Anodal High-definition Transcranial Direct Current Stimulation over the Posterior Parietal Cortex Modulates Approximate Mental Arithmetic

Matthias Hartmann[1,2], Sarah Singer[1], Branislav Savic[1], René M. Müri[1], and Fred W. Mast[1]

Abstract

■ The representation and processing of numerosity is a crucial cognitive capacity. Converging evidence points to the posterior parietal cortex (PPC) as primary "number" region. However, the exact role of the left and right PPC for different types of numerical and arithmetic tasks remains controversial. In this study, we used high-definition transcranial direct current stimulation (HD-tDCS) to further investigate the causal involvement of the PPC during approximative, nonsymbolic mental arithmetic. Eighteen healthy participants received three sessions of anodal HD-tDCS at 1-week intervals in counterbalanced order: left PPC, right PPC, and sham stimulation. Results showed an improved performance during online parietal HD-tDCS (vs. sham) for subtraction problems. Specifically, the general tendency to underestimate the results of subtraction problems (i.e., the "operational momentum effect") was reduced during online parietal HD-tDCS. There was no difference between left and right stimulation. This study thus provides new evidence for a causal involvement of the left and right PPC for approximate nonsymbolic arithmetic and advances the promising use of noninvasive brain stimulation in increasing cognitive functions. ■

INTRODUCTION

The processing of approximate numerosities is a crucial cognitive function for both humans and animals. It allows, for example, to go to the tree that bears the most fruits or leads to the decision about fight or flight when the number of enemies has been estimated (e.g., Wilson, Hauser, & Wrangham, 2001). Given the importance of such a "number sense" for survival and other cognitive functions (Dehaene, 2011), it is no surprise that researchers have tried to reveal its neuronal basis during the last decades. Neurophysiological recordings in the monkey brain revealed that neurons within the posterior parietal and prefrontal cortex are selectively tuned to numerosity (Nieder & Miller, 2004; Nieder, Freedman, & Miller, 2002). Similar numerosity-dependent brain activities have later also been found in the human parietal cortex (Piazza, Izard, Pinel, Le Bihan, & Dehaene, 2004). Since then, evidence has been accumulating that the posterior parietal cortex (PPC), as well as, more specifically, the intraparietal sulcus (IPS), is involved in the processing of numerosity (symbolic and nonsymbolic) and other magnitude-related quantity information (e.g., Bueti & Walsh, 2009).

It has also been argued that higher level cognitive processes, such as symbolic number processing and arithmetic, rely on the innate approximate, nonsymbolic number system, which has been regarded as "neurocognitive start-up tool" for exact numerical cognition (Piazza, 2011). In line with this view, it has been shown that performance in approximate number tasks in children correlates with their school math ability (e.g., Starr, Libertus, & Brannon, 2013; Halberda, Mazzocco, & Feigenson, 2008), and nonsymbolic approximate arithmetic training improves math performance (e.g., Park, Bermudez, Roberts, & Brannon, 2016; Hyde, Khanum, & Spelke, 2014). Despite this evidence, the question whether and to what extent the approximate number system is related to mental arithmetic, as well as the nature of the underlying "number sense," is still debated (e.g., Leibovich, Katzin, Harel, & Henik, 2017; Lindskog & Winman, 2016; Fazio, Bailey, Thompson, & Siegler, 2014). Nonetheless, there is a general agreement that nonsymbolic and symbolic numbers activate shared parietal networks (e.g., Eger et al., 2009; Nieder & Dehaene, 2009; Piazza, Pinel, Le Bihan, & Dehaene, 2007) and that these brain areas are also activated during mental arithmetic (for a meta-analysis, see Arsalidou & Taylor, 2011).

Most of the studies mentioned so far relied on neuroimaging techniques. This approach allows to assess whether certain brain areas are involved in the task at hand but leave open the functional relevance of the activated brain area for the task, which is an important question for the understanding of the brain–behavior relationship. In contrast to neuroimaging, noninvasive

[1]University of Bern, [2]Swiss Distance University Institute

Journal of Cognitive Neuroscience X:Y, pp. 1–15
https://doi.org/10.1162/jocn_a_01514

brain stimulation techniques such as TMS or transcranial direct current stimulation (tDCS) directly interfere with neuronal activity, allowing to study the causal involvement of the stimulated area. Single-pulse (or inhibitory repetitive) TMS "inhibits" the neural activity of the stimulated area, leading to a temporary "virtual brain lesion" in healthy participants. TMS over the PPC impaired performance in both symbolic and nonsymbolic number comparison tasks (Dormal, Andres, & Pesenti, 2008, 2012; Andres, Seron, & Olivier, 2005) and also in mental arithmetic (Montefinese, Turco, Piccione, & Semenza, 2017; Salillas, Semenza, Basso, Vecchi, & Siegal, 2012; Andres, Pelgrims, Michaux, Olivier, & Pesenti, 2011). In contrast to these TMS-induced interference effects, excitatory (anodal) tDCS can lead to an increase in cortical excitability (e.g., Romero Lauro et al., 2014) and consequently boost performance, which could have an important impact on the fields of learning, education, and rehabilitation (see Iuculano & Cohen Kadosh, 2014; Cohen Kadosh, Soskic, Iuculano, Kanai, & Walsh, 2010). There is (limited) evidence for increased performance in symbolic number comparison and exact arithmetic with this technique (Hauser et al., 2016; Artemenko, Moeller, Huber, & Klein, 2015; Grabner, Rütsche, Ruff, & Hauser, 2015; Hauser, Rotzer, Grabner, Mérillat, & Jäncke, 2013; for a minireview, see Schroeder et al., 2017). Moreover, a recent study assessed the enhancing effect of tDCS on symbolic approximate averaging—a specific case of intuitive mental arithmetic (Brezis, Bronfman, Jacoby, Lavidor, & Usher, 2016). In their task, participants were presented with a series of two-digit numbers for which they had to estimate the average without calculating. Brezis et al. (2016) found that participants' estimates were more precise during right parietal anodal tDCS. Numerical averaging involves multiple arithmetic steps (several additions and a division)—thus, it remains unclear why exactly estimates became more precise during parietal stimulation in Brezis et al.'s study.

In this study, we therefore further investigated the functional contribution of the parietal cortex for approximate mental addition and subtraction. Previous fMRI studies showed activity in the IPS during both symbolic and nonsymbolic arithmetic (e.g., Venkatraman, Ansari, & Chee, 2005). We therefore hypothesized that stimulating this target region facilitates approximate mental arithmetic. We used anodal high-definition tDCS (HD-tDCS). HD-tDCS is a new modification of traditional tDCS that uses smaller "high-definition" electrodes (instead of the larger pad electrodes of traditional tDCS), allowing for a more focal stimulation of the target region (Kuo et al., 2013; Datta et al., 2009). We applied HD-tDCS to either the left or right IPS, which allowed us to assess hemispheric specialization, which so far has led to conflicting results. Particularly, some studies found a left hemispheric parietal specialization of number processing and arithmetic (e.g., Hauser et al., 2013; Sasanguie, Göbel, & Reynvoet, 2013; Dormal et al., 2008; Andres et al., 2005; Pesenti, Thioux, Seron, & De Volder, 2000), whereas others found a right hemispheric specialization (e.g., Artemenko et al., 2015; Li et al., 2015; Cohen Kadosh, Bien, & Sack, 2012). Moreover, some studies found a contribution of both the left and right parietal cortex (Artemenko, Soltanlou, Ehlis, Nuerk, & Dresler, 2018; Klein et al., 2013; Salillas et al., 2012; Andres et al., 2011) or operation-dependent hemispheric specialization (e.g., Montefinese et al., 2017; Semenza, Salillas, De Pallegrin, & Della Puppa, 2017; Salillas et al., 2012; Arsalidou & Taylor, 2011; Chochon, Cohen, van de Moortele, & Dehaene, 1999). In the only previous tDCS study on approximate arithmetic, Brezis et al. (2016) applied right-sided stimulation only. Our study will thus be the first brain stimulation study allowing to assess hemispheric specialization for approximate mental arithmetic. Given the mixed findings regarding lateralization of mental arithmetic in general and the absence of brain stimulation studies that specifically compared left and right parietal stimulation for approximate mental arithmetic, we did not specify an a priori hypothesis about differential effects of left and right parietal HD-tDCS.

