Counteracting Implicit Conflicts by Electrical Inhibition of the Prefrontal Cortex

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Abstract

■ Cognitive conflicts and distractions by task-irrelevant information often counteract effective and goal-directed behaviors. In some cases, conflicting information can even emerge implicitly, without an overt distractor, by the automatic activation of mental representations. For instance, during number processing, magnitude information automatically elicits spatial associations resembling a mental number line. This spatial–numerical association of response codes (SNARC) effect can modulate cognitive-behavioral performance but is also highly flexible and context-dependent, which points toward a critical involvement of working memory functions. Transcranial direct current stimulation to the PFC, in turn, has been effective in modulating working memory-related cognitive performance. In a series of experiments, we here demonstrate that decreasing activity of the left PFC by cathodal transcranial direct current stimulation consistently and specifically eliminates implicit cognitive conflicts based on the SNARC effect, but explicit conflicts based on visuospatial distraction remain unaffected. This dissociation is polarity-specific and appears unrelated to functional magnitude processing as classified by regular numerical distance effects. These data demonstrate a causal involvement of the left PFC in implicit cognitive conflicts based on the automatic activation of spatial–numerical processing. Corroborating the critical interaction of brain stimulation and neurocognitive functions, our findings suggest that distraction from goal-directed behavior by automatic activation of implicit, task-irrelevant information can be blocked by the inhibition of prefrontal activity. ■

INTRODUCTION

Automatic activation of task-irrelevant and potentially distracting cognitive processes often counteracts effective behavior by blurring attentional and memory resources and luring cognitive processes into the wrong direction. This can happen implicitly, hence without an external stimulus feature directly prompting such processing. A classic example for an implicit cognitive conflict is the spatial association of numbers. Here, although ubiquitous number symbols traditionally convey objective information about the external world, implicit spatial information is automatically activated during number processing (Cipora, Patro, & Nuerk, 2015; Gevers, Lammertyn, Notebaert, Verguts, & Fias, 2006), following left-to-right spatial activations with ascending number magnitude (the SNARC [spatial–numerical association of response codes] effect; Wood, Willmes, Nuerk, & Fischer, 2008; Dehaene, Bossini, & Giraux, 1993). These spatial–numerical associations can systematically bias overt behaviors such as lateral turns during walking (Shaki & Fischer, 2014) and fair action decisions (Schroeder & Pfister, 2015).

The functional implications of space–number associations are currently controversially discussed: SNARC is sometimes assumed to precede number processing in general (e.g., Rugani, Vallortigara, Priftis, & Regolin, 2015). In contrast, other studies either failed to find correlations between SNARC effects and mathematical ability in human adults (Cipora & Nuerk, 2013; for a review, see Cipora, Patro, et al., 2015) or even suggested that professional mathematicians exhibit diminished rather than increased SNARC effects relative to less mathematically trained participants (Cipora, Hohol, et al., 2015; Hoffmann, Mussolin, Martin, & Schiltz, 2014). Regarding its cognitive foundations, it has been suggested that space–number associations are driven by flexible ordinality representations of the current number set in serial order working memory (WM; van Dijck, Abrahamse, Acar, Ketels, & Fias, 2014; van Dijck & Fias, 2011), possibly emphasized by cultural learning (Patro, Nuerk, Cress, & Haman, 2014; Shaki, Fischer, & Petrusic, 2009). The established neurophysiological view on the representation of number magnitude and its association with space highlights specifically the contribution of parietal areas (Cutini, Scarpa, Scatturin, Dell'Acqua, & Zorzi, 2014; Krause, Lindemann, Toni, & Bekkering, 2014; Cohen Kadosh & Walsh, 2009; Cohen Kadosh, Cohen Kadosh, Kaas, Henik, & Goebel, 2007; Dehaene, Piazza, Pinel, & Cohen, 2003; Fias, Lammertyn,

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Reynvoet, Dupont, & Orban, 2003). Only recently, however, studies indicated that prefrontal contributions to advanced numerical cognition might be essential (Klein et al., 2014; Arsalidou & Taylor, 2011), especially in terms of frontoparietal circuits (Nieder, 2016; Rusconi, Dervinis, Verbruggen, & Chambers, 2013; Göbel, Johansen-Berg, Behrens, & Rushworth, 2004). Similarly, numeric interval bisection critically deviated in individuals with prefrontal damage (Doricchi, Guariglia, Gasparini, & Tomaiuolo, 2005). This corresponds with the idea that WM functions are involved in seemingly basic spatial–numerical processes (van Dijck et al., 2014; van Dijck & Fias, 2011). Yet, the underlying neurophysiological foundations for implicit spatial–numerical conflicts are not resolved.

Empirically, the claim that WM is critically involved in the SNARC effect was motivated from the observations that (i) items (i.e., random numbers) at the beginning of a WM list are responded to more quickly with left rather than right responses, with the reversed pattern for items from the end of a WM list. This pattern suggests links between the sequential positions—not necessarily the numerical magnitude—in WM and spatial left–right response codes (van Dijck & Fias, 2011). Furthermore, (ii) concurrent WM load from maintenance of nonnumerical visuospatial or phonological information disrupted SNARC (van Dijck, Gevers, & Fias, 2009; Herrera, Macizo, & Semenza, 2008). Thus, it was suggested that the common left-to-right spatial–numerical alignment is supported by WM functions maintaining a magnitude-ordered number sequence in SNARC tasks, as opposed to a long-term mental number line representation. Indirectly, these considerations postulate that prefrontal activity may guide the ties between space and number. Critically, however, it is now well established that PFC activities corroborate rather broad sets of cognitive functions that could draw on WM, for example, as maintenance of internal and possibly distributed representations (D'Esposito & Postle, 2015), but also on cognitive control functions such as conflict detection and inhibition (Egner & Hirsch, 2005; Botvinick, Cohen, & Carter, 2004; Miller & Cohen, 2001). In SNARC, comparable to other conflict tasks, spatial–numerical associations can activate a spatial response incompatible with a task rule, thus prefrontal control is required to inhibit incongruent activations and select the appropriate action. By experimentally modulating PFC activity during corresponding tasks, the neurophysiological underpinnings of these viewpoints can be investigated.

