Anodal high-definition transcranial direct current stimulation over the left (but not right) parietal cortex facilitates mental arithmetic

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Abstract

Non-invasive brain stimulation (NIBS) techniques such as transcranial direct current stimulation (tDCS) allow investigating the causal involvement of specific brain areas in mental arithmetic. In this study, we utilized for the first time the enhanced spatial precision of high-definition (HD)-tDCS to study the functional involvement of the left and right intra-parietal sulcus (IPS) in mental arithmetic. A total of 25 participants underwent anodal left IPS, right IPS, and sham stimulation in separate sessions in counterbalanced order while solving single- and multi-step addition and subtraction problems. We found that left but not right IPS stimulation (vs. sham) improved performance across all types of problems. Notably, the observed improvements in arithmetic performance were specific to arithmetic processing, as IPS stimulation had no enhancing effect on performance in a control n-back task. These results provide further evidence supporting the functional involvement of the left IPS in arithmetic problem-solving across a wide range of problem types, and for the use of NIBS for cognitive enhancements.

Keywords: mental arithmetic, tDCS, HD-tDCS, posterior parietal cortex (PPC), intraparietal sulcus (IPS), numerical cognition

Introduction

The processing of numbers and mental arithmetic is a fundamental cognitive function, with mathematical abilities being strongly associated with academic achievements, career prospects, earning potential, and overall quality of life (Parsons & Bynner, 2005; Ritchie & Bates, 2013). Consequently, neuroscientists have dedicated substantial efforts to investigate the neuronal and cognitive mechanisms involved in number processing and mental arithmetic, as well as to explore tools to support mathematical learning (Fischer et al., 2011; Park & Brannon, 2014; Snowball et al., 2013; Wilson et al., 2006). Neuroimaging studies have revealed distinct neural networks associated with number processing. Simple tasks like number comparisons engage a parietal network, while more complex tasks such as mental arithmetic recruit a fronto-parietal network (Arsalidou & Taylor, 2011). The frontal regions of this network, including the middle and superior frontal gyri, likely reflect increased cognitive demands, such as working memory requirements during calculation (Arsalidou & Taylor, 2011). On the other hand, the parietal component, specifically the intraparietal sulcus (IPS), serves as a central hub for magnitude representation (Dehaene, 2011; Eger et al., 2009; Piazza et al., 2007).

Neuroimaging techniques do not provide the means to distinguish between epiphenomenal activity and critical activity (i.e., functionally relevant) within brain areas during mental arithmetic. To address this issue, non-invasive brain stimulation (NIBS) techniques come into play. By modulating neural activity, NIBS offers a valuable tool for establishing causal relationships between specific brain regions and cognition (Garcia-Sanz et al., 2022; Schroeder et al., 2017). The primary line of evidence establishing the causal contributions of fronto-parietal areas in mental arithmetic stems from NIBS studies utilizing transcranial magnetic stimulation (TMS) (Garcia-Sanz et al., 2022). TMS involves the generation of a magnetic field through a coil placed on the skull, which, in turn, induces an electric current across the skull, interfering with neuronal activity in the brain regions proximate to the coil. In TMS research, inhibitory stimulation protocols are commonly employed, and subsequent impairments in task performance are observed (Jahanshahi & Rothwell, 2000).

Despite multiple studies investigating the inhibitory effects of TMS on mental arithmetic, a consistent understanding regarding the role of the IPS in terms of lateralization (i.e., the contribution of the left and right IPS) and its specific involvement in different aspects of arithmetic processing has not yet emerged (Garcia-Sanz et al., 2022). For example, some studies have reported impaired arithmetic performance for left IPS stimulation, while right IPS stimulation showed no effect (Göbel et al., 2006). Conversely, other studies have found no differences between left and right IPS stimulation (Montefinese et al., 2017, for multiplication problems; Salillas et al., 2012, for addition problems). Interestingly, some studies have even reported a stronger or exclusive impairment associated with right IPS stimulation (Montefinese et al., 2017, for addition problems; Salillas et al., 2012, for multiplication problems). On the other hand, there have been studies that did not observe any TMS-related effects on arithmetic performance at all (Fresnoza et al., 2020).

The second line of evidence supporting the causal contributions of parietal brain areas in mental arithmetic stems from studies employing transcranial direct current stimulation (tDCS) as a NIBS technique. tDCS involves the administration of a constant electrical current to the brain, typically ranging from 0.5 to 2 mA, through the placement of anodal and cathodal electrodes on the scalp (Nitsche et al., 2008). Anodal tDCS is generally thought to enhance cortical excitability by increasing the resting membrane potentials of neurons closer to the threshold for activation, without directly inducing action potentials (Bikson et al., 2016; Brezis et al., 2016). In contrast, cathodal tDCS is believed to reduce the excitability of the underlying brain tissue by decreasing the resting membrane potential. tDCS is currently being discussed as promising tool to enhance cognitive performance across different cognitive domains even in healthy individuals (Mancuso et al., 2016; Santarnecchi et al., 2015).

In the initial study demonstrating the beneficial effects of tDCS on mental arithmetic, Hauser et al. (2013) reported enhanced performance for subtraction problems during anodal tDCS applied over the left IPS, while stimulation of the right IPS or bilateral IPS stimulation did not yield similar improvemens. This pattern of results was replicated by the same research group in a study investigating arithmetic learning (Grabner et al., 2015) but not in another subsequent study (Hauser et al., 2016; see also Mosbacher et al., 2020, 2021). Yet another study utilized a bilateral approach with two electrodes of the same polarity to stimulate the left and right IPS regions simultaneously (Klein et al., 2013). While specific modulations in number processing were observed, clear improvements in arithmetic performance were not evident (see aso Artemenko et al., 2015). The potential of NIBS for enhancing arithmetic performance remains to be further assessed.