In contrast to Brezis et al. (2016), we used nonsymbolic stimuli, because it is difficult to study approximate addition and subtraction with number symbols. Particularly, it is difficult for participants to suppress exact calculation strategies even when they are told to perform approximate arithmetic (Venkatraman et al., 2005). The estimation of results from nonsymbolic arithmetic is typically biased in an operation-specific way: Results from addition tend to be overestimated, and those from subtraction tend to be underestimate (McCrink, Dehaene, & Dehaene-Lambertz, 2007). The origin of this so-called "operational momentum" (OM) effect is still unclear (e.g., Knops, Zitzmann, & McCrink, 2013). It has, for example, been hypothesized that the OM effect reflects a "forward bias" when moving along a mental number line during arithmetic (McCrink et al., 2007). Specifically, such a forward bias leads to overestimation of addition results (moving too far toward larger numbers on the number line) and an underestimation of subtraction results (moving too far toward smaller numbers on the number line). However, more recent studies (using a similar task than the one employed in this study) found that results for both addition and subtraction were underestimated, with a stronger underestimation for subtraction (Knops, Dehaene, Berteletti, & Zorzi, 2014; Knops, Viarouge, & Dehaene, 2009). Based on these latter findings, we expected a "relative" OM effect (stronger underestimation for subtraction than for addition) in this study. The hypothesized enhancing effect of parietal HD-tDCS could therefore manifest itself in a reduction of the underestimation of results.

To summarize, we investigated the causal contribution of the left and right parietal cortex by means of HD-tDCS in nonsymbolic approximate mental addition and subtraction. We expected an increase in arithmetic performance during parietal anodal HD-tDCS. This study thus evaluated for the first time a possible enhancing effect of noninvasive brain stimulation for nonsymbolic approximate arithmetic, which has—despite its assumed role as basis for higher numerical cognition—not yet been assessed.

METHODS

Participants

Eighteen healthy participants (eight women, 10 men) took part in this study (mean age = 24.5 years, range = 22–30 years). The number of participants was in the same range than previous brain stimulation studies about numerical cognition (Brezis et al., 2016; Hauser et al., 2013). Participants either received course credit or monetary compensation for their participation. Participants gave written informed consent before the study, and the study was approved by the ethics committee of the University of Bern. All participants confirmed that they had no history of psychiatric and neuronal disorder, did not take any drugs or abused alcohol, and did not suffer from dyscalculia or any other impairment in number processing.

Design

We used a single-blind sham-controlled within-participant design whereby each participant received left parietal, right parietal, and sham stimulation during nonsymbolic approximate addition and subtraction.

Stimuli and Task Procedure

Stimuli were selected and created as in Knops et al. (2009; Experiment 2). Nine different types of solution-matched addition and subtraction problems were used (Table 1). For each problem, eight deviant results were created in addition to the correct result, ranging from half of the correct result to the double of the correct result, linearly spaced on a logarithmic scale. From the

Table 1. Operands and Proposed Results for the 18 Arithmetic Problems

Operands		*Proposed Results (Not Jittered)*								
Op1	*Op2*	*1/2*	*1/1.7*	*1/1.4*	*1/1.2*	*1/1*	*1.2/1*	*1.4/1*	*1.7/1*	*2/1*
						Addition				
14	5	10	11	13	16	**19**	23	27	32	38
14	7	11	12	15	18	**21**	25	30	35	42
14	11	13	15	18	21	**25**	30	35	42	50
28	7	18	21	25	29	**35**	42	49	59	70
28	13	21	24	29	34	**41**	49	58	69	82
28	21	25	29	35	41	**49**	58	69	82	98
56	13	35	41	49	58	**69**	82	98	116	138
56	28	42	50	59	71	**84**	100	119	141	168
56	42	49	58	69	82	**98**	117	139	165	196
						Subtraction				
32	13	10	11	13	16	**19**	23	27	32	38
32	11	11	12	15	18	**21**	25	30	35	42
32	7	13	15	18	21	**25**	30	35	42	50
64	29	18	21	25	29	**35**	42	49	59	70
64	23	21	24	29	34	**41**	49	58	69	82
64	15	25	29	35	41	**49**	58	69	82	98
128	59	35	41	49	58	**69**	82	98	116	138
128	44	42	50	59	71	**84**	100	119	141	168
128	30	49	58	69	82	**98**	117	139	165	196

The actual problems presented to the participants were jittered by a small random amount, so that the correct outcome was never presented. Only seven of the nine possible results were selected, and the 1/1 result was never the middle of the range of the proposed solutions.

resulting nine proposed solutions, only seven were selected for each trial and presented in a circular spatial arrangement (see Figure 1). In half of the trials, the lower range of proposed results was chosen (from 1/2 to 1.4/1), and in the other half, the upper range of proposed results was chosen (from 1/1.4 to 2/1) so that participants could not use a strategy of always selecting the middle of the proposed solutions. Each of the 18 different problems was presented 14 times, resulting in a total of 252 trials. To prevent participants from learning, the problems and their proposed solutions were jittered differently for each trial, so that each of the 14 repetitions of the same problem represented a unique trial. The first operand was jittered by a random value from 0 to ± 2, and the second operand by -1 times the jitter of the first operand, so that the correct result remained unchanged by the jitter of the operands. Moreover, all of the seven proposed results were jittered by the same amount (fixed for a given trial). For each trial, the jitter for the proposed results was selected from a range of $\pm$ half of the numerical interval between the correct result and the first deviant above or below it in a logarithmic space (proposed result $\times\ 2^{(r/i)}$, where r was a random number between -0.5 and $+0.5$ and i was a random number between 0 and 4; see Knops et al., 2009). Thus, the maximum value of the jitter increased as a function of the result size. As in Knops et al. (2009), the jitter for the proposed results was never 0, so that the correct solution would never appear as a response alternative.

Stimuli were created using a custom MATLAB script. For each array, an image file was created with a black circle of 730 $\times$ 730 pixels containing the specified amount of white smaller dots. As in previous studies (Knops et al., 2009, 2014), stimuli were matched for total occupied area of the white dots so that participants could not rely on this visual feature for numerosity estimation. Positions of the white dots were randomly drawn with the restriction that they do not overlap or collapse with the contour of the outer circle.