Building on the idea that mental associations between numbers and space are guided by a WM-related mechanism, we here tested their susceptibility to a noninvasive neuromodulation technique previously used to alter WM performance, while also controlling for online performance on externally available spatial conflicts. In this study, we administered transcranial direct current stimulation (tDCS) to the left PFC during SNARC and explicit spatial stimulus–response conflict tasks. Particularly anodal, activity-increasing tDCS is known to enhance WM (Fregni

et al., 2005; for a review on WM modulations with this montage, see Brunoni & Vanderhasselt, 2014) and other PFC-related processes (Schroeder, Ehlis, Wolkenstein, Fallgatter, & Plewnia, 2015; Dockery, Hueckel-Weng, Birbaumer, & Plewnia, 2009). Conversely, cathodal, activity-decreasing tDCS has been shown to impair PFC functions including WM (Wolkenstein, Zeiller, Kanske, & Plewnia, 2014; Zaehle, Sandmann, Thorne, Jäncke, & Herrmann, 2011). However, a simple dichotomy of beneficial anodal and detrimental cathodal tDCS does not account for the complexity of interactions between cognitive processes, brain activity, and stimulation effects (Plewnia, Schroeder, & Wolkenstein, 2015; Jacobson, Koslowsky, & Lavidor, 2012). Furthermore, distal and network effects can accompany any stimulation that originally targeted PFC. Such effects may lead to a modulation also of parietal sites, for instance, via frontoparietal connectivity and/or inhibitory pathways.

Rather, the critical interplay between modulations of cortical excitability and task-induced activity allows for causal inferences regarding the functional involvement of brain regions that might also include remote and interconnected circuits (Fertonani & Miniussi, 2016). To assess the specificity of this task-dependent interplay, we tested the effect of concurrent cathodal or anodal tDCS to the left PFC on a spatial–numerical SNARC conflict and on a nonnumerical Simon conflict (Hommel, 2011; Simon & Rudell, 1967) as control. Both tasks afford the suppression of either implicitly associated or sensory available spatial information, respectively, and might be mediated by similar mechanisms, that is, spatial attention (Notebaert, Gevers, Verguts, & Fias, 2006; Mapelli, Rusconi, & Umiltà, 2003) and cognitive control (Pfister, Schroeder, & Kunde, 2013; Notebaert et al., 2006). Regarding conflict-related processes, a nonspecific modulation of both effects can be expected with larger conflicts during PFC attenuation by cathodal tDCS. Following the evidence that spatial and numerical processing predominantly recruits parietal areas, Simon and SNARC conflict effects should be unaffected by PFC stimulation. However, following the idea that WM is causally involved in linking numbers with space, tDCS should specifically affect the SNARC effect while leaving intact perceptual spatial response conflicts.

Notably, both tasks are not direct tests of WM functioning. Rather, we utilize the modulation by tDCS to test the consequences of a general conflict resolution or a specific WM function implying frontal and/or frontoparietal involvements differentially in the two tasks. Also, in a nonspatial IAT task, anodal tDCS was already demonstrated to increase an implicit association bias by accelerating responses to congruently paired categories (Gladwin, den Uyl, & Wiers, 2012). With this study, we aimed at shedding light on the role of PFC in forming implicit spatial–numerical associations during number judgments.

More precisely, from the previous proposal of WM involvement in SNARC (van Dijck & Fias, 2011), we hypothesized cathodal, inhibitory tDCS to impede automatic

space–number associations and to thus reduce behavioral conflicts by task-irrelevant implicit spatial information in a parity judgment (Experiment 1) and a magnitude judgment task (Experiment 2). Therefore, a task-specific effect of inhibitory PFC stimulation should occur, but neither spatial information processing nor magnitude processing by itself should be modulated. Finally, by administering anodal tDCS in Experiment 3, we aimed at exposing the polarity specificity of this neuromodulatory effect.

METHODS

Participants

Seventy-two healthy volunteers (17 men, mean age = 23.9 years, range = 18–42 years) were recruited in total, with 24 new participants for each of the three experiments. Each individual participated in two experimental sessions on separate days. Participants were consistently right-handed (Edinburgh Handedness Inventory; Oldfield, 1971; $LI > 75$) and scored without pathological findings in preceding screenings for psychiatric disorders and dyschromatopsia (Ishihara, 1917). Further exclusion criteria were as follows: age < 18 years, epilepsy, neurological disorders, pregnancy, metallic implants, and pacemakers. Participants signed an informed consent as reviewed by the ethics commission of the University Hospital Tübingen (approval ID: 215/2014BO2) and received € 20 or course credit as compensation.

Transcranial Direct Current Stimulation

Direct current was generated by a CE-certified stimulator (DC-STIMULATOR MC, NeuroConn, Ilmenau, Germany) and delivered with a pair of identical $5 \times 7\ cm^2$ rubber electrodes covered with adhesive paste (10/20 conductive EEG paste, Kappamedical, Prescott, AZ). Stimulation lasted 25 min (including a 5-min pretask idle time) with a current of 1 mA, resulting in a current density of 0.028 mA/cm², and impedances were below 10 kΩ. Stimulation was faded in and out with a 5-sec ramp. For participants of Experiments 1 and 2, the cathode electrode was placed over the left PFC (F3 according to the 10–20 EEG system of electrode placement) and fastened with a bathing cap. The reference/anode electrode was placed extracranially on the contralateral upper arm to avoid an opposite polarization of another brain area and thus ensure that tDCS effects could be traced back exclusively to stimulation of the left PFC (Wolkenstein & Plewnia, 2013). For participants of Experiment 3, active and reference electrode polarity were exchanged (anode: F3, cathode: upper arm). Both tasks were initiated and completed during active tDCS. Sham stimulation current was faded out after 40 sec of stimulation (4:20 min before the beginning of the first task) and accordingly the tasks were initiated and completed without active tDCS. Verum and sham

sessions were run on separate days, and stimulation order was counterbalanced across participants.