The present study

Given the inconsistent findings in previous studies, it is important to further investigate the role of the IPS in mental arithmetic by NIBS. This will contribute to a better understanding of the causal relationship between brain function and structure, as well as provide additional insights into the potential of NIBS for enhancing cognitive performance (Kucian & Cohen Kadosh, 2021). To advance this objective, we employ for the first time high-definition tDCS (HD-tDCS) to investigate symbolic mental arithmetic, while also manipulating critical characteristics of arithmetic problems. HD-tDCS offerst two key advantages over conventional tDCS. Firstly, it utilizes smaller “high-definition” electrodes, enabling more precise and focal stimulation of the target region (Datta et al., 2009; Kuo et al., 2013). This allows for a more confident attribution of any facilitatory effects to the IPS, in contrast to conventional tDCS, which modulates neural activity in a broader area between the anode and cathode. Secondly, in HD-tDCS, during anodal stimulation, the cathodal electrode is divided into multiple smaller electrodes with sub-threshold activity. This mitigates the risk of undesired inhibitory effects from the cathodal electrode during anodal stimulation. This aspect is important when studying mental arithmetic, as it involves a fronto-parietal network, considering that the cathode in conventional tDCS is often placed on contralateral frontal regions (Artemenko et al., 2015; Hauser et al., 2016).

One potential source of variance in previous findings is the utilization of different arithmetic tasks across studies (e.g., addition, subtraction, multiplication, or a combination thereof). Different types of arithmetic operations are associated with distinct patterns of neuronal activity. For instance, addition (and multiplication) rely more on retrieval from long-term memory and may therefore exhibit less dependence on the IPS compare to subtraction (Grabner et al., 2009; Yang et al., 2017). However, even within the same type of operation, the level of difficulty may play a significant role. Many previous studies have primarily focused on relatively simple one-step problems (e.g., 13 + 5). As the number of steps increases, the duration and complexity of the computational phase also escalate. More challenging problems are likely to engage the frontal regions of the fronto-parietal arithmetic network to a greater extend (Metcalfe et al., 2013; Yang et al., 2017). In order to gain a better understand of the potential moderating role of the type and difficulty of arithmetic operations on the facilitatory effect of ISP stimulation, we manipulated both the operation and step-size in this study. Specifically, we employed single- and multi-step addition and subtraction problems (e.g., 46 + 7 vs. 46 + 7 + 4 + 6). We believe that this combination of operation (addition, subtraction) and step size (one, three) provides a reasonable range of variability.

Single step addition problems are the easiest and involve the shortest computational phase with the lowest proportion of actual arithmetic computation (Hartmann, 2022). It could be anticipated that the left and right IPS, as core regions of number representation, play a functional role in the arithmetic process for these types of problems (Andres et al., 2011; Dehaene, 2011; Venkatraman et al., 2005). Additionally, since familiarity (i.e., recalling the correct solution of a simple problem) is more strongly associated with the left IPS

(Artemenko et al., 2015; Yang et al., 2017), it is conceivable that a facilitatory effect would be more pronounced for left IPS stimulation.

Conversely, multi-step subtraction problems are the most challenging, presumably recruiting a larger proportion of the frontal part of the parieto-frontal network and placing greater demands on domain-general working memory capacities (Metcalfe et al., 2013). On the one hand, this suggests that the arithmetic process may rely to a lesser extent on the IPS, thereby reducing the impact of IPS stimulation. On the other hand, the extended and more intense computational process of multi-step problems necessitates continuous access to number meanings, which may result in an overall higher dependency on the IPS. It is therefore also plausible that the facilitatory effect of IPS stimulation accumulates over multi-step problems, potentially amplifying the effect of stimulation for these types of problems.

Considering the involvement of the PPC in domain-general functions like working memory and attention (Lazzaro et al., 2022), it is important to assess the extent to which any performance improvements due to IPS stimulation are specific to arithmetic processing (Looi & Cohen Kadosh, 2016). Therefore, we incorporated a n-back working memory task as control task similar to Mosbacher et al. (2020). The n-back task entails processing number symbols, maintaining and updating a sequence of numbers in working memory, necessitating attentional resources, and requiring a motor response. Thus, this task shares several similarities with the arithmetic task, excluding the critical computational aspect.

Materials and Methods

Participants

Twenty-five healthy right-handed participants (17 female, 8 male) took part in this study (mean age: 23.9, ranging from 19-35). Participants either received course credit or monetary compensation for their participation. Participants gave written informed consent prior to the study. The study was approved by the Ethics Committee of the University of Bern and experiments were conducted according to their guidelines. All participants confirmed that they had no history of psychiatric and neuronal disorder, did not take any drugs or abused alcohol, and they did not suffer from dyscalculia or any other impairment in number processing.

Given the heterogenous findings and methods from previous studies, it was difficult to define sample size a priori based on effect size. Instead, the sample size was determined based on the number of participants in previous tDCSs studies on mental arithmetic, where 16-24 participants were employed per stimulation condition (Artemenko et al., 2015; Grabner et al., 2015; Hauser et al., 2013, 2016; Klein et al., 2013; Mosbacher et al., 2020). We initially targeted a sample size of 24 to counterbalance stimulation (left, right, sham) across sessions (1, 2, 3), but 25 participants signed up and we decided to include all participants in the study and randomly allocate the last participants to a stimulation order.

Design

We used a 3 (HD-tDCS: left, right, sham) x 2 (operation: addition, subtraction) x 2 (step size: single, multi) single-blind sham-controlled within-participants design whereby each participant received left parietal, right parietal, and sham stimulation in separate sessions (one week between sessions).