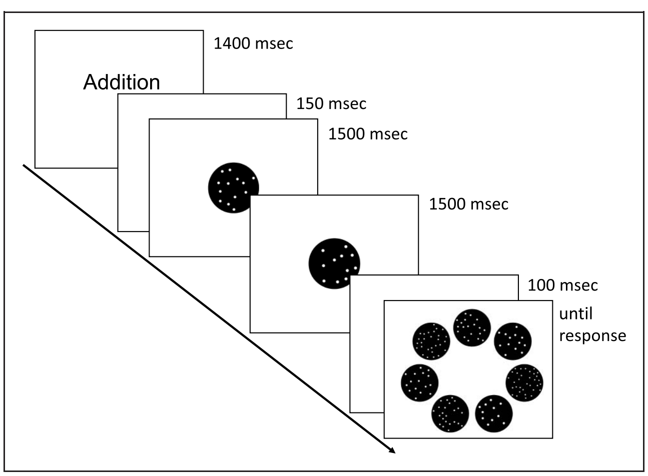

Figure 1. Example of a trial (addition, 14 + 11 = 25; jitter for operands = 0, proposed solutions jittered by −2).

Participants were instructed to estimate as precisely and quickly as possible the outcome of an arithmetic addition or subtraction problem. Participants were informed that they are not supposed to count the dots but rather intuitively select the solution that appears to be most correct. A trial started with the information about the arithmetic operation. The word "addition" or "subtraction" appeared for 1400 msec at the center of the screen (black on a white background). After a short blank screen (150 msec), the first operand appeared at the center of the screen for 1500 msec, immediately followed by the second operand that was also presented for 1500 msec. After another short blank (100 msec), seven possible solutions appeared on the screen in a circular arrangement (see Figure 1). At 1520 msec after the onset of the solution screen, the mouse cursor appeared at the center of the screen, and participants clicked at one of the seven proposed solutions. The delay between solution onset and mouse cursor onset was introduced so that participants view all solutions before they can make a selection. The next trial started 1250 msec after response. An example for a trial (without the blank screens) is illustrated in Figure 1. The operands and the seven proposed solutions had a size of 7 $\times$ 7° of visual angle.

Twelve practice trials were presented at the beginning of the experiment to familiarize participants with the task. The 252 experimental trials were divided into six blocks à 42 trials, separated by a short break. Three blocks were presented during stimulation (online), and the remaining three blocks were presented after stimulation (offline). Experimental trials were presented in random order with the restriction that each of the 18 problems was presented seven times, with the 1/1 proposed result presented once at each of the seven possible positions within each half of the experiment. Three different sets of stimuli were created for the three experimental sessions. In Set 2, stimuli from Set 1 were taken but rotated by 90°, and in Set 3 by 180°, so that participants did not encounter identical visual stimuli during the three experimental sessions. The three sets were administered in a counterbalanced order across participants. Stimuli were presented using PsychoPy (Peirce, 2007).

High-definition tDCS

A one-anode, four-cathode electrode setting was used (4 $\times$ 1). HD-tDCS was administered using a battery-driven, constant-current generator with an HD-tDCS distributor (DC-Stimulator MC, neuroConn GmbH). All electrodes had a size of 1 cm in diameter and were attached to ordinary EEG-caps (Easycap GmbH). Participants' hair under the electrode casings were moved aside to expose the scalp skin, and a conductive gel was injected into the electrode casings (Signa Gel, Parker Laboratories).

The anodal stimulation was set to 2 mA, and consequently, the cathodal stimulation was 0.5 mA per electrode. Previous studies also used 2 mA to modulate parietal activity during mental arithmetic (Houser, Thoma, Fonseca, O'Conner, & Stanton, 2015; Clemens, Jung, Zvyagintsev, Domahs, & Willmes, 2013), and the agreeableness of a 2-mA anodal stimulation with a 4 × 1 electrode setting has been confirmed (Nikolin, Loo, Bai, Dokos, & Martin, 2015; Kuo et al., 2013). Each participant underwent an anodal left IPS, anodal right IPS, and one sham HD-tDCS session in counterbalanced order and with 1 week in between the sessions.

To stimulate the left and right IPS, the anodal electrode was placed over P3 and P4 of the international EEG 10–20 system (Klein et al., 2013; Klein, Nuerk, Wood, Knops, & Willmes, 2009). The optimal electrodes montage was determined by means of software ("HD-Explore," "HD-Target") that simulate the current flow into the brain depending on the given parameters (Soterix Medical). In a first step, electrode positions were determined by the software for selective maximal stimulation of BA 7, and then the proposed positions were manually modified in a way that lead to the highest selective stimulation of the IPS (MNI coordinates 40, −64, 48 according to Preuschhof, Schubert, Villringer, & Heekeren, 2010). These were the positions F5, F2, and PO4 for left parietal stimulation and F6, F1, and PO3 for right parietal stimulation. This stimulation configuration resulted in an electric field over the target region (IPS) of 0.32 V/m, with lower electric field sizes in the surrounding areas (see Figure 2). Previous studies reported tDCS effects for field sizes typically in the range of 0.3–0.4 V/m (Bikson et al., 2016), and some authors implied 0.2 V/m as threshold for neuronal interferences (Zito et al., 2015). We specifically assessed the electric field sizes in several other areas outside IPS, confirming that values were below 0.2 V/m (e.g., V1: < 0.12 V/m, visual association areas BA 18, BA 19: < 0.17 V/m, medial parietal BA 31: < 0.13).

At the beginning of the stimulation, current was increased slowly during the first 30 sec until the stimulation threshold of 2 mA was reached (ramp-up). After 25 min of constant direct current, current was decreased to 0 mA during 30 sec (ramp-down). In the sham condition, current was ramped-up during the first 30 sec as well, until the stimulation threshold was reached. After 30 sec of full stimulation, the current was ramped down to 0 mA during 30 sec and stayed off until the end of the session. This procedure ensured that, in both real and sham stimulation, participants experienced the initial tickling sensation of the current and made both conditions indistinguishable (as confirmed by questionnaires, see Results section). For the sham condition, the left parietal stimulation setting was used for half of participants, and the right parietal stimulation setting was used for the other half. Impedance values were examined during the stimulation and were all below 10 kΩ for the duration of the entire session (typically around 4–7 kΩ).

Participants started with the task immediately after the ramp-up. tDCS is not effective at the beginning of stimulation (Nitsche et al., 2008; Nitsche & Paulus, 2000), and

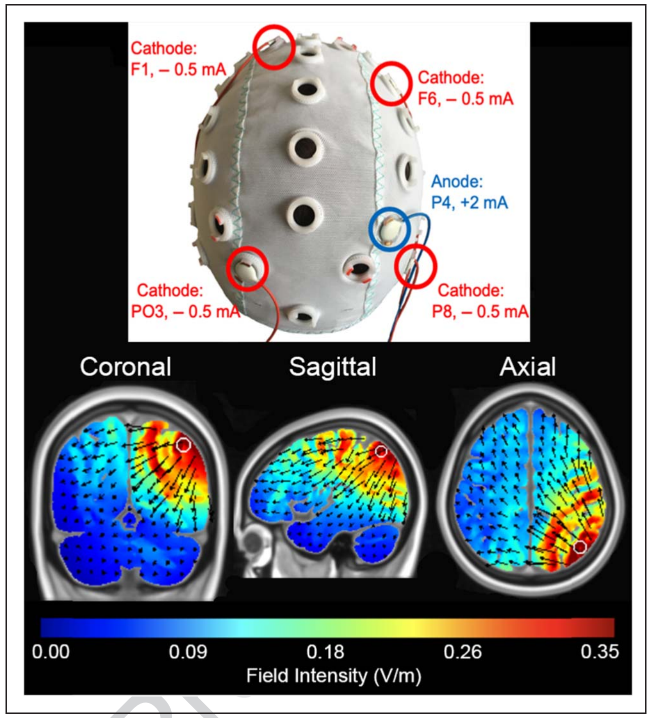

Figure 2. The top panel shows the electrode placement for right parietal anodal HD-tDCS. The lower panel shows the result of the computer simulation for this setting for the coronal (left, right), sagittal (front, back), and axial (left, right) slice.

several minutes of delay between stimulation onset and onset of critical task is employed in most studies (e.g., Artemenko et al., 2015; Martin, Liu, Alonzo, Green, & Loo, 2014; Klein et al., 2013). We therefore considered the first block (42 trials) as "warm-up" block that was not included in data analysis. It took about 6 min from stimulation onset until the critical trials started.