Procedure

All experiments followed a sham-controlled crossover design. Participants were seated in front of a 17-in. monitor with 60-cm distance to the screen and all stimuli appeared at a size of 2.0° as implemented in PsychoPy software (Peirce, 2007). All sessions consisted of one practice and three test blocks for each of the two tasks. Stimulation sequence (sham/verum) and task order (Simon/SNARC) were counterbalanced across participants, but a fixed response mapping was determined to keep possible influences of parity or color on spatial decisions constant (Elliot & Maier, 2014; Nuerk, Iversen, & Willmes, 2004). Participants were instructed to respond with a right (left) key press to blue/even (yellow/odd) circle targets or single digits in the respective tasks (Figure 1) and thus had to ignore actual positions on screen or spatial–numerical associations in response-incongruent trials (50% of all trials). Cathodal/sham/anodal tDCS was applied online to the task to the left PFC (see Figure 1C for a computational model of the stimulation effect; Jung, Kim, & Im, 2013). After 5 min of (sham) stimulation, onscreen instructions signaled the beginning of the first experimental task.

Both parity judgment (Experiments 1 and 3) and magnitude judgment (Experiment 2) SNARC tasks comprised single-digit targets 1–9 except 5. In the Simon task,
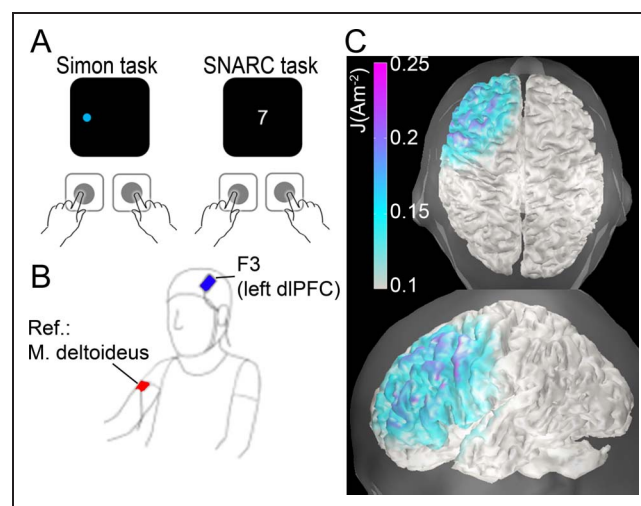

Figure 1. Experimental tasks and electrode montage. (A) Participants judged colors (Simon task) and digit parity (Experiments 1 and 3) or digit magnitude (Experiment 2; SNARC tasks) by index finger key presses. (B) The active tDCS electrode (cathode) was placed over the left PFC (F3), and the reference electrode (anode) was placed on the contralateral upper arm to avoid an opposite polarization of another cortical region (Zwissler et al., 2014; Wolkenstein & Plewnia, 2013). Electrode positions were interchanged for Experiment 3. (C) Current density distribution as modeled using the COMETS toolbox (Jung et al., 2013).

participants judged circle colors (blue vs. yellow) and had to ignore circle locations (distance from central fixation: −4°, −2°, 2°, and 4°). Via onscreen instructions, mapping rules and short encouragements to react correctly as fast as possible were provided and repeated in each short break between the blocks. Additional instructions announced the second experimental task and provided the new task rules. Parity, magnitude, and color judgments were given with the left or right index finger on identically marked keys "s" and "l" of a standard German QWERTZ keyboard, yielding an interkey distance of 11.6 cm.

Trials started with a short central fixation (+; 300 msec), followed by a centrally presented white digit in the SNARC tasks or a laterally shifted colored circle in the Simon task. All stimuli were presented equally often in randomized order. Incorrect or late responses (>2000 msec) triggered immediate feedback in form of the German words "Fehler" (Eng. "error") or "Bitte schneller antworten!" (Eng. "please respond faster!") for 500 msec. An additional blank intertrial interval of 300 msec ended each trial. Responses were regarded congruent (incongruent) if a left (right) response was given to a leftward positioned circle or a digit <5, and vice versa. Each experimental block contained 40 congruent and 40 incongruent trials, and an error count was provided in each break between blocks.

Questionnaires

We assessed participants' mood pre- and poststimulation by the PANAS questionnaire (Watson, Clark, & Tellegen, 1988), adverse effects of tDCS (cf. Brunoni et al., 2011), and blinding efficacy (sham vs. verum stimulation guesses) in all sessions.

Data Treatment

Trials with errors and trials following errors were excluded from the analyses (5.5%; cf. Rabbitt, 1979), as were stimulus repetition trials (6.4%; cf. Pfister et al., 2013; Tan & Dixon, 2011). Outlier trials with RTs differing more than 2.5 standard deviations from the mean RT of the corresponding design cell were omitted (1.7%). These criteria left 86.4% of all trials for the analyses. Mean RTs and error rates from the SNARC and Simon tasks were submitted to separate 2 (Congruency$_{congruent,incongruent}$) × 2 (Stimulation$_{cathodal,sham}$) repeated-measures ANOVAs, followed up by paired t tests.