Stimuli and task procedure

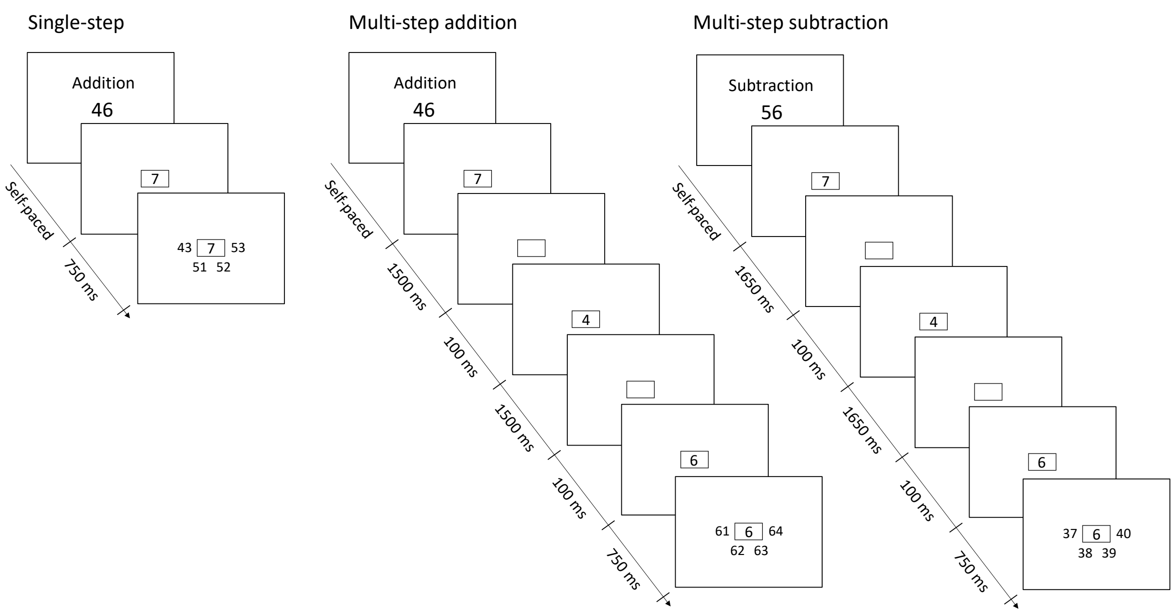
Arithmetic task. In each session, participants solved 96 arithmetic problems, comprising 24 single-step addition, 24 single-step subtraction, 24 multi-step addition, and 24 multi-step subtraction problems, presented in random order. Participants were instructed to prioritize both speed and accuracy in selecting the correct solution. Each trial started with a screen displaying information regarding the operation (addition or subtraction) and the initial number (i.e., the “starting number”). The starting number ranged between 22 and 78 for addition problems, and between 32 and 88 for subtraction problems. Participants initiated the computation process by pressing the “space” key when prepaired. The operands (one for single-step problems, three for multi-step problems) where presented sequentially in a square in the center of the screen (see **Fig. 1**). Operands were either 4, 5, 6, or 7. Operands of different magnitudes were used within the same trial, and the final result of a single-step problem, or the intermediate result of a multi-step problem, never yielded a multiple of ten. Across all trials within each condition (single-step addition, single-step subtraction, multi-step addition, and multi-step subtraction), the average operand size remained constant. Trial sequences are illustrated in **Fig. 1**. Since we expected greater difficulty of subtraction problems compared to addition problems, operands in multi-step subtraction problems were presented for a slightly longer duration (+150 ms) than in multi-step addition problems. This additional time is aimed to prevent the speed of the sequentially presented operands for multi-step subtraction problem from being too high.

After the presentation of the last operand, four potential solution numbers were displayed in a semicircular arrangement around the center of the screen, with ascending magnitudes from left to right (see **Fig. 1**). To correspond with the spatial layout of the solution numbers on the screen, participants positioned their left-hand index and middle fingers on the keys “v” and “f”, and their right-hand index and middle fingers on the keys “n” and “j”. The ascending alignment of the potential solution numbers in combination with the spatially congruent finger placement allowed for a straightforward selection of responses. The incorrect solutions deviated from the correct solution by +/- 1, +/- 2, +/- 10, +/- 11, or +/- 12. The deviations of the three incorrect solution numbers were modified from trial to trial, ensuring that participants could not employ shortcuts or strategic decision-making (e.g., selecting the number that matches only in parity status, decade, or the units digit of the correct solution). To encourage participants to select the potential solution number only after they have finished the computation, a time delay of 750 ms was induced between the last operand and the four potential solution numbers. (Presenting the solution numbers at the same time as the last operand might prevent participants from finishing their ongoing computation and intuitively select the best fitting solution.). The correct solution was presented equally often at each of the four possible positions. An error feedback (“wrong”) was displayed following an incorrect response for a duration of 2500 ms. After correct response or the display of the error message, the subsequent trial commenced after a blank screen of 1000 ms.

Three distinct sets of problems were created for the three sessions (referred to as Set A, B, and C). Each set contained a minimum of 85% unique problems, and no problem was presented in all three sets, ensuring minimal repetition and a diverse range of problems throughout the three sessions. The mean starting number, mean operand size, and mean result size were kept constant across the three problem sets. This ensured that participants encountered similar levels of complexity and difficulty regardless of the set they were assigned. An example of a stimulus list is shown in Table 1. The assignment of problem sets, stimulation condition and session was counterbalanced across participants. The experiment was run on an ordinary laptop using PsychoPy2 (Peirce et al., 2019).

Figure 1

Trial sequence



Note. Example of trial sequences for a single-step addition (left), multi-step addition (middle) and multi-step subtraction problems (right).

Table 1

One-step and multi step arithmetic problems

Addition		Subtraction	
Single-step	Multi-step	Single-step	Multi-step
22 + 4	23 + 4 + 7 + 6	32 - 4	33 - 4 - 7 - 6
23 + 4	24 + 5 + 7 + 6	33 - 6	34 - 5 - 7 - 6
27 + 5	26 + 5 + 6 + 7	37 - 5	36 - 5 - 6 - 7
28 + 5	27 + 4 + 6 + 7	38 - 5	37 - 4 - 6 - 7
32 + 6	33 + 5 + 7 + 4	42 - 6	43 - 5 - 7 - 4
33 + 6	34 + 5 + 6 + 4	43 - 7	44 - 5 - 6 - 4
37 + 6	36 + 6 + 4 + 5	47 - 6	46 - 4 - 6 - 5
38 + 6	37 + 4 + 7 + 5	48 - 6	47 - 4 - 7 - 5
42 + 6	42 + 7 + 5 + 6	52 - 6	52 - 6 - 7 - 5
44 + 7	44 + 7 + 6 + 4	54 - 7	54 - 7 - 6 - 4
46 + 7	46 + 7 + 4 + 6	56 - 7	56 - 7 - 4 - 6
48 + 4	48 + 7 + 6 + 5	58 - 4	58 - 7 - 6 - 5
52 + 7	52 + 6 + 5 + 4	62 - 6	62 - 6 - 5 - 4
54 + 7	54 + 7 + 4 + 5	64 - 7	64 - 7 - 4 - 5
56 + 7	56 + 7 + 5 + 4	66 - 7	66 - 7 - 5 - 4
58 + 7	58 + 4 + 5 + 6	68 - 7	68 - 4 - 5 - 6
63 + 5	62 + 6 + 4 + 7	73 - 5	72 - 6 - 4 - 7
64 + 5	63 + 6 + 7 + 5	74 - 5	73 - 7 - 5 - 6
66 + 6	67 + 6 + 5 + 7	76 - 4	77 - 6 - 5 - 7
67 + 4	68 + 6 + 7 + 4	77 - 4	78 - 6 - 7 - 4
73 + 4	72 + 4 + 5 + 7	83 - 4	82 - 4 - 5 - 7
74 + 5	73 + 4 + 6 + 5	84 - 5	83 - 6 - 4 - 5
76 + 5	77 + 5 + 4 + 6	86 - 5	87 - 5 - 4 - 6
77 + 4	78 + 5 + 4 + 7	87 - 4	88 - 5 - 4 - 7

