and action binding was a common dependent variable, in all seven experiments. We did not perform any other experiments involving these conditions and measures. Therefore, we had a large dataset, free from publication bias, in which we could investigate the following series of research questions:

1. Is there an overall effect of DLPFC tDCS on action binding?
2. Is there heterogeneity between our experiments that cannot be explained by chance alone?
3. If there is heterogeneity, is there a plausible classification of the experiments into subsets of studies that can explain the heterogeneity?
4. Is there a significant effect of frontal tDCS within each such subset?

Meta-analysis of laboratory interventions are rare [26,27] and have received less statistical attention than clinical trials – a point to which we will return in the discussion.

Two methodological points about our meta-analysis require specific mention. First, we performed both fixed-effects and random-effects analyses. Whether fixed or random-effects analyses are more appropriate remains controversial and has not been systematically explored for laboratory experiments, particularly for cases where heterogeneity between subsets of studies may be present [26,28]. We return to this point in discussion.

Second, meta-analyses are much more common for between-subject designs than for within-subject designs, reflecting the traditional association between meta-analysis and clinical trials. The effect size for a within-subject design can be calculated from the difference scores between the two conditions of interest, whereas the effect size for between-subject designs is based on estimates of variability in each of the two conditions. Meta-analyses of within-subject studies often report effect sizes based on between-subject effect sizes [24,26], for comparability with other meta-analyses, and because information about variability of difference scores is rarely given explicitly in published reports of within-subjects designs. If the variability in each condition of a within-subjects design is largely due to factors common to all conditions, such as individual differences in personality, task performance etc., then the variability of difference scores may be substantially lower than the pooled variance of each experimental condition. In that case, using a between-subject method of calculating error variance would underestimate the true within-subject effect size. We have used a measure of effect size that has been recommended for within-subjects designs, and uses the average standard deviation of both conditions [24].

The results of the meta-analysis are summarised in Table 3. Regarding our first question of overall effect size, we found a near-significant overall effect of frontal tDCS when using fixed effects, but

Table 2
Experimental results of experiments 1–6 and dataset 7.

Experiment	The effect of anodal stimulation on action binding compared to sham	
Exp. 1 *Endogenously selected actions* *Different outcome identities*	No significant effect	t(15) = 1.27, p = 0.22, g_{av} = 0.31
Exp. 2 *Endogenously selected actions* *Same outcome identity*	Significant increase	t(15) = 2.55, p = 0.02, g_{av} = 0.81
Exp. 3 *Rule-based endogenously selected actions* *Different outcome identities*	Significant increase	t(15) = 2.21, p = 0.04, g_{av} = 0.95
Exp. 4 *Endogenously selected actions* *Different outcome values*	No significant effect	t(15) = 1.11, p = 0.28, g_{av} = 0.19
Exp. 5 *Exogenously selected actions* *Same outcome identity*	No significant effect	t(15) = 0.48, p = 0.63, g_{av} = 0.16
Exp. 6 *Endogenously selected actions* *Uncertain outcomes*	No significant effect	t(17) = –0.24, p = 0.81, g_{av} = –0.07
Dataset 7 *Fixed action* *Fixed outcome*	No significant effect	t(15) = –1.26, p = 0.22, g_{av} = –0.42

Table 3
Meta-analysis of the experimental results, presented separately for fixed and random effect models. Significant results are presented in bold.

Research question	Analysis model	Effect size/test statistic
Is there an overall effect of stimulation?	Fixed effects	Mean (se) gav = 0.25 (0.13) z-test = 1.84, p = 0.06 95% CI = [–0.02 0.51]
	Random effects	Mean (se) gav = 0.26 (0.18) z-test = 1.45, p = 0.15 95% CI = [–0.09 0.61]
Is there heterogeneity among experiments?	Fixed effects	**I^2 = 44% (moderate heterogeneity)** **Q_{Total} (6) = 10.66, p < 0.1**
	Random effects	I^2 = 1% (negligible heterogeneity) Q_{Total} (6) = 6.05, p > 0.1
Is there a convincing subset of studies where an effect is present? *Grouping based on action selection*	Fixed effects	**$I^2_{Between}$ = 71% (high heterogeneity)** **$Q_{Between}$ (1) = 3.47, p < 0.1**
	Random effects	$I^2_{Between}$ = 50% (moderate heterogeneity) $Q_{Between}$ (1) = 2.00, p > 0.1