At the end of each session, participants were asked to indicate on a paper–pencil questionnaire how comfortable/uncomfortable the stimulation appeared to them (ranging from −3 = *very uncomfortable* to 3 = *very comfortable*) and how much pain they perceived during the stimulation (ranging from 0 = *no pain* to 10 = *very strong pain*). Moreover, after the last session, participants were informed that real brain stimulation was applied only in two out of the three sessions and that a control stimulation (sham) was applied in one of the sessions. They were asked to guess which of the three sessions was the sham condition and to indicate their confidence in this guess (ranging from 1 = *very unsure* to 5 = *very sure*).

Data Analysis

It has been repeatedly shown that mental calculation with nonsymbolic numerosities follows Weber's law (Knops et al., 2009; McCrink et al., 2007; Barth, Kanwisher, & Spelke, 2003). This means that both the mean number chosen by the participants and the variability of the chosen numbers increase with increasing result size. We therefore followed Knops et al.'s (2009) suggestion and used the logarithms of the numbers involved. Specifically, for each trial, the log of the deviation between the chosen and correct result was computed and served as dependent variable (Knops et al., 2009). Negative values indicate underestimation, and positive values indicate overestimation of the correct result.

Preliminary Analyses

Two preliminary analyses were conducted before the main analysis of HD-tDCS effects. First, participants' task compliance was assessed. To this end, we computed for each participant and session a Pearson correlation between the log correct solution and the log solution selected by the participants (see Brezis et al., 2016). Second, to assess potential training effects due to the repetition of the task, we computed a repeated-measures ANOVA with session (1, 2, 3) as within-subject variable on the log deviation values (averaged across all trials per participant and session).

Main Analysis

In the main analysis, the influence of HD-tDCS on approximate arithmetic was tested by means of a repeated-measures ANOVA with the variables HD-tDCS (left, right, sham), operation (addition, subtraction), and phase (online, offline). Phase was included in the analysis because Brezis et al. (2016) found selective effects of tDCS on approximate arithmetic only in the online (vs. offline) phase of stimulation. Pairwise comparisons (simple main effect *t* tests) were complemented by Bayes factors (BFs). Specifically, BFs_{10} are reported to quantify the evidence of data for H1. According to conventions, a $BF_{10} > 3$ can be interpreted as evidence for H1, whereas a $BF_{10} < 1/3$ can be interpreted as evidence for H0. Values between 1/3 and 3 provide inconclusive evidence for H1 or H0. Because we expected improved performance under stimulation, H1 was defined as "log deviation during stimulation < log deviation during sham" when computing BFs.

Statistical analyses were conducted using the free software JAMOVI (JAMOVI Project, 2017) and JASP using default priors for BFs (JASP Team, 2016).

RESULTS

Data that deviated more than ± 3 *SD* from the individual log deviation means were excluded from analysis, as well as very long responses (+ 10 sec). This procedure led to the exclusion of 1.4% of responses.

Preliminary Analysis

Task Compliance

The Pearson correlation between the log "correct" solution and the log "selected" solution was highly significant for all participants in all three session (all *p*s < .001), with correlations ranging from .78 to .94 ($M = .87$). This confirms that participants' responses were not at random and that all participants complied to the task in all three sessions.

Training Effect

The repeated-measures ANOVA with session (1, 2, 3) as within-subject variable on the log deviation values revealed neither a main effect of session, $F(2, 34) = 0.30$, $p = .742$, $\eta_p^2 = .02$, nor a linear contrast effect of session, $F(1, 17) = 0.60$, $p = .450$, $\eta_p^2 = .03$. This shows that participants did not increase their approximate arithmetic performance as a function of task repetition. We therefore did not consider the variable session in all further analyses.

Main Analysis

The mean log deviation values for left, right, and sham HD-tDCS for addition and subtraction problems in the online and offline phase of stimulation are shown in Figure 3. The repeated-measures ANOVA with the variables HD-tDCS (left parietal, right parietal, sham), operation (addition, subtraction), and phase (online, offline) revealed a significant main effect of operation, $F(1, 17) = 61.62$, $p < .001$, $\eta_p^2 = .78$, and a by trend significant three-way interaction, $F(1, 17) = 2.98$, $p = .064$, $\eta_p^2 = .15$ (see Table 2 for complete statistical report). The main effect of operation indicated that deviation values were larger for subtraction ($M = -0.13$, $SEM = 0.01$) than for addition problems ($M = -0.04$, $SEM = 0.01$). The fact that solutions were generally underestimated and that the underestimation was larger for subtraction is in line with the expected OM effect.

The results showed that there was no overall effect of HD-tDCS on approximate arithmetic. However, the by trend significant three-way interaction suggests that there might be a more specific effect of HD-tDCS, depending on operation and phase of stimulation. We therefore further disentangled the three-way interaction by computing separate repeated-measures ANOVAs with the variables HD-tDCS (left parietal, right parietal, sham) and operation (addition, subtraction) for the online and offline phase of the stimulation.

For the online phase, the ANOVA revealed a significant main effect of operation, $F(1, 17) = 61.62$, $p < .001$, $\eta_p^2 = .78$, but no main effect of stimulation, $F(2, 34) = 0.47$, $p = .630$, $\eta_p^2 = .03$. The main effect showed again that deviation values were larger for subtraction ($M = -0.14$, $SEM = 0.01$) than for addition problems ($M = -0.04$, $SEM = 0.01$). Most importantly, the two variables interacted, $F(1, 17) = 3.33$, $p = .048$, $\eta_p^2 = .16$. We therefore ran separate repeated-measures ANOVAs with the variable HD-tDCS (left parietal, right parietal, sham) for addition and subtraction. Although there was no main