Control task. In the n-back task, participants were instructed to press the “j” key with the index finger of their right hand as quickly as possible if the number on the screen was the same than two numbers before (n = 2 back). A total of 100 numbers from 1-9 were presented in pseudo-random order, so that a total of 20 hits were included in the task. As the operands in the arithmetic task, numbers in the n-back task were presented in the center of the screen inside of a box of 3.5 x 2 °of visual angle. Each number was presented for 1000 ms, with an ISI of 550 ms. If participants missed a target or incorrectly pressed the button, the central box turned into red for 500 ms.

HD-tDCS

A 1-anode, 4-cathode electrode setting was used (4 x 1). HD-tDCS was administered using a battery-driven, constant-current generator with a HD-tDCS distributor (DC-Stimulator MC, neuroConn GmbH, Germany). All electrodes had a size of 1cm in diameter and were attached to ordinary EEG-caps (Easycap GmbH, Germany). 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, NJ, USA).

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 in order to modulate parietal activity during mental arithmetic (Clemens et al., 2013; Hartmann et al., 2020; Houser et al., 2015), and the agreeableness of a 2 mA anodal stimulation with a 4 x 1 electrode setting has been confirmed (Hartmann et al., 2020; Kuo et al., 2013; Nikolin et al., 2015). Each participant underwent an anodal left IPS, anodal right IPS, and one sham HD-tDCS session in counterbalanced order and with one week in between the sessions.

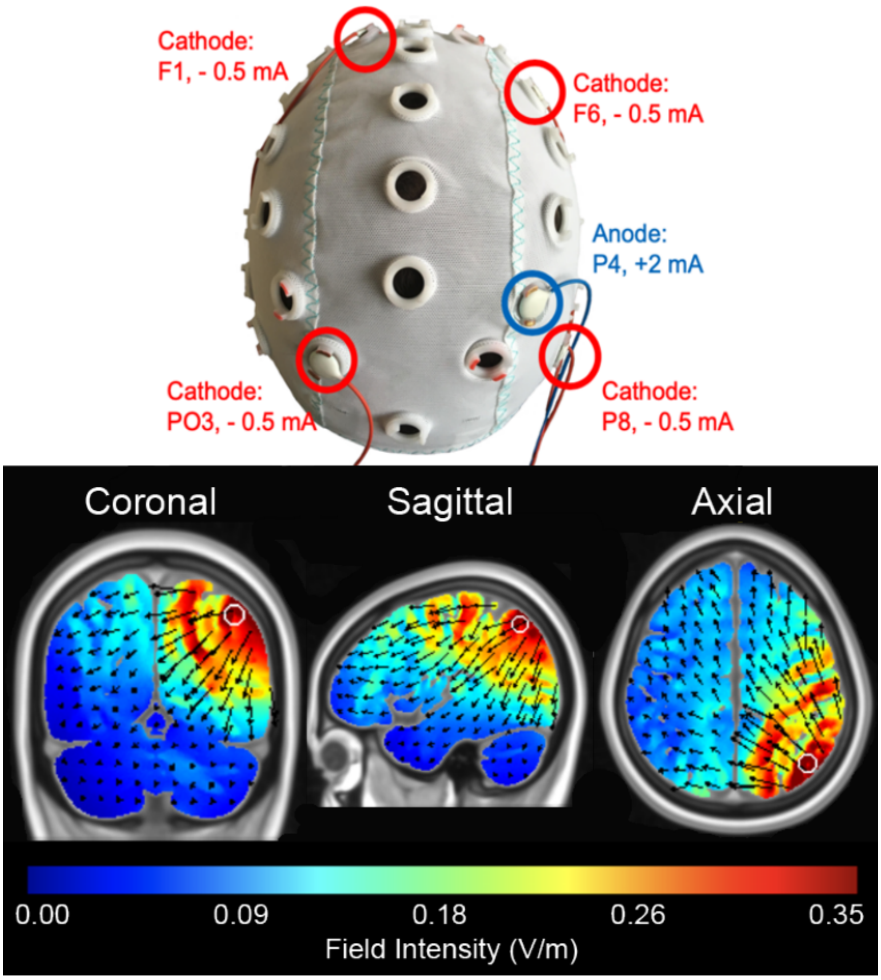
Electrode placement was the same as in Hartmann et al. (2020). In order to stimulate the left and right IPS, the anodal electrode was placed over P3 and P4 of the international EEG 10-20-system (Klein et al., 2009, 2013). The optimal electrodes montage was determined by means of software ("HD-Explore", "HD-Target") that simulate the current flow into the brain depending on the given parameters (Soterix Medical, NY, USA). 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 et al., 2010)). These were the positions F5, F2, P7 and PO4 for left parietal stimulation, and F6, F1, P8 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 **Fig. 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 BA18, BA19: < 0.17 V/m, medial parietal BA 31: < 0.13).

The procedure of stimulation was the same as in Hartmann et al. (2020). At the onset of the stimulation, current was gradually increased over a period of 30 sec until reaching the stimulation threshold of 2 mA (ramp-up phase). Following this, a constant direct current of 2 mA was applied for 25 minutes. Subsequently, the current was decreased to 0 mA over a 30-sec period (ramp-down phase). In the sham condition, the same ramp-up procedure was applied, gradually increasing the current over 30 sec until reaching the stimulation threshold. Once the threshold was reached, a full stimulation of 2 mA was delivered for 30 sec, after which the current was ramped-down to 0 mA over another 30-sec interval. The current remained off for the rest of the session. This procedure aimed to ensure that participants in both the real and sham stimulation condition experienced the initial tickling sensation of the current, rendering the two conditions indistinguishable (as validated by questionnaires, see the result section). For the sham condition, the left parietal stimulation setting was used for half of participants, and the right parietal stimulation setting 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).