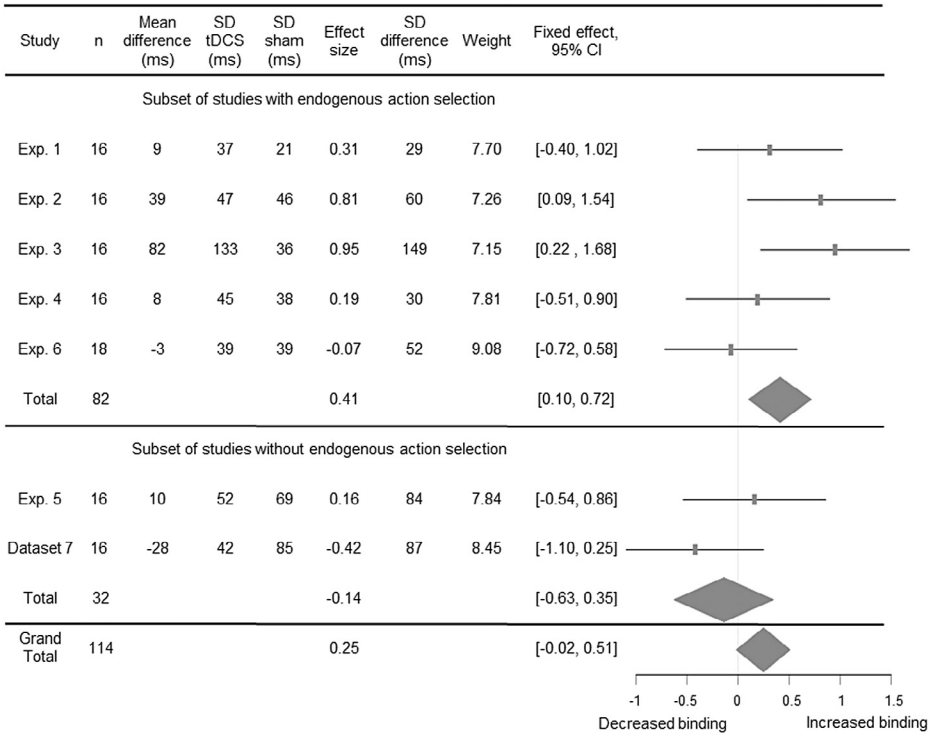


Figure 1. Forest plot comparing subsets of studies with and without endogenous action selection.

not random effects analysis. Thus, we found a trend for frontal tDCS to influence our measure of sense of agency.

Regarding our second research question of heterogeneity, we used the established I^2 measure to estimate the variability among effect sizes that could not be explained by chance. This amounted to 44% (moderate heterogeneity [25]) under the fixed effects model. Because we purposely designed the experiments with different behavioural paradigms, some heterogeneity is expected a priori. Nevertheless, we also applied the conventional Cochrane's Q test, and confirmed presence of heterogeneity under the fixed effects model, but not the random effects model. Note that we used the recommended significance level of 0.1 for the Q test, rather than the conventional 0.05, given the acknowledgedly conservative nature of the test [29].

Where heterogeneity exists, the Q test can also be used to identify potential subsets of studies that have a common pattern of results, since heterogeneity should be high between subsets, but low within. Based on previous literature [17], we hypothesised that DLPFC stimulation might influence action binding differently when participants themselves select between alternative actions (experiments 1, 2, 3, 4, 6), compared to when they did not (experiment 5, dataset 7). This subsetting of studies explained a high (71%) proportion of the variability between experiments and revealed a significant difference between experiments with and without endogenous action selection (Table 3 and Fig. 1). Importantly, within the action selection subset, we found a highly significant effect of stimulation (mean (se) $g_{av} = 0.41(0.16)$, z-test = 2.56, p = 0.01, 95% CI = [0.10 0.72]) with low and non-significant heterogeneity ($I^2_{Subset} = 31\%$, $Q_{SubsetTotal}(4) = 5.79$, $p > 0.1$). In the subset of experiments lacking action selection, we found no effect of stimulation (mean (se) $g_{av} = -0.14(0.25)$, z-test = –0.57, p = 0.57, 95% CI = [–0.63 0.35]).

