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Original Article

Making the rich richer: Frontoparietal tDCS enhances transfer effects of a single-session distractor inhibition training on working memory in high capacity individuals but reduces them in low capacity individuals

Marlen Schmicker[a,*], Inga Menze[a], Christine Schneider[a], Marco Taubert[b,d], Tino Zaehle[c,d], Notger G. Mueller[a,d]

[a] *Neuroprotection Lab, German Center for Neurodegenerative Diseases (DZNE), Magdeburg, Germany*
[b] *Chair for Training Science, Faculty for Humanities, Otto-von-Guericke University, Magdeburg, Germany*
[c] *Department of Neurology, Otto-von-Guericke University, Magdeburg, Germany*
[d] *Center for Behavioral Brain Sciences, Magdeburg, Germany*

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ABSTRACT

Working memory (WM) performance depends on the ability to extract relevant while inhibiting irrelevant information from entering the WM storage. This distractor inhibition ability can be trained and is known to induce transfer effects on WM performance. Here we asked whether transfer on WM can be boosted by transcranial direct current stimulation (tDCS) during a single-session distractor inhibition training. As WM performance is ascribed to the frontoparietal network, in which prefrontal areas are associated with inhibiting distractors and posterior parietal areas with storing information, we placed the anode over the prefrontal and the cathode over the posterior parietal cortex during a single-session distractor inhibition training. This network-oriented stimulation protocol should enhance inhibition processes by shifting the neural activity from posterior to prefrontal regions. WM improved after a single-session distractor inhibition training under verum stimulation but only in subjects with a high WM capacity. In subjects with a low WM capacity, verum tDCS reduced the transfer effects on WM. We assume tDCS to strengthen the frontostriatal pathway in individuals with a high WM capacity leading to efficient inhibition of distractors. In contrast, the cathodal stimulation of the posterior parietal cortex might have hindered usual compensational mechanism in low capacity subjects, i.e. maintaining also irrelevant information in memory. Our results thus stress the need to adjust tDCS protocols to well-founded knowledge about neural networks and individual cognitive differences.

1. Introduction

Successful working memory (WM) performance relies on the ability to select relevant information and to inhibit distractors. The posterior parietal cortex has been associated with WM storage as WM capacity was correlated with the bilateral activity in the intraparietal and intraoccipital sulcus (Todd and Marois, 2005, 2004). In contrast, the inhibition of distractors is linked to prefrontal activity, especially in the middle frontal gyrus, but also with activity in the basal ganglia (Chao and Knight, 1998; McNab and Klingberg, 2008). Hence, working memory is suggested to rely on a frontoparietal network (Cabeza and Nyberg, 2000; Constantinidis and Klingberg, 2016) in which attentional top-down control (i.e. distractor inhibition) over posterior parietal storage areas is attributed to prefrontal areas, implicating a close neurophysiological connection of these two regions (Awh, E; Jonides, 2001; Brass et al., 2005; Curtis and D'Esposito, 2003; Nobre et al., 2011; Zanto et al., 2010).

Electrophysiological investigations indicate, however, that the functioning of the frontoparietal network varies with working memory capacity. As such, it was found that individuals with a high WM capacity (high capacity individuals, HCI) show successful distractor inhibition which results in efficient WM maintenance. In contrast, low WM capacity individuals (low capacity individuals, LCI) unnecessarily store unfiltered distractors in memory and strain their WM capacity limit (Vogel et al., 2005; Vogel and Machizawa, 2004). An fMRI study (McNab and Klingberg, 2008) showed that frontal activity, reflecting preparation of distractor inhibition, positively correlates with an individual's WM capacity, whereas unnecessary storage of distractors in posterior parietal regions negatively correlates with basal ganglia activity.

Abbreviations: WM, working memory; WMC, working memory capacity task; HCI, high capacity individuals; LCI, low capacity individuals; DIIN training, distractor inhibition training; WM-, condition without distractors; WM+, condition including distractors.

[*] Corresponding author.

E-mail address: Marlen.Schmicker@DZNE.de (M. Schmicker).

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These results indicate different accentuations of the frontoparietal network nodes in HCI and LCI, which are reinforced by positive correlations of WM performance with the activity and connectivity of this network (Gray et al., 2003; Klingberg, 2006; Kwon et al., 2002).

Since WM performance and inhibition of distractors are closely related, both behaviorally and physiologically, training of one of these cognitive functions should have an impact on the other. In fact, it was reported that training of distractor inhibition leads to transfer effects that were quantified by WM improvement (Li et al., 2017; Schmicker et al., 2016).