Because tDCS is not effective at the beginning of stimulation (Nitsche et al., 2008; Nitsche & Paulus, 2000), participants started with the arithmetic task 5 minutes after stimulation onset. During the first 5 minutes of stimulation, participants performed 32 practice trials in which they trained the finger response mapping. Such a trial was identical to the screen of the arithmetic task where the four solution numbers were presented around the central box (see **Fig. 1**, last screen), except that the target number was an “X”, and the three lure cues were “O”. Participants then also performed 16 arithmetic practice trials before starting with the experimental trials. All participants completed these two practice blocks within 5 minutes after the onset of stimulation in all sessions. Participants completed the arithmetic task in about 15 minutes, and then started with the n-back task, which took about 4 minutes. Thus, both tasks were completed during stimulation.

Figure 2

Electrode placement and simulated brain activity of HD-tDCS



Note. 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.

As in Hartmann et al. (2020), participants were asked at the end of each session 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

RTs. RT analysis was based on correct trials (85.0%). Data trimming was performed in a two-step procedure as described by Mann et al. (2011). In a first step, responses shorter than 200 ms and longer than 5000 ms for single-step, or 8000 ms for multi-step problems were excluded (305 trials, 5.0% of correct trials). In a second step, all RTs deviating from the individual's condition mean (step size x stimulation x operation) by more than 2.5 *SD* were excluded. This procedure was repeated iteratively until no more outliers were detected, resulting in the exclusion of another 45 trials (0.8% of remaining correct trials). RTs were log-transformed for analysis, and untransformed means are reported. RTs reflect the time between the onset of the solution and participant's response.

RTs were analyzed by means of a repeated measure linear mixed-effects model using the lme4-package in R (Bates et al., 2015). The model included the fixed effect predictors stimulation (left, right, sham), operation (addition, subtraction), step size (single, multi), and all interactions of these three predictors. We also added the fixed effect predictor session (1, 2, 3) to account for training effects across sessions. Session was defined as ordered factor (Session 1 < Session 2 < Session 3), thus a significant effect of session indicates that participants improve over sessions. Given the repeated measure design, a random intercept for participant was added, as well as a random slope of stimulation per participant. Lastly, a random intercept effect was added for each problem in order to account for variance in RTs that were caused by the specific problems within each category of operation and step size (see Artemenko et al., 2015 for a similar approach). Statistical report was based on Type III Analysis of Variance (ANOVA) using Satterthwaite approximation for the calculation of degrees-of-freedom. The lme-4 analysis syntax and the normal quantile-quantile plot of the model confirming normality of residuals can be found in the supplemental material.

Errors. We did not expect HD-tDCS to have an impact on the accuracy of arithmetic problem solving. However, for the sake of completeness, we also analyzed the error rate by means of a logistic regression mixed-effect model with 1 = correct and 0 = error, using the same model specifications as described for RTs.

Control task. For the n-back task, accuracy and RTs of correctly detected targets were analyzed. For each participant, the mean accuracy over all 100 trials for each session was computed and analyzed by means of a linear mixed effect model with the fixed effects of stimulation (left, right, sham) and session (1, 2, 3), and with a random intercept for participant. Since there was no random effect for trial (as in the arithmetic task), analysis is performed on the aggregated data, thus no random slope of stimulation by participants was included into the model.

For the analysis of RTs, outliers were removed using the same procedure as described for the arithmetic task. One trial with a RT < 200 ms was excluded, and another 6 trials were excluded that deviated more than 2.5 SD over the individual mean per session. Thus, a total of 7 trials (0.6% of correct responses) were removed from analysis of RTs. Aggregated RTs were then analyzed by means of the same linear mixed effect model as for accuracy. Statistical report was based on Type III Analysis of Variance (ANOVA) using Satterthwaite approximation for the calculation of degrees-of-freedom. The lme-4 analysis syntax and the normal quantile-quantile plot of the model confirming normality of residuals can be found in the supplemental material. Data from one session was missing due to technical problems.

Results

RTs

Mean RTs for each condition (addition – single step, subtraction – single step, addition – multi step, subtraction – multi step) are illustrated in **Fig. 3a**, and the ANOVA results of the linear mixed effect model analysis are summarized in Table 2. As expected, there was a main effect of operation, $F(1,276.8) = 18.59$, $p < .001$, and a main effect of step size, $F(1,277.1) = 196.47$, $p < .001$. Participants were faster when solving addition ($M = 2111$, $SEM = 88$) than subtraction ($M = 2331$, $SEM = 91$) problems, and they were faster when solving single ($M = 1640$, $SEM = 47$) than multi step ($M = 2802$, $SEM = 97$) problems. Most importantly, there was a main effect of stimulation, $F(2,23.9) = 3.64$, $p = .042$. Pairwise comparison showed that participants were significantly faster in arithmetic problem solving during left ($M = 2136$, $SEM = 103$) when compared to sham stimulation ($M = 2318$, $SEM = 123$, $p_{\text{left vs. sham}} = .017$), and also faster when compared to right stimulation ($M = 2210$, $SEM = 103$, $p_{\text{left vs. right}} = .042$), as illustrated in **Fig. 3b**. There was no difference between sham and right stimulation ($p = .391$). The additional main effect of session, $F(2, 43.7) = 73.54$, $p < .001$, indicated that participants became faster over the three sessions (Session 1: $M = 2481$, $SEM = 119$; Session 2: $M = 2180$, $SEM = 110$; Session 3: $M = 2002$, $SEM = 95$). None of the interactions were significant. We also plotted the effect size of stimulation (difference in log RTs between left stimulation and sham) for each condition in **Fig. 3c**. This additional figure shows that the single-step addition contributed the least, while the multi-step subtraction problems contributed the most to the effect of stimulation.

Table 2

ANOVA table for the linear mixed effect model (RTs) and the linear mixed effect logistic regression model (errors).

	RT		Error	
Effect	*F*	*p*	*F*	*p*
Stimulation	3.64	.042	0.27	.767
Operation (Op)	18.59	< .001	0.57	.450
Step size (Ss)	196.47	< .001	108.92	<.001
Session	73.54	< .001	11.82	<.001
Stimulation x Op	0.39	.679	0.50	.604
Stimulation x Ss	0.59	.554	1.62	.198
Op x Ss	3.70	.055	< 0.00	.967
Stimulation x Ss	0.64	.53	1.62	.198
Stimulation x Op x Ss	0.01	.996	0.67	.510

Note. Type III ANOVA table with Satterthwaite's method.