Unusually for a meta-analysis, we had ready access to the original data, not just effect sizes. We therefore also conducted a mixed effects ANOVA across the 114 participants, using a within-subject factor of the stimulation (anode vs. sham) and a between-subject factor of experiment (7 levels, Exp. 1–6 + dataset 7), with experiment as a fixed effect. We found no significant main effect of experiment ($F(6,107) = 0.88$, $p = 0.51$, $\eta 2 = 0.05$), but a significant overall increase in action binding with stimulation ($F(1,107) = 5.13$, $p = 0.03$, $\eta 2 = 0.05$), and a significant interaction between the stimulation and experiment ($F(6,107) = 3.09$, $p < 0.01$, $\eta 2 = 0.15$) (Fig. 2).

We conducted a further ANOVA, collecting the experiments into the subsets of studies identified by meta-analysis. This showed no significant main effect of stimulation ($F(1,112) = 1.06$, $p = 0.30$, $\eta 2 = 0.01$) nor of subsets ($F(1,112) = 0.48$, $p = 0.50$, $\eta 2 < 0.01$), but a significant interaction between the stimulation and the subsets ($F(1,112) = 4.10$, $p = 0.04$, $\eta 2 = 0.04$). Anodal stimulation increased action binding within the endogenous action-selection subset of studies ($t(81) = 2.93$, $p < 0.01$, $g_{av} = 0.47$), but not in the other subset ($t(31) = -0.56$, $p = 0.58$, $g_{av} = -0.13$).

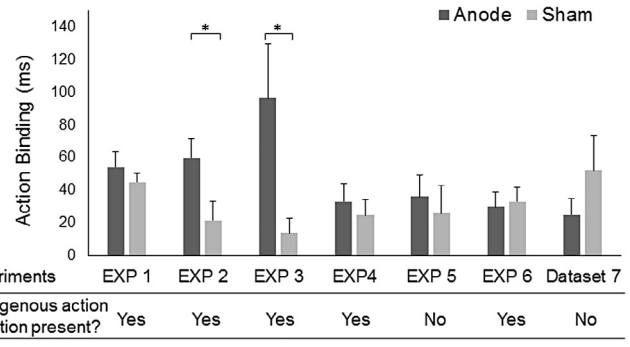


Figure 2. The effect of anodal stimulation of the left DLPFC on action binding in each of seven studies. Error bars show standard error of the mean. *p < .05.

Discussion

Effect of anodal stimulation of DLPFC on action binding: a meta-analytic approach

DLPFC is routinely activated in studies of human voluntary action [13], particularly when a strong action selection component is present [17]. Moreover, a recent study involving explicit agency judgement found that when action selection was facilitated by compatible primes, the DLPFC influenced sense of agency over outcomes, through its connectivity with angular gyrus [30]. Our previous neurostimulation experiment found some evidence in support of the involvement of lateral frontal areas in sense of agency [12]. However, that task lacked any action selection component. To further explore the contribution of DLPFC to sense of agency, we performed a series of tDCS experiments, altering task parameters related to action selection and action outcome, and measuring the temporal association between a voluntary action and its outcome, as an implicit measure of sense of agency.

In a series of experiments, participants were asked to endogenously select an action from two action alternatives. Actions were then followed by a sensory outcome (tone) of different identities (Exp. 1 and 3), same identity (Exp. 2), different outcome values (Exp. 4), or uncertain outcomes (Exp. 6). In other experiments, participants were explicitly told which action to choose (Exp. 5) or had no alternatives (dataset 7). Primary analysis of individual experiments showed that anodal stimulation of the left DLPFC sometimes increased action binding but sometimes did not. We then used meta-analysis to investigate the results across the several experiments.