RESULTS

Experiment 1

We tested 24 right-handed participants (mean age = 24.2 years, SD = 4.4 years, 3 men) during sham and cathodal tDCS on a color judgment Simon task and a parity judgment SNARC task. Mean RTs for both tasks and stimulation conditions are depicted in Figure 2 (leftmost panel). For the SNARC task, a significant main effect of Congruency$_{congruent,incongruent}$ emerged, $F(1, 23)$ = 5.68, p = .026, η_p^2 = 0.20, signaling reliable SNARC effects. Importantly, the two-way interaction of Congruency$_{congruent,incongruent}$ and Stimulation$_{cathodal,sham}$ was significant, $F(1, 23)$ = 9.42, p = .005, η_p^2 = 0.29, whereas the main effect of Stimulation$_{cathodal,sham}$ was not
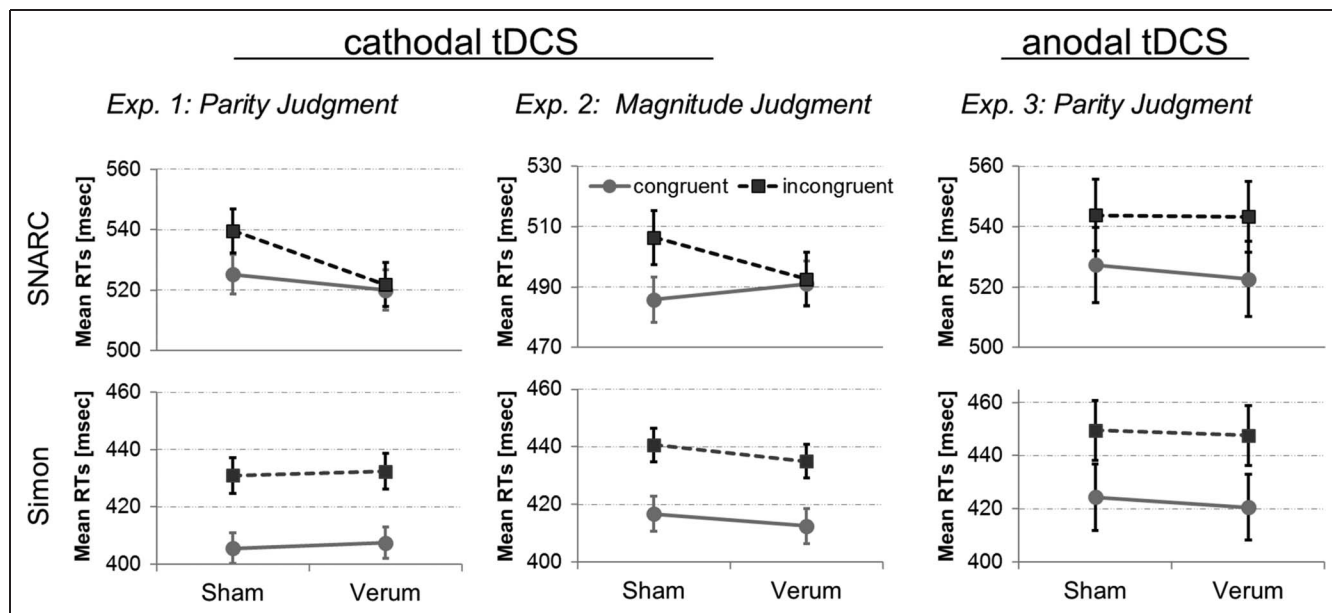

Figure 2. Specific modulation of implicit conflicts by cathodal tDCS. Mean RTs of congruent and incongruent SNARC and Simon trials in verum and sham stimulation conditions of the three experiments. Error bars indicate standard errors of paired differences (Pfister & Janczyk, 2013). During cathodal (Experiments 1 and 2) or anodal tDCS (Experiment 3), participants judged single digits by their parity (odd or even) or magnitude (<5 or >5; SNARC tasks) and laterally shifted circles by their color (Simon task).

significant, $F(1, 23) = 2.72, p = .11$. Follow-up paired t tests confirmed that responses were significantly faster during cathodal stimulation (compared with sham stimulation) in incongruent SNARC trials, $t(23) = 2.33, p = .029, d = 0.49$, but not in congruent SNARC trials, $t(23) = 0.75, p = .46$.

For the control Simon task, a reliable main effect of Congruency$_{congruent,incongruent}$ emerged, $F(1, 23) = 99.93, p < .001, \eta_p^2 = 0.81$, signaling reliable Simon effects. However, neither the main effect of Stimulation$_{cathodal,sham}$, $F(1, 23) = 0.08, p = .77$, nor the two-way interaction approached significance, $F(1, 23) = 0.01, p = .91$, suggesting that the tDCS modulation was specific to incongruent SNARC trials. By subjecting the data from both tasks to another repeated-measures ANOVA, this hypothesis was substantiated in terms of a significant three-way interaction of Task$_{SNARC,SIMON}$, Congruency$_{congruent,incongruent}$, and Stimulation$_{cathodal,sham}$: $F(1, 23) = 8.12, p = .009, \eta_p^2 = 0.26$.

In error rates, the 2×2 ANOVAs again showed the main effect of Congruency$_{congruent,incongruent}$ to be significant for the SNARC task, $F(1, 23) = 6.82, p = .016, \eta_p^2 = .23$, and for the Simon task, $F(1, 23) = 16.67, p < .001, \eta_p^2 = .42$. In contrast to RTs, the Stimulation$_{cathodal,sham} \times$ Congruency$_{congruent,incongruent}$ interaction in the SNARC task was not significant, $F(1, 23) = 0.90, p = .35$, and neither was the main effect of Stimulation$_{cathodal,sham}$, $F(1, 23) = 2.20, p = .15$. The same picture emerged for the Simon task, ps > .40.

Experiment 2: Magnitude Judgment

To delineate the relevance of magnitude processing for the formation of the stimulation effect and to cross-validate our results, another group of 24 participants (mean age = 22.8 years, $SD = 4.6$ years, 7 men) was asked to make explicit magnitude judgments in the SNARC task. Experimental design and the control Simon task were identical to Experiment 1. In the magnitude judgment task, two blocks of each 240 trials were completed by all participants and the response mapping order (i.e., congruent, left hand [incongruent, right hand] response for digits <5 in the first block) was counter-balanced across participants but held constant for the two sessions.

Resembling the data of Experiment 1, a significant two-way interaction of Congruency$_{congruent,incongruent}$ and Stimulation$_{cathodal,sham}$ emerged for the SNARC task, $F(1, 23) = 10.58, p = .004, \eta_p^2 = 0.32$, but not for the Simon task, $F(1, 23) = 0.19, p = .66$ (Figure 2, center panel). Again, task specificity was tested with data from both tasks, which yielded a significant three-way interaction of Task$_{SNARC,SIMON}$, Congruency$_{congruent,incongruent}$, and Stimulation$_{cathodal,sham}$, $F(1, 23) = 7.85, p = .010, \eta_p^2 = 0.26$. Importantly, although the stimulation-driven response acceleration in SNARC-incongruent trials was not significant, $t(23) = 1.54, p = .14$, SNARC effects (i.e., the RT difference between congruent and incongruent trials) did not differ

significantly from zero during cathodal tDCS, $t(23) = 0.32, p = .75$, but SNARC effects were pronounced during sham tDCS, $t(23) = 3.06, p < .01, d = 0.62$. Again, error rates were not affected by the stimulation, all ps > .83, which implies that effective magnitude comparison (for instance, correct retrieval of magnitude facts) was not eliminated by PFC down-regulation.