For the previous analysis of single-step problems, problems with carry (e.g., 46 + 7 or 64 – 7) and without carry (e.g., 23 + 4 or 87 – 4) were analyzed together. Problems with carry are more complex and rely more strongly on procedural processes than problems without carry. To additionally assess whether carry moderated the effect of stimulation for the single-step problems, we repeated the analysis described above for single-step problems adding carry and all higher order interactions between carry, operation and stimulation as additional fixed effects. The separate analysis of single-step problems confirmed an effect of stimulation, although slightly below significance threshold, $F(2,3039.67) = 2.89$, $p = .056$

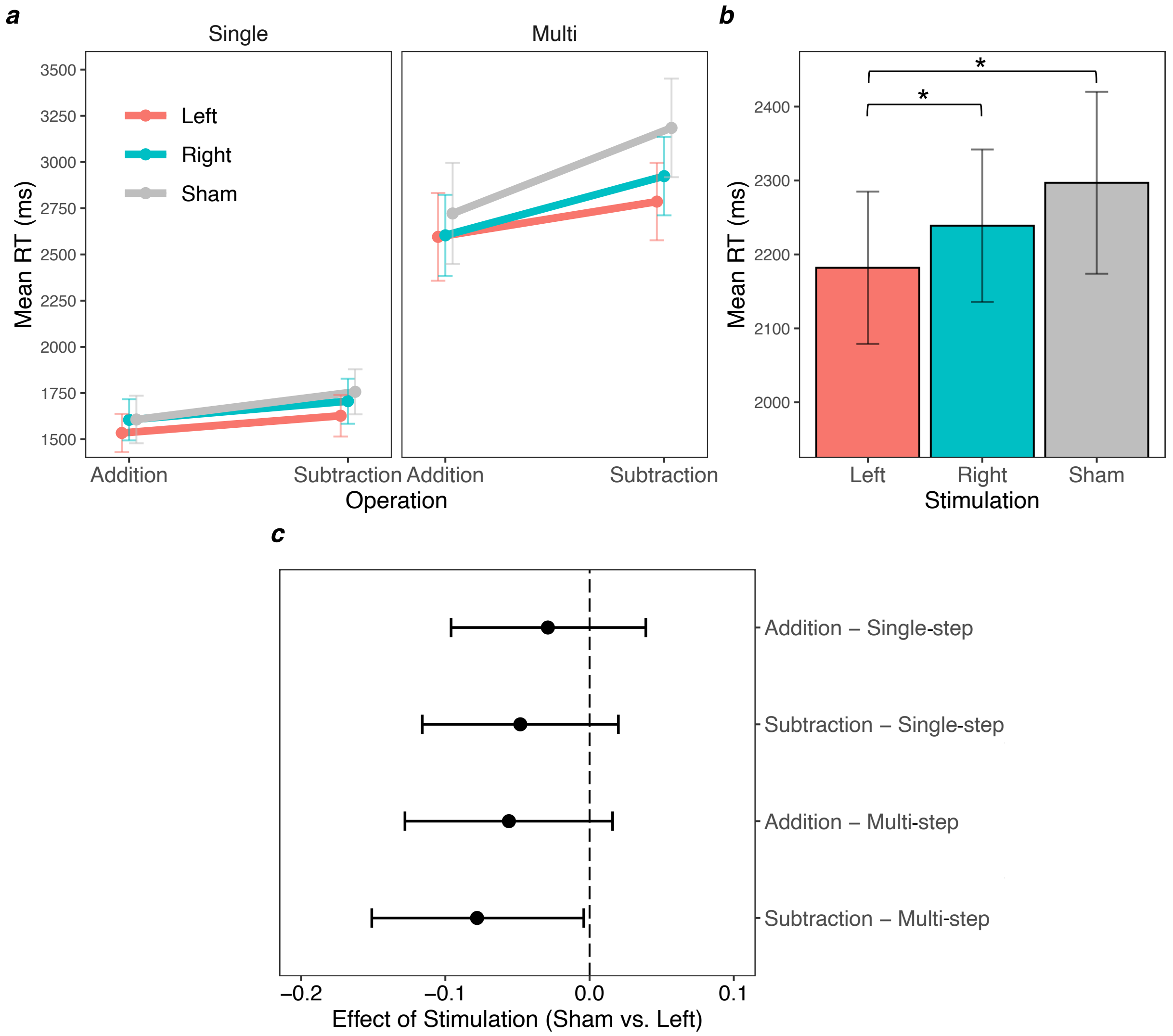
(M_{Left} = 1544, *SEM* = 63, M_{Right} = 1623, *SEM* = 69, M_{Sham} = 1654, *SEM* = 73), an effect of carry, $F(1,136.83) = 121.19$, $p < .001$ (M_{Carry} = 1893, *SEM* = 56, $M_{NoCarry}$ = 1321, *SEM* = 44), an effect of operation, $F(1,136.82) = 4.93$, $p = .028$ ($M_{Addition}$ = 1554, *SEM* = 53, $M_{Subtraction}$ = 1660, *SEM* = 58), and an effect of session, $F(2,2931.16) = 46.94$, $p < .001$ ($M_{Session1}$ = 1755, *SEM* = 71, $M_{Session2}$ = 1596, *SEM* = 71, $M_{Session3}$ = 1470, *SEM* = 59). Most importantly, there was no interaction between carry and stimulation, $F(2,3039.43) = 0.59$, $p = .552$, and no three-way interaction between carry, stimulation and operation, $F(2,3039.58) = 1.16$, $p = .313$.

Errors

Results are summarized in Table 2. There were significant main effects of step size, $F(1,279.94) = 108.92$, $p < .001$, and session, $F(2,40.74) = 11.82$, $p < .001$. Participants solved more single (*M* = 91.1%, *SEM* = 0.7) than multi (*M* = 78.8%, *SEM* = 1.1) step problems correctly, and they improved over sessions (Session 1: *M* = 82.3%, *SEM* = 1.4; Session 2: *M* = 85.5%, *SEM* = 1.2; Session 3: *M* = 87.1%, *SEM* = 1.2). As expected, there was no main effect or interaction effects of stimulation (all *p*'s > .202). There was also no main effect of operation, $F(1, 281.22) = 0.48$, $p = .490$, (addition: *M* = 85.4%, *SEM* = 1.0; subtraction: *M* = 84.6%, *SEM* = 1.1) suggesting that the adjustment of trial timing for subtraction problems was successful.