Furthermore, Schmicker and colleagues (Schmicker et al., 2016) found transfer effects on WM after a five-day distractor inhibition training (DIIN training). However, it remains elusive which exact processes were influenced by the DIIN training. A direct modulation of task-related brain activity would allow causal inferences.

A common method for such causal brain modulation is the transcranial direct current stimulation (tDCS). The current flow between the anode and the cathode causes shifts of the membrane's resting potential, with the anode increasing and the cathode decreasing excitability of stimulated brain areas (Nitsche and Paulus, 2000; Utz et al., 2010).

Previous results concerning tDCS modulation of WM and distractor inhibition have been contradicting, even in studies targeting the same brain regions. As such, a number of studies have found an improvement in the ability of inhibiting distractors and WM performance by frontal anodal and parietal cathodal stimulation (Cosman et al., 2015; Heimrath et al., 2012; Heinen et al., 2016; Moos et al., 2012; Weiss and Lavidor, 2012) but also anodal stimulation of the parietal cortex was able to improve WM performance (Heinen et al., 2016; Hsu et al., 2014; Tseng et al., 2012).

Yet, these studies have only addressed the modulation of either WM storage or distractor inhibition, without considering their direct interaction. An important contribution to this question was made by Li et al. (2015), who examined the specific involvement of prefrontal and posterior parietal regions in the interplay of WM and distractor inhibition processes via tDCS. Anodal tDCS was applied either over prefrontal or parietal regions during a WM change detection paradigm. The stimulation of the prefrontal areas increased inhibition efficiency in conditions with distractors, whereas posterior parietal stimulation increased performance in conditions without distractors.

All the aforementioned studies have in common that they only targeted one brain region and only investigated the immediate changes in the tDCS-modulated task. In such conventional set-ups the active electrode is placed over the brain region that is considered most relevant to the task, while the reference electrode is located over a hypothetically irrelevant region (Nasseri et al., 2015). However, the current flow, and thus which brain areas are stimulated, depends on the placement of both electrodes (Faria et al., 2011). Hence, it is fair to assume that tDCS not only modulates local activity in one network node, but causes a reaction within whole neuronal networks (Fertonani and Miniussi, 2017; Filmer et al., 2014; Krause and Cohen Kadosh, 2014; Meinzer et al., 2012). There are in fact findings that hint to the relevance of stimulating entire neuronal networks. Over the course of a multi-day WM training (Jones et al., 2017) anodal tDCS over frontal and parietal regions (alternating per day), led to a significant improvement in WM performance as well as in cortical network efficiency and connectivity, compared to sham. However, inter-individual differences were not taken into account.

Here, we therefore investigated whether tDCS during a single-session DIIN training can modulate the effects on a change-detection WM task in high and low WM capacity individuals (HCI and LCI). For this purpose, we adapted an established paradigm (Schmicker et al., 2016) by reducing the DIIN training to a single-session and applying tDCS online. Our single-session DIIN training asked the participants to compare the orientation of color-cued rectangles on the left and right half of the test display. As such, it put a demand solely on selective attention, in particular distractor inhibition. To assess transfer effects on the non-trained function of WM, participants completed a change-detection task with or without distraction (WM-/WM+). Target-rectangles had to be memorized and after a delay it had to be reported if there was a change in orientation. This task primarily required working memory and is therefore qualified as a transfer task.

Due to the reduced duration, the single-session DIIN training should actually be termed “practice”. However, DIIN “training” remains consistent with common terminologies of the corresponding research context, so we use this term.

We decided to use a theory-driven, network-oriented tDCS approach that allowed the simultaneous modulation by both electrodes, thereby considering the specialization of the frontoparietal network's key regions: We placed the anode over prefrontal areas to increase distractor inhibition related activity and the cathode over the posterior parietal cortex to reduce unnecessary storage activity in preparation for the following WM transfer task. The idea was to boost WM performance by driving frontal distractor inhibition activity rather than parietal storage. We thereby wanted to attenuate maladaptive strategies of maintaining distractors in WM storage, which seems especially characteristic in LCI, and instead promote a more efficient WM performance by supporting distractor inhibition related activity in frontal areas. In this way, the stimulation was assumed to gate an optimal utilization of the frontoparietal network that facilitates transfer. Taking into consideration that HCI and LCI differ concerning distractor inhibition and storage processes (McNab and Klingberg, 2008; Vogel et al., 2005; Vogel and Machizawa, 2004) and that individual response to tDCS varies in relation to baseline network functioning (Krause and Cohen Kadosh, 2014), the main aim was to investigate whether there are capacity-specific effects following network-oriented tDCS. Accordingly, we compared HCI and LCI by dividing our sample by means of an independent capacity measure. We compared pre-post changes in WM after single-session DIIN training alone (sham) and after stimulated single-session training (verum).