Numerical Distance Effect

Unrelated to the resolution of cognitive conflicts, the difficulty (and, consequently, mean response latency) of a magnitude judgment decreases with the numerical distance between the two compared digits (Moyer & Landauer, 1967). Reflecting the analogue nature of magnitude representations, numerical distance effects are not necessarily linked to a spatial mapping (Bonato, Zorzi, & Umiltà, 2012) and diverge from SNARC effects (Nuerk, Bauer, Krummenacher, Heller, & Willmes, 2005). Moreover, although distance effects draw on activations in the intraparietal sulcus, they might also be related to general response selection processes (Göbel et al., 2004) as required throughout our tasks. However, if numerical magnitude processing per se was affected by the stimulation, the numerical distance effect should also appear modified. We therefore extracted congruency-independent RTs for individual target digit distances from the reference digit "5" ($|distance| = 1, 2, 3,$ or 4) from both stimulation sessions separately and tested for modulatory effects in a 2 (Stimulation$_{cathodal,sham}$) $\times$ 4 (Distance$_{1,2,3,4}$) ANOVA (cf. Holloway & Ansari, 2009). As indicated by Figure 3A, reliable distance effects emerged during both sham and cathodal stimulation and gave rise to a significant main effect of Distance$_{1,2,3,4}$, $F(3, 69) = 42.53, p < .001, \eta_p^2 = 0.65$. However, neither the main effect of Stimulation$_{cathodal,sham}$, $F(1, 23) = 0.34, p = .57$, nor the interaction term approached significance, $F(3, 69) = 0.28, p = .84$.

These findings indicate that the modulation of SNARC effects by PFC stimulation observed in Experiments 1 and 2 was not driven by altered magnitude processing, but the modulation was exclusively related to the emergence of (and distraction by) spatial–numerical associations.

Experiment 3: Polarity Specificity

Finally, we repeated Experiment 1 with a new group of 24 participants (mean age = 24.7 years, $SD = 5.1$ years, 7 men) and administered 1 mA anodal, activity enhancing tDCS to the left PFC to test whether the previous results were polarity-specific (Figure 2, rightmost panel). Following our previous findings, we now predicted a task-specific increase in spatial–numerical conflicts from anodal tDCS relative to sham stimulation.

A main effect of Congruency$_{congruent,incongruent}$ signaled reliable SNARC effects, $F(1, 23) = 11.16, p = .003, \eta_p^2 = 0.33$. However, we neither obtained a significant main effect of Stimulation$_{anodal,sham}$, $F(1, 23) = 0.57, p = .814$
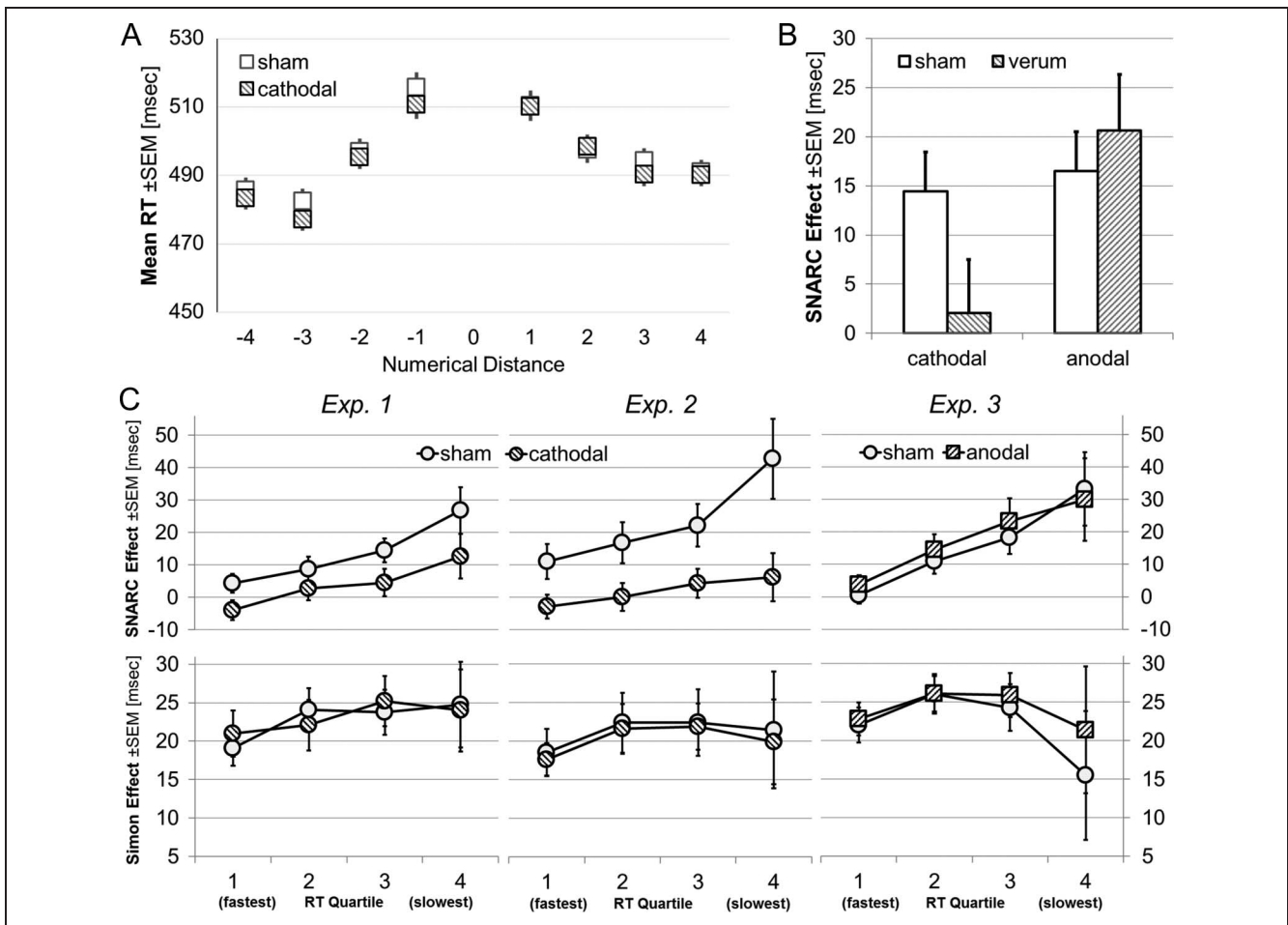
Figure 3. Numerical distance effect, polarity specificity and time-course analysis. Regular numerical distance effects (A) emerged in Experiment 2 and independent of tDCS. (B) Polarity-specific modulation of SNARC effects in parity judgment. (C) Time-course analyses of SNARC and Simon conflict effects. A modulation by cathodal tDCS was already observed for the fastest SNARC trials, but not for the slowest Simon trials.

nor a two-way interaction, $F(1, 23) = 2.18$, $p = .153$. As with cathodal stimulation, there were no significant stimulation effects on Simon conflict nor in error rates, $ps > .28$. Thus, although descriptively a slight increase in SNARC was observed (see Figure 3B), the effect of anodal stimulation alone was not significant.