Figure 3

Results of the arithmetic task



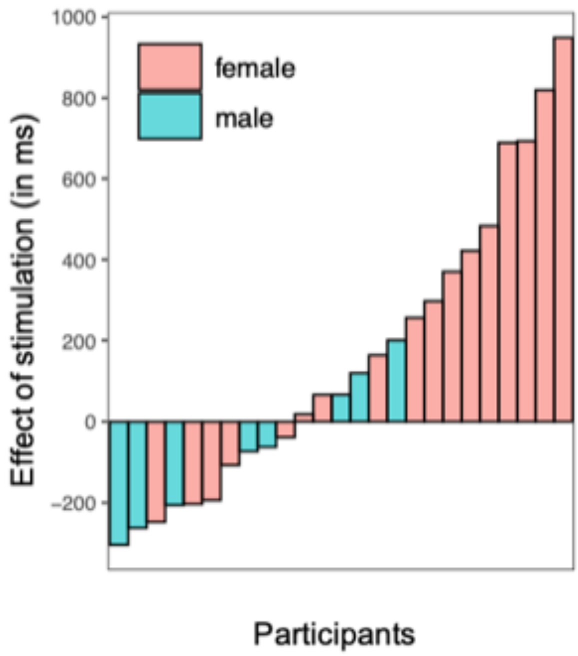
Note. Mean RTs for each type of arithmetic problem (a) and averaged for each stimulation condition (b). Asterisks indicate significant pairwise comparison ($p < .05$). (c) shows effect size of stimulation (log difference between sham and left IPS stimulation) for each type of arithmetic problem. In (a) and (b), error bars show +/- 1 SEM, and 95 CI in (c).

Individual differences

Individual differences in ms between sham and left stimulation are illustrated in **Fig. 4**, sorted by magnitude of the difference (positive values reflect faster RTs during left stimulation). The figure shows that the majority of participants showed faster RTs during left compared to sham stimulation.

Figure 4

Individual data



Note. The effect of stimulation (left – sham; in ms) for each participant. Gender it is marked in different colors.

Control task

Accuracy. The linear mixed effect analysis revealed a main effect of stimulation, $F(2, 44.48) = 4.24$, $p = .021$, and also a main effect of session, $F(2, 44.48) = 5.36$, $p = .008$. Pairwise comparison revealed that participants were less accurate during left stimulation (M = 90.6%, SEM = 1.1) when compared to sham stimulation (M = 92.7%, SEM = 0.7, $p_{\text{left vs. sham}} = .017$) and also less accurate when compared to right stimulation (M = 92.7%, SEM = 0.7, $p_{\text{left vs. right}} = .014$). There was no difference between sham and right stimulation ($p = .904$).

Participants improved accuracy over the three sessions (Session 1: *M* = 90.6%, *SEM* = 0.9; Session 2: *M* = 92.2%, *SEM* = 0.8; Session 3: *M* = 93.4%, *SEM* = 0.08).

RTs. The linear mixed effect analysis revealed no effect of stimulation, $F(2, 45.27) = 0.35$, $p = .709$ (left: *M* = 625, *SEM* = 20; right: *M* = 615, *SEM* = 21; sham: *M* = 607, *SEM* = 20), and participants did not become faster over sessions, $F(2, 45.27) = 1.44$, $p = .247$ (Session 1: *M* = 633, *SEM* = 19; Session 2: *M* = 609, *SEM* = 21; Session 3: *M* = 605, *SEM* = 20).

Stimulation-related questionnaires (discomfort, pain, recognizing sham).

A repeated measures ANOVA with the variable stimulation (left, right, sham) revealed no difference in discomfort (1 = very comfortable, 7 = very uncomfortable) across conditions, $F(2,48) = 1.42$, $p = .251$, $\eta^2_p = .06$ ($M_{\text{Left}} = 4.68$, *SEM* = 0.17; $M_{\text{Right}} = 4.60$, *SEM* = 0.18; $M_{\text{Sham}} = 4.44$, *SEM* = 0.20). The same analysis on the mean pain score revealed a significant difference in perceived pain (0 = no pain, 10 = unable to move) across stimulation conditions, $F(2,48) = 5.30$, $p = .008$, $\eta^2_p = .18$. Pain ratings during sham were significantly lower when compared to left ($p = .025$) or right ($p = .008$) stimulation, but mean pain ratings were low and varied between 1 (minimal) and 2 (mild) ($M_{\text{Left}} = 1.56$, *SEM* = 0.25; $M_{\text{Right}} = 1.68$, *SEM* = 0.25; $M_{\text{Sham}} = 1.04$, *SEM* = 0.19).

When asked at the end of the third session to guess post-hoc which of the three sessions was the sham condition, 13 out of 25 participants correctly guessed the sham session. This proportion (13/25 = 0.52) is not significantly different from the guessing chance rate of 1/3 ($p = .078$). There was no difference in confidence for this guess between participants who correctly indicated the sham session and those who did not ($M_{\text{correct}} = 2.92$, *SEM* = 0.45; $M_{\text{incorrect}} = 2.42$, *SEM* = 0.38), as revealed by independent sample *t*-test ($p = .334$). These analyses confirm the tolerability of the stimulation setting used in this study and that participants were not able to identify the different stimulation conditions accurately/confidently.

Discussion

NIBS techniques such as tDCS hold significant promise as tool for both investigating the causal involvement of specific brain areas in mental arithmetic and also for increasing arithmetic performance, which could have implications for the treatment of individuals suffering from dyscalculia and other impairments in number processing (Hauser et al., 2016; Kucian & Cohen Kadosh, 2021). However, previous studies have yielded inconsistent findings, necessitating further investigation. Therefore, the objective of this study was to shed light on the role of the left and right IPS in mental arithmetic using HD-tDCS, which, to the best of our knowledge, had not been employed for this purpose previously.