2. Methods and Material

2.1. Sample

Eighty-six healthy, young subjects (18–30 years; $\text{mean}_{\text{age}} = 23.36$, $SD = 2.93$; female = 65.1 %) participated in the study. A prior G*Power Analysis (Faul et al., 2007) for interaction effects of within- and between-subject factors with an expected low to medium effect size of f = 0.2 and a target power of = .85 resulted in a suggested total sample size of 84 participants. Exclusion criteria involved left-handedness, visual impairments, neurological disorders and metal implants in/on the head. Subjects were randomly assigned to either the sham or the verum condition. After correcting for outliers, the sham group contained 40 subjects, the verum group 38 subjects. Both groups neither differed in age ($\text{age}_{\text{sham}} = 23.43$; $\text{age}_{\text{verum}} = 23.21$, $p = .740$) nor in their education (education in $\text{years}_{\text{sham}} = 15.72$; education in $\text{years}_{\text{stim}} = 15.66$, $p = .907$).

Subjects participated voluntarily in the experiment and gave their written, informed consent in accordance with the Declaration of Helsinki. They either received course credit or money (9 €/h) as compensation. The study was approved by the ethics committee of the University of Magdeburg (Germany).

2.2. Experimental tasks

All tasks were programmed, presented and recorded with Presentation® (Version20.1 12.04.17, Neurobehavioral Systems, Inc., Berkeley, CA, www.neurobs.com). Subjects were placed in front of a 22 inch monitor (resolution: 1920 × 1080 Pixel, refreshing rate: 60 Hz) and used the left (right index finger) and right (right middle finger) arrow key of a standard keyboard to respond. Stimuli in all tasks were red (RGB: 242|12|12) and green (RGB: 0|229|0) rectangles, presented against a

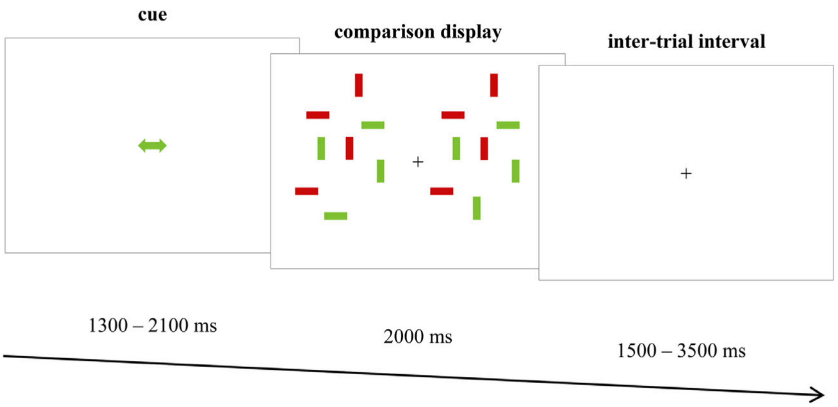

Fig. 1. Schematic depiction of the single-session DIIN training. In this example, the subject had to indicate whether the orientation of green rectangles is identical in the left and right half of the display or if they differed.