Fixed effects meta-analysis confirmed moderate heterogeneity among studies. Classifying studies into subsets, according to presence or absence of endogenous action selection, explained 71% of the variability across the experiments. Within the subset of experiments involving action selection, anodal tDCS significantly increased action binding compared to sham. We conclude that anodal stimulation may have a modest (mean $g_{av} = 0.41$) facilitatory effect on a component of intentional binding related to selection between alternative voluntary actions. Thus, our meta-analysis suggests a causal role of frontal action selection signals in prospective sense of agency. A similar suggestion was made previously in the context of a neuroimaging study using explicit agency judgements [30]. Our result provides the first evidence using neurostimulation and implicit measures.

DLPFC, action selection, and sense of agency

Few causal studies have investigated the neural correlates of agency and those focused primarily on medial frontal cortex. Direct stimulation of medial frontal cortex in neurosurgical patients can induce an experience of volition ("urge to move") [31]. In contrast, stimulation of lateral frontal cortex produced movements without any subjective experience of urge [32], though the stimulation sites were largely posterior to DLPFC.

Three studies have reported neurostimulation effects on sense of agency over outcomes. One study combined a choice reaction-task with single pulse TMS stimulation of the inferior parietal cortex (IPC), or the DLPFC, or sham stimulation [33]. Participants made explicit judgements of control over action outcomes. There was no main effect of TMS on judgements of control, but stimulation of IPC at the time of action selection reduced the influence on judgements of compatible vs. incompatible subliminal primes preceding the instructional cue. The absence of any significant effect of DLPFC TMS may seem inconsistent with the present results. However, in that task, the action selection was direct and exogenous. In contrast, in our experiments, action selection always involved some endogenous element, such as learning to identify a 'correct' response, or an indirect cue–action mapping requiring a working memory component. Two other studies focused on medial frontal areas. A cTBS virtual lesion study of pre-supplementary motor area (pre-SMA) was shown to reduce effect binding, but not action binding, in a task where participants could make only a single action, but chose the time at which to do so [16]. Finally, a recent tDCS experiment [34] combined intentional binding with stimulation of pre-SMA. Those authors found reduced action binding, but not effect binding, again in a task that lacked action selection.

Limitations

We always placed the return (cathode) electrode on the right supraorbital area. Although this montage is common in tDCS studies of prefrontal areas [35], it involves a high current density close to the right frontopolar area. Hence, we cannot completely rule out effects of right cathodal frontopolar stimulation. However, we think this alternative interpretation is unlikely for a number of reasons. First, a recent review found that cathodal stimulation has only weak effects on cognitive (as opposed to motor) measures [36]. Second, in previous experiments focusing on the parietal contribution to sense of agency, we found strong effects of parietal anodal stimulation, both with cathode placed over the right supraorbital area or placed elsewhere [12]. Third, an overview of studies of anodal left DLPFC studies shows effects both with supraorbital and other cathodal locations, including left mastoid [37] and Cz [38]. Thus, while we cannot strictly rule out a right frontopolar cathodal effect, we favour an interpretation based on a left DLPFC anodal effect.

Meta-analytic methods originated in the context of clinical trials and do not transfer straightforwardly to experimental settings. In the 'ideal' clinical trial case, meta-analysis would include several large studies all using a common intervention, on comparable populations, and with a single outcome measure. In contrast, the neurostimulation literature typically provides many low-powered studies. Variations in equipment, electrode placement, and experimenter technique may influence effect size [39]. Finally, the neurostimulation literature is probably strongly affected by publication bias.