Across both single-and multi-step addition and subtraction problems, we observed that HD-tDCS applied over the left IPS resulted in increased speed of arithmetic performance. Notably, stimulation of the right IPS did not yield any significant benefits. To ascertain the specificity of these effects, we also assessed performance on a control n-back task and found no advantageous impact of left IPS stimulation. This indicates that the observed improvements in arithmetic performance were specific to arithmetic processing itself, rather than reflecting general enhancements in attention or working memory. Consequently, our results provide evidence that the IPS serves as a fundamental hub for number representation and arithmetic (e.g., Arsalidou & Taylor, 2011; Dehaene, 2011; Knops, 2017; Piazza et al., 2007), and more specifically that the left IPS is functionally involved in arithmetic problem solving across a broad range of problem types.

The observed selective effect of left IPS stimulation aligns with previous NIBS studies that have reported left hemispheric parietal specialization in number processing and arithmetic (e.g., Andres et al., 2005; Grabner et al., 2015; Hauser et al., 2013; Pesenti et al., 2000; Sasanguie et al., 2013). Our initial hypothesis proposed that the dependency on the left

IPS would vary according to the complexity of the arithmetic problem. However, our results did not support this hypothesis, suggesting that the effect of left IPS stimulation may not depend as heavily on specific characteristics of arithmetic problems as previously believed. Examination of effect sizes for the different types of problems revealed that single-step addition problems contributed the least to the facilitatory effect of left IPS stimulation, while the most challenging multi-step subtraction problems contributed the most. This descriptive observation suggests that more difficult arithmetic problems involving an extended computation phase may potentiate the effects of left IPS stimulation. It is possible that complex tasks require multiple access to number representation, thereby benefiting more from enhanced access to this representation. This finding may help explain why previous studies utilizing single-step problems have not consistently observed an effect of IPS stimulation on arithmetic performance (Hauser et al., 2016; Mosbacher et al., 2020, 2021), or why the facilitatory effect of left IPS stimulation has sometimes been restricted to more complex problems (Rütsche et al., 2015; see also Salillas et al., 2012).

Our findings holds promise for the potential use of HD-tDCS as a tool to enhance cognitive performance in individuals with impairments in number processing (Cohen Kadosh et al., 2010; Lazzaro et al., 2022). However, it is important to acknowledge that our sample did not include participants with diagnosed or self-reported number processing impairments. Therefore, it remains to be examined whether HD-tDCS-induced improvements hold true also for extreme groups, such as individuals with dyscalculia. Additionally, we found that females demonstrated higher improvements compared to males, suggesting that previous studies should have a closer look at gender effect.

In the arithmetic task, we included a time delay between the last operand and the solution. A time delay was induced to motivate participants to continue the mental arithmetic process (cf. stimuli and task procedure). The duration of the delay was determined based on a pretest and was set to be rather short (750 ms), but we cannot rule out that in some trials, participants might might have already solved the problem before the solution numbers appeared, particularly when they quickly retrieved the solution from memory. This might reduce the chance to find a subtle facilitatory effect of IPS stimulation for quickly solved problems. Since there was a selective enhancing effect of left but not right IPS stimulation, and since all type of problems contributed to this effect (**Fig. 3c**), we do not think that this methodological issue had a critical effect on our results. However, it limits the conclusions about a possible moderating effect of problem difficulty, which should be further addressed in future research.

Furthermore, our experimental approach did not allow to disentangle the specific effects of IPS stimulation on number representation and numerical computation. It is plausible that the observed effects were driven by an enhanced access to number meaning, an augmentation of mental manipulation processes, or a combination of both. To gain a deeper understanding of these underlying mechanisms, future research should consider integrating IPS stimulation with neuroimaging techniques such as fMRI or electroencephalography (EEG). A combination of these approaches would enable the exploration of neural processes and provide valuable insights into the precise mechanisms involved in IPS stimulation effects (Hauser et al., 2016; Mosbacher et al., 2020; Rütsche et al., 2015). For example, Rütsche et al. (2015) discovered that the effects of IPS stimulation were associated with modulations of oscillatory EEG activity in different frequency bands. Specifically, they found distinct patterns of modulation in the alpha band related to procedural arithmetic processes, while modulations in the theta band were linked to memory-based arithmetic processes. Furthermore, they observed that larger arithmetic problems were associated with increased lower-alpha desynchronization, whereas smaller problems resulted in decreased theta synchronization. These findings indicate a differential engagement of the left IPS in arithmetic problem-solving of varying complexity. This underscores the considerable variability in brain stimulation effects based on the specific neuro-cognitive processes involved. Integrating NIBS with neuroimaging methods might also provide valuable insights not only into the different effects of individual brain regions, such as the IPS, but also into the broader cortical network (Pisoni et al., 2018).

Additionally, it is worth noting that our study unexpectedly revealed impairment in the n-back-task during left IPS stimulation, for which we currently lack an explanation. This finding may warrant further investigation in future research. As a limitation of this study, we did not counterbalance the order of the tasks (arithmetic task, control tasks), which further restricts conclusions about the differential effect of IPS stimulation on the two tasks.

Despite the aforementioned limitations, we believe that this study significantly contributes to the growing body of evidence supporting the functional involvement of the left IPS in mental arithmetic. It serves as an important steppingstone for future research in this domain. Previous studies have demonstrated that conventional tDCS applied to the IPS can not only enhance performance but also improve mathematical learning (Grabner et al., 2015). With the current study establishing performance improvements through left IPS stimulation using HD-tDCS, it opens up exciting avenues for investigating the potential use of HD-tDCS as a tool to enhance arithmetic learning. The enhanced spatial precision and reduced inhibitory effects of HD-tDCS make it a particularly promising intervention, targeting specific brain regions more precisely and possibly leading to more effective and targeted enhancements in arithmetic performance and learning.

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Statements and Declarations

Competing interests

The authors declare no competing interests.

Data availability statement

Data and analysis code are available at: https://osf.io/f2jgn (analysis code is in the supplemental material file)

We confirm that we have reported all measures, conditions, data exclusions and information regarding the sample size used in this study. Analysis code can be found in the supplemental material.

Ethics declaration and consent to participate

Participants gave written informed consent prior to the study. The study was approved by the Ethics Committee of the University of Bern and experiments were conducted according to their guidelines.

Author contribution declaration

M.H. created the experiment, conducted data curation, data analyses and visualization, wrote the first draft and edited the manuscript. M.D. contributed to data interpretation and contributed in writing and editing the manuscript. All authors reviewed the manuscript.