To resolve the differential effects of cathodal and anodal tDCS on SNARC, we next directly compared the results of Experiments 1 and 3 in a between-experiment analysis. The ANOVA on the SNARC task comprised the within-subject factors Stimulation$_{verum,sham}$ and Congruency$_{congruent,incongruent}$ as well as the between-experiment factor Polarity$_{anodal,cathodal}$. A significant interaction of Stimulation$_{verum,sham}$, Congruency$_{congruent,incongruent}$, and Polarity$_{anodal,cathodal}$ emerged, $F(1, 46) = 10.86$, $p = .002$, $\eta_p^2 = 0.19$, which substantiates our polarity specificity hypothesis.

Joint Analyses: Time Course of Conflict Effects

Because it is conceivable that tDCS effects could have emerged on the basis of overall prolonged responses, we evaluated the effect functions of both tasks (with conflict effects defined as the RT difference between incongruent and congruent trials) by a quantile analysis and split the RT data individually into four equally large quartiles of participants' response speed. If the stimulation effect was due to the current time on task, a tDCS modulation of both SNARC and Simon effect functions should emerge for prolonged responses only.

As illustrated in Figure 3C, the task-specific impact of tDCS on the SNARC effect was not particularly modulated by response speed as quantified by the quartile split (and there were no significant interactions, $ps > .34$). Interestingly, the magnitude of sham SNARC, at the same time, increased with prolonged responses ($ps < .04$), in line with previous findings (Gevers et al., 2006). Importantly, and in both experiments employing cathodal stimulation, a significant tDCS effect emerged already in the fastest SNARC trials that also contained the smallest conflict sizes at sham (Experiment 1: $t(23) = 2.44$, $p = .023$, $d = 0.56$; Experiment 2: $t(23) = 3.00$, $p = .006$, $d = 0.60$). In contrast, no significant effect was detected for the slowest Simon trials (Experiment 1: $t(23) = 0.12$, $p = .91$; Experiment 2: $t(23) = 0.19$, $p = .85$). For these two quartiles

Table 1. TDCS Adverse Effects

Sensation	Verum tDCS, M (SD)	Sham tDCS, M (SD)	p
Tingling at the site of the electrode	2.90 (1.19)	2.34 (1.17)	.001
Tingling elsewhere	1.33 (0.68)	1.18 (0.49)	.16
Exhaustion	1.68 (0.88)	1.39 (0.77)	.007
Itching	2.04 (1.20)	1.64 (0.96)	.003
Headache	1.30 (0.58)	1.28 (0.64)	.73
Nausea	1.07 (0.31)	1.00 (0.00)	.058

Adverse sensations were assessed on a 5-point Likert-like scale after each session (1 = *none*, 5 = *extensive*). Ratings from the two sessions were subjected to paired t tests. There were no main effect nor interactions between experiments ($ps > .21$), thus collapsed data are presented.

of the respective tasks, mean RTs in the SNARC task (Experiment 1: 443 msec; Experiment 2: 420 msec) were faster than mean RTs in the Simon task (Experiment 1: 507 msec; Experiment 2: 520 msec), all $ps < .001$, which renders unlikely that the modulation depended on response speed or within-task conflict strength.

Adverse Effects and Blinding Efficacy

Participants experienced weak sensations of tingling and exhaustion in both sham and verum stimulation sessions (Table 1). There were no significant differences between the experiments (all $ps > .21$), but the main effect of tDCS on adverse effects ratings was highly significant, $F(1, 66) = 20.79$, $p < .001$, $\eta_p^2 = 0.24$. Blinding guesses did not exceed chance level: In the first session, 57% guesses were correct, $\chi^2(1, N = 72) = 1.39$, $p = .24$. In the second session, 61% guesses were correct, $\chi^2(1, N = 71) = 3.17$, $p = .08$. Participants' mood (as quantified by the PANAS questionnaire; Watson et al., 1988) was not significantly altered after anodal or cathodal versus sham stimulation, $ps > .41$.

DISCUSSION

The results of our experiments outline a polarity-specific and task-dependent elimination of interference from implicit cognitive conflicts by concurrent PFC inhibitory tDCS. Specifically, parity as well as magnitude judgments were no longer affected by task-irrelevant but distracting space–number associations during cathodal tDCS, whereas such implicit cognitive conflicts emerged during sham and anodal tDCS. In contrast, the distracting influence of externally available visuospatial information in the Simon task affected task performance in all stimulation conditions (for comparable results, see Zmigrod, Zmigrod, & Hommel, 2016).

Of note, significant numerical distance effects that indicate typical magnitude representations remained unaffected throughout Experiment 2. Functionally, this result indicates that the concurrently abolished intrinsic spatial property of number—be it as maintenance in WM or recall from parietal sites—is not required for simple comparisons of numerical magnitudes, an interpretation corroborated by the reduced SNARC in professional mathematicians (Cipora, Patro, et al., 2015) and by observations of magnitude-based effects in absence of magnitude–space associations (Nuerk et al., 2005). It is further consistent with the idea that magnitude processing precedes spatial mappings in a separable step (Santens & Gevers, 2008; Gevers, Verguts, Reynvoet, Caessens, & Fias, 2006), possibly along a hierarchical frontoparietal pathway (Nieder, 2016). Therefore, these findings point toward a specific suppression of implicit dysfunctional spatial–numerical information by PFC down-regulation, but not of effective magnitude representations. In turn, our results underline the necessity of prefrontal activity for implicit conflict generation in case of the SNARC effect and thus corroborate the significant role of prefrontal activity for space–number associations.