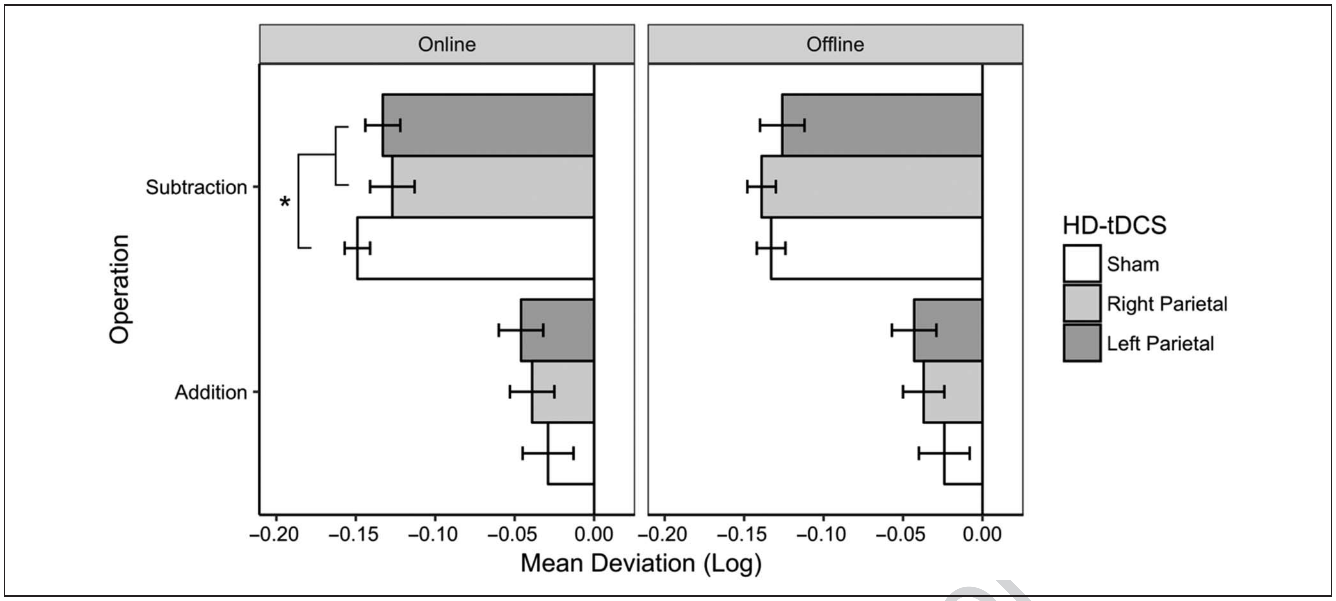

Figure 3. Mean log deviation values for all conditions. Note that, for the main analysis, values from the left and right side of stimulation were averaged and tested against sham. The asterisk indicates a significant difference between parietal and sham HD-tDCS for subtraction in the online phase of stimulation. Error bars depict ± 1 *SEM*.

effect of HD-tDCS for addition problems, $F(2, 34) = 0.92$, $p = .408$, $\eta_p^2 = .05$, there was a significant main effect for subtraction problems, $F(2, 34) = 3.66$, $p = .036$, $\eta_p^2 = .18$. Pairwise comparisons (paired *t* tests) revealed that the underestimation was significantly reduced during left parietal versus sham stimulation, $t(17) = 2.31$, $p = .034$, $BFs_{10} = 3.82$ ($M_{\text{Left HD-tDCS}} = -0.13$, $SEM = 0.01$; $M_{\text{Sham HD-tDCS}} = -0.15$, $SEM = 0.01$) and also during right parietal versus sham stimulation, $t(17) = 2.12$, $p = .049$, $BFs_{10} = 2.85$ ($M_{\text{Right HD-tDCS}} = -0.13$, $SEM = 0.01$; $M_{\text{Sham HD-tDCS}} = -0.15$, $SEM = 0.01$). There was no difference between left and right HD-tDCS, $t(17) = 0.76$, $p = .461$, $BFs_{10} = 0.31$. Thus, the data provide (partial) evidence in favor of an increased performance during HD-tDCS (H1) and also evidence that there is no difference between left and right HD-tDCS (H0). Given the latter, we averaged data from the left and right parietal stimulation condition and compared it against sham to assess the combined effect of stimulation (left and right).

Table 2. Results of the ANOVA (Main Analysis)

Effect	*F*	*p*	η_p^2
HD-tDCS	0.18	.839	.01
Operation (O)	61.62	<.001	.78
Phase (P)	0.97	.338	.05
HD-tDCS × O	2.39	.107	.12
O × P	0.01	.931	<.01
HD-tDCS × P	1.63	.210	.09
HD-tDCS × O × P	2.98	.064	.15

This comparison revealed a significant combined effect of HD-tDCS for subtraction problems, $t(17) = -2.39$, $p = .028$, $BF_{10} = 4.42$ ($M_{\text{HD-tDCS}} = -0.13$, $SEM = 0.01$; $M_{\text{sham}} = -0.15$, $SEM = 0.01$).

For the offline phase, the ANOVA revealed a significant main effect of operation, $F(1, 17) = 51.71$, $p < .001$, $\eta_p^2 = .75$, but no main effect of HD-tDCS, $F(1, 17) = 2.06$, $p = .170$, $\eta_p^2 = .12$, and no interaction, $F(1, 17) = 1.49$, $p = .239$, $\eta_p^2 = .08$. The main effect of operation showed that, also in the offline-phase, deviation values were larger for subtraction ($M = -0.13$, $SEM = 0.01$) than for addition problems ($M = -0.03$, $SEM = 0.01$).

The results from the main analysis suggest that parietal HD-tDCS increased performance in approximate mental arithmetic (by reducing the underestimation) selectively for mental subtraction during the online phase of stimulation (see Figure 3). This conclusion is further evaluated by additional analyses.

Additional Analyses

RTs

To assess whether the effect of HD-tDCS on approximate arithmetic performance during stimulation was associated with a change in speed–accuracy trade-off, we analyzed (median) RTs with the same procedure as for accuracy. The results from the overall analysis is shown in Table 3. Participants responded faster for subtraction than for addition problems ($M_{\text{Subtraction}} = 1289$, $SEM = 174$; $M_{\text{Addition}} = 1530$, $SEM = 222$), and also faster in the offline than in the online phase of the experiment ($M_{\text{Offline}} = 1319$, $SEM = 170$; $M_{\text{Online}} = 1499$, $SEM = 228$). Because there was no

Table 3. Results of the Global ANOVA on RTs

Effect	*F*	*p*	η_p^2
HD-tDCS	0.61	.550	.04
Operation (O)	19.26	<.001	.53
Phase (P)	5.82	.027	.26
HD-tDCS × O	0.20	.819	.01
O × P	0.01	.980	<.01
HD-tDCS × P	0.49	.618	.03
HD-tDCS × O × P	2.40	.106	.12

interaction between phase and HD-tDCS, the latter effect simply reflects a within-session practice effect in response speed that is not related to stimulation.

As for accuracy, we further decomposed the three-way interaction by computing separate repeated-measures ANOVAs with the variables HD-tDCS (left parietal, right parietal, sham) and operation (addition, subtraction) for the online and offline phase of the stimulation. There was no main effect of HD-tDCS or interaction between operation and HD-tDCS, neither in the online nor in the offline phase of stimulation (all Fs < 1.16). These results show that the effect of HD-tDCS on approximate arithmetic performance was not due to a stimulation-induced change in speed–accuracy trade-off.

Operand Size

We used solution-matched problems in this study (e.g., $14 + 11 = 25$; $32 - 7 = 25$). Thus, the mean magnitude of the solution was the same for addition and subtraction problems. As a consequence of the solution-match approach, the mean magnitude of operands was smaller for addition than for subtraction problems (see Table 1). A possible interpretation of our results would therefore be that HD-tDCS only improved performance for larger operands (i.e., when more dots needed to be processed). Thus, it is not clear whether the selective effect of HD-tDCS for subtraction is truly related to the mental operation (subtraction) or rather due to the operand-size confound (larger operands). If the latter was the case, an improved performance under HD-tDCS would be expected for larger operands for both addition and subtraction. To address this issue, we computed a hierarchical linear mixed effects model for the log deviation values from the online phase of stimulation using the mean operand size of each problem as continuous predictor at the trial level, along with HD-tDCS and operation and all interactions between the three variables as fixed effects. To account for the repeated measurement, we included a random intercept for participants and a random slope for HD-tDCS by participants. To account for other problem-specific characteristics, we also added a random intercept for arithmetic problem (1–18). For a straightforward interpretation of coefficients, sum coding was applied for operation (addition = 1, subtraction = −1), and operand size was mean-centered. Moreover, the contrasts for HD-tDCS were set in a way that the fixed effect coefficient represents the difference between sham and parietal stimulation (sham = 1, left parietal = −0.5, right parietal = −0.5). Consequently, the critical interaction term between HD-tDCS and operation size would reflect a systematic increase in the effect of parietal HD-tDCS for increasing operands. This analysis was performed using the lme4 package in R (Bates, Mächler, Bolker, & Walker, 2015).