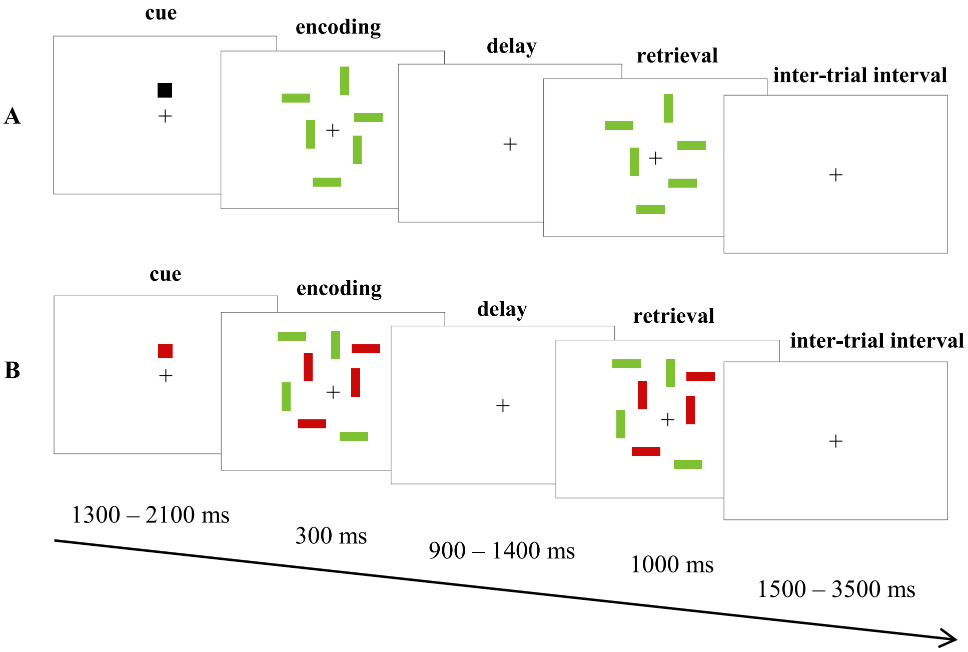

Fig. 2. Schematic depiction of the WM-/WM+ transfer task. (A) change trial of the WM- condition without distraction, in which all green rectangles are to be remembered. (B) no-change trial of the WM+ condition with distraction, in which the red rectangles are to be remembered. The green rectangles serve as distractors that are to be ignored.

grey background (RGB: 128|128|128). The size of stimuli was 1.43° x 0.29° viewing angle. A central fixation cross was presented in all tasks.

2.2.1. Independent working memory capacity (WMC)

In this adaption of the change-detection task by Vogel et al. (2005) subjects were presented red or green rectangles (100 ms), whose orientation had to be encoded and remembered. After a short delay (900 ms), the test display was presented (2000 ms). Subjects indicated whether there was a change in orientation of one of the rectangles. A change occurred in 50 % of the trials, whereby stimuli tilted 30°, 60°, 90°, 120° or 150°. The set-size ranged from 2 to 7 items. The task comprised 4 blocks with a total of 144 trials and took 10 min. The WMC paradigm served the allocation of subjects to the HCI and LCI group by using a median split.

2.2.2. Single-session DIIN training

The single-session DIIN training was adapted according to Schmicker et al. (2016). Subjects were asked to compare the orientation of green or red rectangles and indicate whether the orientation of target items in the left and right half of the comparison display was identical or different (fig. 1). A colored cue (red or green double arrow, balanced over the task) indicated the target color. The set-size ranged from 4 to 6 target rectangles with the same number of counter-colored distractors. The left and right halves of the display were each 1.79° viewing angle away from the fixation. Subjects underwent 6 blocks of 50 trials each. The duration of the DIIN training was ca. 45 min.

2.2.3. WM without and with distraction (WM-/WM+)

This change-detection task, adapted according to Schmicker et al. (Schmicker et al., 2016), was the primary outcome to measure transfer on WM performance. Similar to the WMC task, subjects had to encode and remember the orientation of red or green rectangles and decide after a delay whether rectangles changed their orientation. The task comprised a condition without (WM-; fig. 2A) and with distraction (WM+; fig. 2B). In the latter, a cue indicated the color of the target-rectangles while the distractors of the other color were presented concurrently. Set-size ranged from 4 to 6 target stimuli. In WM+, the same number of distractors in the counter-color were added. In 50 % of the trials a target changed its orientation. The task was divided into 4 blocks of 36 trials each and lasted 30 min.