Nevertheless, alternative physiological effects have to be considered (Tremblay et al., 2014; Nitsche et al., 2008): Instead of inducing a focal PFC activity decrease, cathodal tDCS could have down-regulated a frontoparietal number network including PFC and relevant parietal cortex areas, for example, intraparietal sulcus (Klein et al., 2014; Eger, Sterzer, Russ, Giraud, & Kleinschmidt, 2003). Via PFC-parietal intercommunication, the observed stimulation effect could also partly draw on parietal representations, for instance in form of an enhanced number fact retrieval from relevant parietal sites (Smirni, Turriziani, Mangano, Cipolotti, & Oliveri, 2015; Klein, Moeller, Glauche, Weiller, & Willmes, 2013; Dehaene et al., 2003). As for the latter, cathodal stimulation has been attributed a noise filter function before (Miniussi, Harris, & Ruzzoli, 2013) that allowed more effective distinctions between target and flanker or lure stimuli (Zwissler et al., 2014; Weiss, Lavidor, O'Neil, & Adamson, 2012). Seeing the flexible emergence of SNARC also observed from different context manipulations (Fischer, Mills, & Shaki, 2010; Bächtold, Baumüller, & Brugger, 1998), slight membrane threshold modulations by tDCS might have just blocked the jittery and task-irrelevant spatial–numerical signal chain. Considering also that pure (and task-relevant) magnitude processing as indicated by the numerical distance effect necessarily recruits parietal areas, as outlined by recent rTMS and tDCS studies (Klein, Mann, et al., 2013; Cappelletti, Barth, & Spelke, 2008), attributing the stimulation effect to a down-regulation of PFC efficiency seems the most parsimonious mechanism, albeit not the only one possible. In future studies, concurrent imaging methods (i.e., NIRS and/or tES-EEG) could be used to investigate network effect activation changes by focal stimulations, that is, at parietal sites. By relating

our results to previous behavioral studies and including further theoretical accounts, we propose attributing the stimulation effect to the neurocognitive downregulation of WM efficiency.

Functional Implications of PFC in Number Processing

Currently, PFC involvement in numerical cognition is integrated in corresponding neurocognitive models (Klein et al., 2014; Arsalidou & Taylor, 2011), emphasizing its relevance for arithmetic performance. For instance, in children with mathematical disabilities, increased prefrontal activation, among parietal and occipitotemporal cortex activation, was observed during arithmetic problem solving and traced back to hyperconnectivity of several networks, including frontoparietal hyperconnectivity (Rosenberg-Lee et al., 2015). Also, children with mild traumatic brain injury displayed specific arithmetic difficulties associated with visual WM deficits (Van Beek, Ghesquière, Lagae, & De Smedt, 2015). Moreover, using noninvasive brain stimulation, it has been demonstrated that the administration of excitatory anodal tDCS (Cohen Kadosh, Soskic, Iuculano, Kanai, & Walsh, 2010) and transcranial random noise stimulation to the bilateral PFC during arithmetic training improved learning effects (Snowball et al., 2013).

Although both learning paradigms and advanced arithmetic competencies thus point to prefrontal involvement in numerical cognition in general, our study highlights a critical role of prefrontal circuits in the very basics of number representation and spatial–numerical processing. Our experimental design allows for specific conclusions regarding the underlying cognitive mechanisms that produced differential effects of tDCS on SNARC and Simon conflicts. Previous studies dissociated slightly different posterior parietal processing pathways for these types of conflict (Rusconi, Turatto, & Umiltà, 2007), as well as different time courses and a lack of additivity of the two conflict effects (Mapelli et al., 2003). Yet, different regional activations can still be explained by a common dual-route architecture with abstract spatial representations on an intermediate layer (Gevers & Notebaert, 2008; Gevers, Caessens, & Fias, 2005). Functionally, it appears consistent with a framework in which prefrontal cathodal tDCS blocks the emergence, maintenance, or recall of an abstract spatial code, resulting in the observed reduction of interference with response selection processes. Nevertheless, in both tasks, suppression of distracting spatial content by a cognitive control mechanism is required to respond correctly. So, if cognitive control in general had been impaired by cathodal stimulation of the PFC (Wolkenstein et al., 2014), task performance should have suffered in both the Simon and the SNARC task, leading to generally increased conflict effects. Here, in this respect, tDCS was ineffective, possibly undermined by compen-

satory processes (Pirulli, Fertonani, & Miniussi, 2014) or by the intermediate role of dorsolateral PFC (i.e., as compared with the ACC; Botvinick et al., 2004) during nonemotional conflict processing (i.e., as compared with emotional processing; Plewnia et al., 2015). Similar behavioral results have been obtained from applying tDCS over medial PFC during an Eriksen flanker conflict task, that is, there was no modulation of executive attention from 2 mA anodal tDCS (Coffman, Trumbo, & Clark, 2012).

Do PFC Modulations of SNARC Effects Draw on WM?

To relate our findings to WM, it is essential to conciliate previous behavioral and theoretical results, because it is a broad set of cognitive processes involved in the PFC including but also exceeding WM processes (D'Esposito & Postle, 2015). Specifically, previous work repeatedly demonstrated WM maintenances to corrupt spatial–numerical activations (van Dijck & Fias, 2011; van Dijck et al., 2009; Herrera et al., 2008). Furthermore, by maintaining random number sequences during number judgment tasks, the regular left-to-right SNARC effect was replaced flexibly by the ordinal positions of the exact number sequence kept in mind (van Dijck et al., 2014; van Dijck & Fias, 2011). As these short-term representations were constructed during task execution, it was suggested that ascending order representations of target digit *positions* (and not magnitudes) account for the SNARC effect by drawing on WM maintenance of the existing or artificial ties between number and space. A similar elimination of regular space–number associations occurred in the presented single-task setting. In this framework, the present findings could imply separate functional mechanisms to be disentangled in future research: (1) Participants might fail to adapt to the current task set (though this mechanism is improbable due to the correct maintenance of response mapping), (2) the systematic association of task set stimuli with space might have been corrupted, and/or (3) spatial task set information maintained in WM is blocked from transfer to task-relevant response selection. Although any of these possibilities is in line with a WM account on SNARC, other prefrontal functions could also account for the observed results. Nevertheless, using tDCS, we here demonstrate and replicate that prefrontal activity is critical for distraction by implicit cognitive conflicts based on SNARC.