The analysis revealed a close-to-significant effect of operation, estimate = 0.0636, *SEM* = 0.0299, $t = 2.13$, $p = .052$. Most importantly, the interaction term between HD-tDCS and operand size was not significant, estimate = −0.0003, *SEM* = 0.0002, $t = -1.20$, $p = .232$. Thus, the effect of parietal HD-tDCS did not increase as a function of operand size. Instead, the interaction term between HD-tDCS and operation was significant, estimate = 0.0313, *SEM* = 0.0158, $t = 1.99$, $p = .047$, confirming the results from the main analysis. This interaction was independent of operation size, as indicated by the absence of a three-way-interaction, estimate = −0.0001, *SEM* = 0.0004, $t = -0.30$, $p = .763$. All other effects were also not significant (all ps $> .215$).

As shown in Figure 4, parietal HD-tDCS improved the estimates for subtraction equally for the different operand sizes. Moreover, inspecting the range of operand size that was used for both addition and subtraction (around 20–50) reveals a different pattern for addition and subtraction. This analysis therefore rules out the possible explanation that operand size was responsible for the selective effect of tDCS for subtraction. Thus, the effect of HD-tDCS that we found for subtraction in the main analysis cannot be attributed to the larger operands but rather reflects some operation-specific modulation.

Operational Momentum

The general trend for underestimation of results sizes was expected (see Introduction) and can be traced back to a general tendency to underestimate the number of perceived dots in visual displays (e.g., Izard & Dehaene, 2008; Krueger, 1984), possibly as a result of the logarithmically compressed representation of non-symbolic magnitudes (differences between adjacent numbers decrease with increasing magnitudes; e.g., Dehaene, 2003). The finding that the underestimation was larger for subtraction than for addition is in line with the definition of OM for nonsymbolic approximate arithmetic (Knops et al., 2009, 2014). To assess more explicitly a possible effect of HD-tDCS on the OM effect, we computed a "relative OM effect," quantified as the difference between addition and subtraction (log deviation addition − log

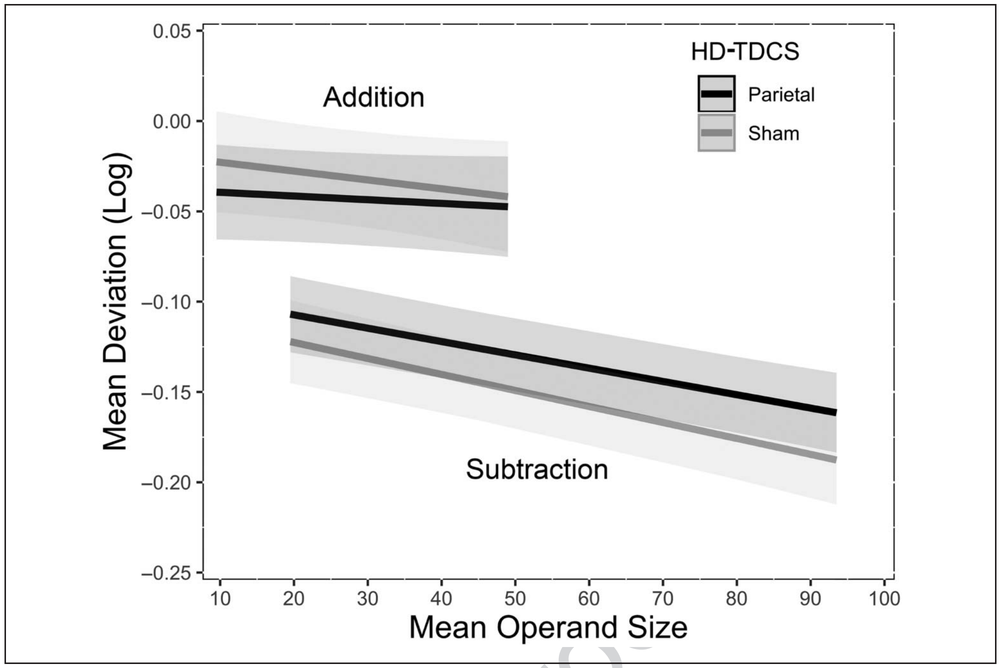

Figure 4. The effect of HD-tDCS as a function of the operand sizes of the arithmetic problems, plotted separately for addition and subtraction. Area around the lines depict 95% confidence interval.

deviation subtraction; see Knops et al., 2009). We termed it "relative OM" because positive values reflect underestimation of subtraction "relative" to addition results, independent of the absolute deviation values (i.e., ignoring the general trend for underestimation). A repeated-measures ANOVA with the variable HD-tDCS (left parietal, right parietal, sham) was computed for the relative OM values during the online phase of stimulation. There was a significant main effect of HD-tDCS, $F(2, 34) = 3.33$, $p = .048$, $\eta_p^2 = .16$. Pairwise comparison revealed a just significant differences between left parietal HD-tDCS and sham ($p = .050$, $BF_{10} = 1.44$) and also a close-to-significant difference between right parietal HD-tDCS and sham ($p = .051$, $BF_{10} = 1.43$). The combined effect of stimulation ($M_{\text{Left and right parietal}}$ vs. sham) was significant, $t(17) = 2.3$, $p = .034$, $BF_{10} = 1.94$. As shown in Figure 5, the relative OM is lower during left and right parietal when compared with sham stimulation, but the evidence is not conclusive.

Given that all results tended to be underestimated, we would not expect an effect of HD-tDCS on the relative OM when stimulation reduces the underestimation for addition and subtraction to the same extent (log deviation addition–log deviation subtraction would still be the same). The effect of HD-tDCS on the relative OM might therefore simply reflect the fact that HD-tDCS only reduced the underestimation for subtraction and had no effect on addition.

Stimulation-related Questionnaires (Comfort/Discomfort, Pain, Recognizing Sham)

A repeated-measures ANOVA with the variable HD-tDCS (left parietal, right parietal, sham) revealed no difference in comfort/discomfort across HD-tDCS conditions, $F(2, 34) = 0.69$, $p = .507$, $\eta_p^2 = .04$ ($M_{Left} = -0.11$, $SEM = 0.17$; $M_{Right} = -0.22$, $SEM = 0.17$; $M_{Sham} = 0.00$, $SEM = 0.17$). Similarly, a repeated-measures ANOVA with the variable HD-tDCS (left parietal, right parietal, sham) revealed no significant difference in perceived pain across HD-tDCS conditions, $F(2, 34) = 2.71$, $p = .093$, $\eta_p^2 = .14$, and pain ratings were generally low ($M_{Left} = 1.17$, $SEM = 0.23$; $M_{Right} = 1.11$, $SEM = 0.23$; $M_{Sham} = 0.72$, $SEM = 0.23$).