Fixed effects models assume that all studies share a common true effect size, while random effects models assume that the true effect sizes may vary across studies [21]. Previous meta-analyses of cognitive effects of tDCS argued in favour of fixed-effects models [40], on the grounds that the intervention was a uniform and precisely-quantified intervention. In contrast, random-effects meta-analyses are often used in systematic reviews of clinical trials to address likely but uncontrolled variation across trials, including factors such as differences in protocol, trial setting, etc. In our case, we varied the details of the cognitive task, and therefore might *expect* our intervention to have varying effects. However, our experimental designs followed the classic logic of cognitive neuropsychology, in which a task involves a particular combination of cognitive processes, each implemented by a specific functional circuit within the brain, which is targeted by tDCS. Finally, combining a fixed-effects model with heterogeneity analysis may seem paradoxical, since the former assumes a common effect, while the latter looks for variability. However, since the meta-analysis aims to identifying possible subsets of studies, the assumption of a single true effect size would be warranted *within each subset*. Here, we identified a subset of agency tasks involving endogenous selection between alternatives, for which DLPFC stimulation increased sense of agency. This result fits well with the neurocognitive theory of localisation of function [41] and is consistent with the role for DLPFC in both action selection [17]

and prospective agency [30]. Other meta-analytic approaches have also been proposed to address such research questions. In particular, clinical trial and policy meta-analyses often favour random-effects meta-regression, using covariates to identify heterogeneity and possible subsets. However, these methods are not recommended when fewer than ten studies are available [42].

The effect of anodal stimulation on action binding was not observed in every experiment, even within the subset of studies involving endogenous action selection. In the fixed-effects statistical model, the measured effects combine both the "true" effect, and measurement error. Measurement error may thus explain why not all individual studies showed the significant effect found in the subset of action selection studies. Indeed, estimating the true effect size, independent of measurement error, is one explicit aim of meta-analysis. Furthermore, our studies differed in other aspects, such as outcome identity and value, in addition to the common feature of endogenous action selection. We cannot exclude the possibility that left anodal DLPFC stimulation might also have some influence on other cognitive processes involved in some of the experiments – and this could partly explain the varied effect of stimulation on action selection subset of studies. In this vein, we also applied similar meta-analytic analyses of heterogeneity to investigate whether stimulation effects depended on the nature of action outcomes in our data. These analyses did not reveal any significant pattern in the results. However, small additional effects, related to cognitive processes other than action selection, might still be present in some individual experiments.

Conclusions

We performed a series of experiments to test whether we can interfere with sense of agency in the context of action selection by combining frontal tDCS with an implicit measure of sense of agency based on mental chronometry. Anodal stimulation of DLPFC increased binding of actions towards outcomes, but only in tasks where participants endogenously selected between alternative actions. One previous behavioural study noted a relation between action selection and intentional binding [43], but the underlying neural basis remained unclear. Our result has important implications for the sense of agency. In particular, it seems incompatible with a strongly reconstructionist view that people infer agency from the mere conjunction of action execution and sensory outcomes [44]. Rather, neural processes in DLPFC of selecting *which action* to make, which necessarily precede action initiation, make a prospective contribution to sense of agency. A recent meta-analysis on the efficacy of tDCS in the treatment of depression indicated that anodal stimulation of left DLPFC was superior to sham tDCS [45]. Depression and sense of agency may be related. We speculate that clinical benefits in depression could be related to increased feeling that one's decisions and actions can make a difference – an enhanced sense of agency. Finally, we note that the size of our effect is modest and that no established statistical analysis plan exists for meta-analysing laboratory intervention studies. Our approach was based on fixed effect meta-analysis and used heterogeneity analysis to identify subsets of studies, as a means of identifying the specific cognitive processes in DLPFC that contribute to sense of agency. We hope that this article will trigger future methodological developments in using meta-analysis of neurostimulation data to localise cognitive functions in the human brain.

Acknowledgements

This work was supported by the European Research Council Advanced Grant HUMVOL (Grant number: 323943). PH was additionally supported by a Professorial Research Fellowship from the ESRC (grant number ES/J023140/1). The funding sources had no involvement, in study design; in the collection, analysis or interpretation of data; in the writing of the report; or in the decision to submit the article for publication. We are grateful to Prof. Chris McManus for comments.

Appendix: Supplementary material

Supplementary data to this article can be found online at doi:10.1016/j.brs.2016.01.005.

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