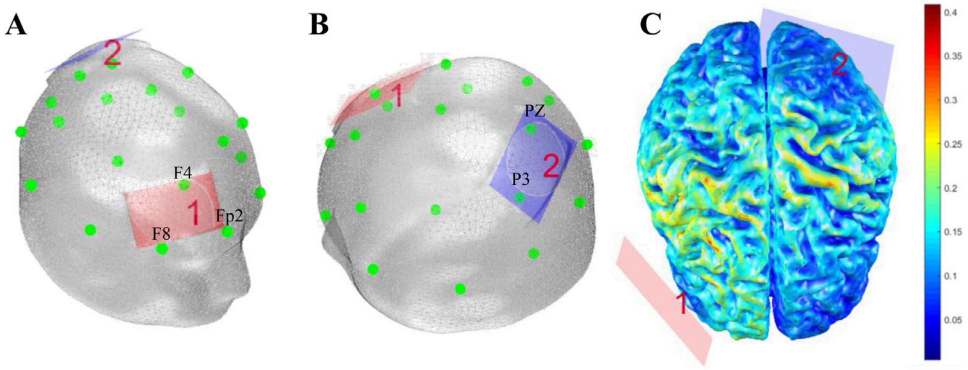

Fig. 3. Simulation of electrode montage via COMETS 2.0. The international 10–20 system was used for positioning. (A) Positioning of anode over prefrontal region. (B) Positioning of cathode over posterior parietal region. (C) Simulated current density in Joule.

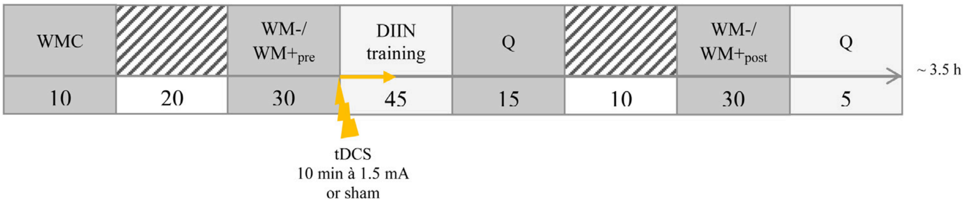

Fig. 4. Experimental procedure. WMC = independent assessment of working memory capacity; WM-/WM+ = working memory task without (-) and with (+) distraction; DIIN training = single-session distractor inhibition training; Q = Questionnaires. Within the striped areas further neuropsychological tests (Iowa Gambling Task and Corsi-Block Tapping) were assessed which are not reported here.

2.3. *tDCS protocol*

tDCS was applied via the DC-Stimulator by neuroConn and was single-blinded to the subjects. Examiners followed a standardized protocol to handle participants and questions in order to avoid any bias. The two sponge electrodes (5 × 7 cm) were soaked in 0.9 % saline solution. The placement of electrodes was planned with COMETS 2.0 (Matlab R2018a, The MathWorks, Inc., Natick, Massachusetts, United States; Lee, Jung, Lee, & Im, 2017). In order to target the right prefrontal cortex via the anode, particularly the middle frontal gyrus (McNab and Klingberg, 2008), and the left posterior parietal cortex via the cathode, especially the intra-parietal sulcus (Vogel et al., 2005), the electrode positions according fig. 3 were chosen.

We opted for a lateralized set-up foremost to lower the risk for side-effects due to increased current density. Several reasons supported the set-up of the right frontal anode and left parietal cathode. Firstly, pronounced activity in the right middle frontal gyrus was found under distractor inhibition (McNab and Klingberg, 2008; Schmicker et al., 2016). Secondly, higher task demands resulted in a right-dominant prefrontal activation, reflecting higher executive control (D'Esposito et al., 2000; Mayer et al., 2007; Rypma et al., 1999; Wager and Smith, 2003). Thirdly, the main argument to target the left posterior parietal cortex was absence of hemispheric specialization of posterior parietal storage activity (Todd and Marois, 2005, 2004). Electrodes' positions were determined with the international 10-20 system and EEG-caps were used for appropriate placement and fixing of electrodes.

The current strength was 1.5 mA with a fade-in and fade-out interval of 1 s. The stimulation was delivered during the beginning of the single-session DIIN training. Whereas the sham stimulation lasted 30 s, the verum stimulation lasted 10 min. The aim of this procedure was to cause facilitation effects of distractor inhibition-related frontoparietal network activity by accentuating neural activity in prefrontal regions. We ensured a delay of approximately 45 min between application of tDCS and post assessment of WM-/WM+ performance, in order to avoid sensational or motoric after effects (Ohn et al., 2008). tDCS should only boost advantageous distractor inhibition activity which was thought to be transferrable to the WM-/WM+ task.

2.4. *Procedure and design*

At first, subjects did the independent assessment of their WM capacity (WMC). The pre-assessment of WM-/WM+ followed. Then, the tDCS electrodes were positioned and the proper start of stimulation was ensured before the single-session DIIN training commenced. Afterwards, the tDCS set-up was removed and subjects filled out a questionnaire asking for side-effects of the stimulation (5-point Likert scale) and checking for successful blinding. At last, the post-assessment of the WM-/WM+ was conducted (fig. 4).