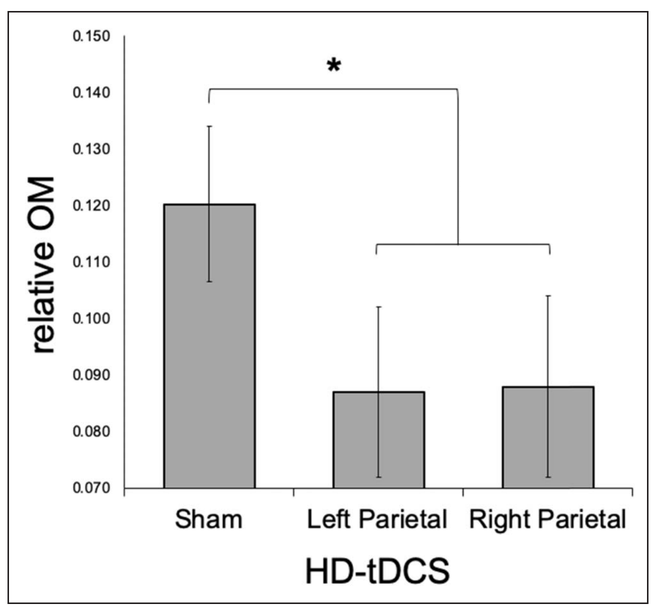

Figure 5. The relative OM effect (log deviation addition–log deviation subtraction) during left and right parietal and sham HD-tDCS. Error bars depict ± 1 *SEM*.

When asked to guess which of the three sessions was sham stimulation, six out of 18 participants correctly guessed the sham session. This proportion (6/18 = 0.33) is equal to the chance level (1/3 = 0.33). Moreover, none of the participants who correctly indicated the sham session reported strong confidence. In fact, there was no difference in confidence ratings between participants who correctly indicated the sham session and those who did not (M_{correct} = 2.67, *SEM* = 0.49; $M_{\text{incorrect}}$ = 2.50, *SEM* = 0.31). These analyses confirm the tolerability of the stimulation setting used in this study and that it was truly a single-blind sham-controlled design.

DISCUSSION

The aim of this study was to investigate whether approximate nonsymbolic mental arithmetic could be improved by means of parietal anodal HD-tDCS. We found that accuracy of subtraction results increased during parietal (vs. sham) HD-tDCS. We showed that the increase in accuracy cannot be explained by a change in speed–accuracy trade-off. Moreover, the fact that the improvement in accuracy was specific for subtraction rules out that parietal HD-tDCS leads to a domain-unspecific increase in performance, for example, by attentional enhancement (cf. Brezis et al., 2016; Roy, Sparing, Fink, & Hesse, 2015). This study therefore extends previous work that found an enhancing effect of parietal tDCS on number processing and symbolic arithmetic (Hauser et al., 2013, 2016; Artemenko et al., 2015; Grabner et al., 2015). Specifically, our study provides first evidence for a modulation of approximate (subtraction) arithmetic by means of HD-tDCS and provides further support for a causal involvement of the IPS in approximate mental arithmetic (Brezis et al., 2016).

Anodal tDCS is assumed to depolarize the stimulated neurons' membrane potential, resulting in lower firing threshold (Nitsche & Paulus, 2000). Brezis et al. (2016) proposed that lower thresholds increase the neuronal response function of the units in the parietal network. Specifically, the increase in neuronal response elevates the population signal-to-noise level of numerosity sensitive neurons, resulting in increased tuning curves and finally in enhanced sensitivity of the network and improved precision of numerosity perception (Brezis et al., 2016). Such an explanation might also apply for the present results. However, if the increase in arithmetic performance was based on a more precise estimate of input numerosity (numerosity of the operands and of the proposed results), then a similar improvement in addition and subtraction could have been expected, which was not the case in this study. It is therefore likely that the modulation in parietal activity due to anodal HD-tDCS influenced the approximate arithmetic computation process, at least for subtraction.

The selective effect of parietal HD-tDCS for subtraction was not expected. It is a common finding in mental arithmetic that subtraction is more difficult than addition (Campbell, 2005; Ashcraft, 1992). In line with this, there was a greater deviation from the true solution for subtraction (vs. addition) problems across all levels of problem sizes in this study. A possible explanation for the selective effect of parietal HD-tDCS for subtraction could be that stimulation only improved performance for more difficult arithmetic problems. Particularly, one could argue that there was not enough room for improvement for addition because participants' performance was already quite accurate. This is in line with studies showing enhanced performance during tDCS for more difficult tasks or for low performing participants, both providing room for improvements (e.g., Arciniega, Gözenman, Jones, Stephens, & Berryhill, 2018; Gill, Shah-Basak, & Hamilton, 2015; Tseng et al., 2012). However, this explanation is not entirely satisfying because medium and large addition problems also yielded reliable deviations from the true results (see Figure 4) and thus provided room for potential improvements.

Besides interpreting the results as selective enhancement of the more difficult subtraction problems, we want to discuss an alternative (or complementary) interpretation of the results in the sense that parietal HD-tDCS modulated the OM effect. In general, the OM effect is a systematic cognitive bias resulting in overestimation of addition and underestimation of subtraction results (McCrink et al., 2007), but based on previous research relying on a similar task, we expected a general tendency for underestimation in this study and defined the OM effect as "relative" larger underestimation of subtraction (vs. addition) results (Knops et al., 2009, 2014). Even though we only found inconclusive evidence that parietal HD-tDCS reduced the relative OM effect, it is still possible that the OM effect played a role for the selective effect of HD-tDCS on subtraction: In the case of subtraction, an increase in estimates is equal to a decrease in underestimation and thus to an increase in accuracy. However, in light of the general trend for underestimation in this study, the situation is more complex for addition: A reduction in estimated results for addition was in contrast to an increase in accuracy, and these two processes may have counteracted each other. However, in other situations (e.g., when operating with smaller magnitudes or symbolic numbers), it is more likely that addition results are overestimated (Knops et al., 2009; McCrink et al., 2007), and therefore, a reduction in estimated results may be generally advantageous. It is possible that stimulating the IPS might trigger a corrective mechanism, thus leading to a reduction in OM effect (i.e., an increase in estimates for subtraction and a decrease in estimates for addition). Although this interpretation is speculative at this point in time, we think that it complements the interpretation of the pattern of results for subtraction and addition. A possible modulating effect of parietal HD-tDCS on the OM during mental arithmetic should be addressed in future studies. Moreover, it would also be interesting to compare the OM effect and its modulation by parietal brain stimulation to the representational momentum effect. The representational momentum effect reflects a “forward bias” in the perception of the vanishing position of a moving object along its motion trajectory (Freyd & Finke, 1984). Similar to the physical space, such a forward bias has also been hypothesized for movements in the representational number space (McCrink et al., 2007), leading to the classical OM pattern (underestimation of addition, overestimation of addition; see Introduction). The parietal cortex does also play an important role for the processing of spatial information, and overlapping parietal networks for the processing of spatial and numerical information are likely to be the neuronal basis for “spatial” biases in the processing of numbers (e.g., Fischer & Shaki, 2014; Göbel, Calabria, Farnè, & Rossetti, 2006; Hubbard, Piazza, Pinel, & Dehaene, 2005). If both the representational momentum and OM effect rely on a common spatial metric (for a discussion, see Hubbard, 2014; Knops et al., 2009), parietal stimulation should lead to similar modulations of these two biases.