Consequently, the stimulation was less efficient in modulating the Simon effect, which builds on the sensory processing of externally available spatial information. Here, it should be noted that both effects require WM representations of the response mapping to occur (Ansorge & Wühr, 2004). Thus, it would be misleading to consider the observed tDCS effect a complete downregulation of WM. Mitigating our interpretations, it was

not assessed whether other established measures of WM functioning were addressed by the stimulation (but see Wolkenstein et al., 2014; Zaehle et al., 2011; Wager & Smith, 2003). Also, both tasks require spatial information processing; however, spatial information in the SNARC task is not directly available in the external stimulus. Thus, interference with a spatial response in the SNARC effect depends on the internally and automatically generated spatial–numerical code (Gevers, Verguts, et al., 2006) and not on external visuospatial information. Although leaving open to further investigation how exactly the spatial–numerical tie is created by PFC and/or communication networks, our results are also consistent with a WM account of the SNARC effect (i.e., van Dijck & Fias, 2011).

Alternatives to a WM Explanation

Revisiting conflict detection and resolution, one interesting speculation can be drawn from previous findings on the relation of conflict strength and recruitment of PFC (Tsushima, Sasaki, & Watanabe, 2006). More precisely, subthreshold conflicting information does not seem to recruit LPFC as compared with suprathreshold information. Given that the SNARC effect was markedly weaker than the Simon effect in the present experiments (and participants were presumably also less aware of it), the conflicting spatial signals from number representations could similarly fail to recruit prefrontal control mechanisms. Such a perspective may further suggest alternative interpretations of our results that do not necessarily draw on WM and its supposed role in retrieving spatial–numerical associations. For instance, reduced prefrontal noise from cathodal tDCS could improve the detection (and the subsequent resolution) of internal conflict.

Furthermore, the mere fact that the Simon task provoked greater conflict than the SNARC task—that is, as reflected in latency effect size—might mediate its resilience to tDCS. From this idea of a simple quantitative—and not qualitative—difference in conflict strength signals, it can also be predicted that within-task conflict strength differences should modulate stimulation efficacy. For the SNARC effect, it is known that the magnitude of conflict evoked is the higher for greater spatial distances (i.e., "1" and "2" are more strongly associated with "left" than "3" and "4," and so on; $Fs > 8.2$, $ps < .01$). Turning to the stimulation effects observed in our data, however, we did not detect different tDCS effects within the SNARC tasks ($ps > .22$), but—introducing this within-task factor to the corresponding ANOVAs—we were only able to replicate the global SNARC modulations with cathodal tDCS (Experiment 1: $p = .014$; Experiment 2: $p = .004$). This result corresponds to significant stimulation effects throughout the SNARC RT distribution, thus regardless of conflict increases with longer responses. Thus, the current data do not support a view of merely quantitative different conflict signals. Nevertheless, these mentioned

accounts do provide interesting alternatives to the WM-based explanation discussed above, to be tested in confirmatory tasks (i.e., by introducing other subthreshold conflicts and manipulating response compatibility or conflict strength in further stimulation experiments).

Limitations

Further investigations into WM functioning are required to specify the theoretical interpretation and functional implications of our findings. By finding even the fastest SNARC trials to be modulated by tDCS, we can rule out that the stimulation effect was merely driven by prolonged responses. Yet, the rather large tDCS stimulation site (cf. Figure 1C) necessarily comes with a reduced focal specificity, and the observed effects therefore might partially draw on regions such as the frontal junction or (left) FEF (Rusconi, Bueti, Walsh, & Butterworth, 2011). Stimulation of parietal control sites may further amend to the focal specificity of our observed effects and had been effective in the past to modulate magnitude-related processing, which is not necessarily connected to spatial–numerical associations (Sarkar & Cohen Kadosh, 2016; Artemenko, Moeller, Huber, & Klein, 2015; Hauser, Rotzer, Grabner, Mérillat, & Jäncke, 2013; Rusconi et al., 2007). Finally, the established active control from the Simon task and our additional analyses on the numerical distance effect paint a very clear picture of the outlined modulation's specificity.

Overall, verum stimulation triggered more intense sensations of tingling, itching, and exhaustion. Thus, it might be argued that any cognitive effect was due to a sensory experience of the stimulation (i.e., distraction). However, the polarity-specific cognitive effects were not reflected in differential reports on adverse effects in our study, and blinding guesses were not given beyond chance, which eventually underpins the neuromodulatory mechanism as outlined. In fact, anodal tDCS even seemed to pronounce SNARC (see Figure 3B), but here we would like to draw conclusions only from the significant polarity-specific effect as obtained in the between-subject analysis. Because we reproduced SNARC effects in all sham conditions, a ceiling effect possibly restricted additional increases in spatial–numerical activations by anodal tDCS. Finally, although the causal dependence of spatial–numerical associations on prefrontal activity sharply fosters a WM account of SNARC, the exact cognitive mechanisms need to be specified theoretically and empirically in further studies. In our experiments, the perfect correspondence between sequence position and magnitude neither favors linking the abolished SNARC to either of these possibly distinct representations, although the dissociation of SNARC and distance effects requires to consider multiple magnitude representations. For instance, our results leave open whether spatial–numerical activations are due to serial-order task set adaptations (Abrahamse, van Dijck, Majerus, & Fias,

2014; van Dijck et al., 2014) or due to the spatial representation of number retrieved by PFC (i.e., from the angular gyrus; Göbel, Walsh, & Rushworth, 2001).

Conclusions

The task- and polarity-specific elimination of the SNARC effect by cathodal, activity-decreasing tDCS to the left PFC during parity and magnitude judgment (i) demonstrates PFC (network) involvement in the generation of spatial–numerical associations, (ii) suggests a significant and distracting influence of PFC in implicit processing, and (iii) exemplifies that inhibition of dysfunctional processes by cathodal tDCS can improve task performance. These results extend our knowledge on the neural mechanisms and malleability of implicit cognitive conflicts and further expose the complex interactions between non-invasive brain stimulation and cognition. The inhibition of dysfunctional cognitive processes by cathodal tDCS may provide interesting new options for a targeted treatment of neuropsychiatric disorders.

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