In this study, there was no difference between left and right parietal stimulation. Our results therefore do not support earlier claims of a predominant role of either the right parietal cortex (Semenza et al., 2017; Brezis et al., 2016; Li et al., 2015; Dormal et al., 2012) or the left parietal cortex (Hauser et al., 2013; Dormal et al., 2008; Andres et al., 2005) for the processing of numerosity and arithmetic. Rather, our results are in line with studies that reported left and right parietal contributions in arithmetic (Artemenko et al., 2018; Semenza et al., 2017; Salillas et al., 2012; Andres et al., 2011; Dehaene, Piazza, Pinel, & Cohen, 2003; Dehaene & Cohen, 1997). For example, Andres et al. (2011) found bilateral activation of the IPS during mental subtraction in fMRI and showed that TMS over either the left or the right IPS impairs arithmetic performance. It requires more brain stimulation studies using the same stimulation settings on a variety of arithmetic tasks (symbolic, nonsymbolic, different operations) until final conclusions regarding the specific involvement of the left and right parietal cortex can be drawn. Moreover, future studies could also compare the effect of bilateral stimulation (left and right anodal stimulation) to that of left and right unilateral stimulation (see Hauser et al., 2013; Klein et al., 2013; Andres et al., 2005).

Another interesting aspect of our results is that the effect of HD-tDCS was limited to the online phase of stimulation. This corresponds to the previous study on symbolic approximate arithmetic where an increase in accuracy of numerical estimates was only found during the online delivery of tDCS (Brezis et al., 2016). The timeline of the effect of tDCS depends on stimulation parameters (e.g., intensity, location) and also on the task (Stagg et al., 2011; Nitsche & Paulus, 2000). Aftereffects of tDCS (both conventional and HD) are typically reported for 30 min or even longer at the level of motor cortex excitability (e.g., Kuo et al., 2013) but have not yet been systematically investigated for cognitive functions. In some cognitive studies, only offline performance was analyzed (e.g., Hauser et al., 2013) or the cognitive task outlasted the stimulation phase, whereby online versus offline phase was not considered in the analysis (e.g., Savic, Cazzoli, Müri, & Meier, 2017; Savic, Müri, & Meier, 2017; Artemenko et al., 2015). Our own study and Brezis et al.’s (2016) study point toward an important role of taking the stimulation phase (online vs. offline) more thoroughly into account (see also Martin et al., 2014).

Limitations and Outlook

Numerosity of nonsymbolic stimuli is correlated with various visual features. For example, when numerosity of equally sized stimuli changes, the total occupied area changes, along with convex hull and density. It is therefore impossible to dissociate numerosity from all other continuous visual magnitude features (Salti, Katzin, Katzin, Leibovich, & Henik, 2017). The stimuli used for this study were controlled for total occupied area, so that the perception of numerosity was based on the number of dots rather than the salient spatial information of the total occupied area. As a consequence, numerosity was confounded with other visual features such as dot size. We decided to use total occupied area-controlled stimuli because this has been done in most previous nonsymbolic arithmetic studies (e.g., Knops et al., 2009, 2014). Moreover, studies that systematically assessed the effect of different visual features on approximate number processing concluded that numerosity (i.e., the number of dots) is the primary feature that most participants rely on (DeWind, Adams, Platt, & Brannon, 2015; Park, DeWind, Woldorff, & Brannon, 2016; but see also Gebuis & Reynvoet, 2012a, 2012c). Similarly, in a nonsymbolic numerosity estimation task, a high correlation (r = .89) was found between numerosity estimates of dots with a constant size (and thus area covered by the array increased with increasing numerosity) and numerosity estimates of dots with a constant occupied area across all numerosities (and thus dot size decreased with increasing numerosity; Reinert, Hartmann, Huber, & Moeller, 2019). We therefore argue that the confound of other visual features did not play a crucial role for arithmetic performance in this study (see also Knops et al., 2009). Nevertheless, we acknowledge that more sophisticated methods have been proposed to generate nonsymbolic number stimuli that allow for better control of visual features that could be used in future studies (Salti et al., 2017; Gebuis & Reynvoet, 2012b).

Additional research is needed to further assess the possibilities and limits of enhancing exact and approximate arithmetic by means of noninvasive brain stimulation. Future studies could, for example, combine brain stimulation with arithmetic learning and/or assess whether (stimulation-induced) increased performance in approximate arithmetic could transfer to exact arithmetic or vice versa (cf. Popescu et al., 2016; Snowball et al., 2013; Cohen Kadosh et al., 2010). Such studies will have implications, especially for people suffering from dyscalculia (Iuculano & Cohen Kadosh, 2014; Cohen Kadosh et al., 2010).

This study provided further proof of the feasibility and agreeableness of a 4 × 1 HD-tDCS setting with 2 mA. This setting overcomes limitations of conventional tDCS by stimulating more focal (Datta et al., 2009) and particularly by removing inhibitory effects of the return electrode, which is often placed over frontal positions (Schroeder et al., 2017). Given that mental arithmetic relies on a frontoparietal network (e.g., Artemenko et al., 2018; Arsalidou & Taylor, 2011), it is crucial to avoid frontal interferences when studying the role of parietal networks. The increased focality of HD-tDCS might allow to test specific contributions of different parts of the parietal network (and beyond) for numerical cognition in future studies (e.g., horizontal vs. ventral IPS, angular gyrus, superior parietal lobe, supramarginal gyrus; see Montefinese et al., 2017; Semenza et al., 2017; Salillas & Semenza, 2015; Dehaene et al., 2003).

In this study, we argued that the modulation in arithmetic performance due to HD-tDCS was based on increased excitability in the IPS (see Figure 2). However, given that approximate arithmetic involves a larger parietal network involving different parts of the IPS and (among others) the medial frontal and left precentral gyrus (Venkatraman et al., 2005), we do not know exactly whether the effects found in this study were solely based on the processing of numerosity and arithmetic within the IPS or whether the higher excitability of the IPS also modulated processing in other areas with close neuronal connections to the IPS, which might also have contributed to the effect. To further clarify the causal role of different areas within the frontoparietal network, future studies are needed, in which different areas along the processing pathway of arithmetic are systematically stimulated. This may require the integration of brain stimulation with neuroimaging and electrophysiological methods. Although technically challenging, previous results showed that such integration could yield valuable insights into tDCS effects on not only one region but also whole cortical networks (see Pisoni et al., 2018; Romero Lauro et al., 2016).

Conclusions

This study provided first evidence for a modulation of approximate (subtraction) arithmetic by means of anodal HD-tDCS and provides further support for a causal involvement of the (bilateral) IPS in approximate mental arithmetic (Brezis et al., 2016). Approximate number processing has been discussed as precursor of exact arithmetic (Park, DeWind, et al., 2016; Hyde et al., 2014; Park & Brannon, 2014; Gilmore, McCarthy, & Spelke, 2007), and our study therefore advances the promising use of noninvasive brain stimulation in increasing cognitive functions that are essential for everyday life situations (e.g., dealing with money). We hope that this study encourages others to use a HD-tDCS setting to investigate numerical cognition and that accumulating research findings with this method will eventually untangle the causal involvement of different brain areas in numerical cognition.

Acknowledgments

This research was funded by the Swiss National Science Foundation (Grant No. PZ00P1_167995).

Reprint requests should be sent to Matthias Hartmann, Department of Psychology, University of Bern, Fabrikstrasse 8, 2012 Bern, Switzerland, or via e-mail: matthias.hartmann@psy.unibe.ch.

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