The study was designed as a *mixed design.* The within-subject factor *time* resulted from the multiple measurements of WM-/WM+ task. The between-subject factors included *stimulation* (sham vs. verum) and *WM capacity* (LCI vs. HCI). The classification in LCI and HCI was based on a median split in the WMC. *WM capacity* was calculated after data collection according to the formula by Pashler (Pashler, 1988), which is more sensitive for whole display recognition (Rouder et al., 2011). The cutoff for the median split was *Pashler's* $K = 2.2575$. By the combination of the factor levels of *stimulation* and *WM capacity*, four groups resulted (Table 1).

2.5. *Data Analyses*

Data Analyses were conducted with IBM SPSS Statistics 21. Trials with RT < 100 ms were excluded from analyses. Missed answers were rated as incorrect, as subjects weren't able to fulfill the expected task demands. Outliers, defined as 2 *SD* from the mean percentage of correct answers (%correct) in the single-session DIIN training or the pre-assessment of the WM-/WM+, were excluded from the statistical evaluation (sham: 4 subjects; verum: 3 subjects). Due to a technical issue, the *WM capacity* of a subject in the verum group couldn't be determined.

Table 1
Number of participants according to stimulation groups and working memory capacity.

		Working Memory Capacity		
		LCI	HCI	
stimulation	sham	24 (1.78 ± 0.34)	16 (2.79 ± 0.37)	*40*
	verum	15 (1.96 ± 0.24)	23 (2.72 ± 0.47)	*38*
		39	*39*	

Annotations. LCI = low working memory capacity individuals. HCI = high working memory capacity individuals. Under the number of participants for each factor combination, the mean working memory capacity and standard deviation is reported in parentheses.

Overall, 78 subjects remained for the statistical analyses (n_{sham} = 40, n_{stim} = 38).

Interaction effects were of primary interest to check for dependence of individual tDCS effects on *WM capacity*. For the single-session DIIN training we analyzed overall performance (%correct) and reaction times (RT) via 2 × 2 ANOVAs with the between-subject factors *stimulation* and *WM Capacity*. Subsequently, we analyzed performance patterns based on %correct. Therefore, we ran a 2 × 2 × 6 repeated measures ANOVA (rmANOVA) with the between-subject factors *stimulation, WM capacity* and the within-subject factor *experimental blocks*.

For our primary outcome WM-/WM+ we conducted 2 × 2 × 2 rmANOVAs for %correct and RT, with the between-subject factors *stimulation, WM capacity* and the within-subject factor *time* (pre vs. post) on the overall performance. We additionally ran these 2 × 2 × 2 rmANOVA separately for %correct in WM- and WM+ to analyze if effects were specific to one condition. Furthermore, we subsequently analyzed whether performance gains, defined as the change in performance from pre- to post, differed between groups. Post-hoc comparisons between groups were corrected according to the Tukey-Kramer method as it is more robust for unequal sample sizes. For post-hoc comparisons of levels of within-factors, Bonferroni correction was used. Preconditions were tested and satisfied for all statistical analysis. The defined significance level of all calculations was set at α = .05.

3. Results

Pretest equivalence in the primary outcome of the WM-/WM+ transfer task was checked with a one-way ANOVA taking all four factor combinations into account (HCI_{sham}, $\text{HCI}_{\text{verum}}$, LCI_{sham}, $\text{LCI}_{\text{verum}}$). Pretest-equivalence was observed as the four groups did not differ in their performance before the single-session DIIN training ($F(3,74) = 0.387$, $p = .762$, $\eta p^2 = .015$). Overall, 74.4% of the verum group and 70% of the sham group believed that they had received the real stimulation. A binomial test against chance probability (50%) confirmed that blinding can thus be considered successful ($p_{\text{sham}} = .017$; $p_{\text{verum}} = .003$). The rated tingling sensation and itching, however, was more present in the verum group (*mean* = 3.62) compared to sham (*mean* = 2.73, $p = .001$). Both groups did not differ in other side effects (burning sensation/pain, headache, nausea, concentration problems, discomfort).

3.1. Effects within the single-session DIIN training

With regard to overall performance in the single-session DIIN training, there were no significant effects and group differences concerning %correct and RT (*supplementary table 1*). The analysis of the performance patterns was based on the performance (%correct) within each of the six experimental blocks of the DIIN training. There were no significant interaction effects (fig. 5). Only the main effect for *experimental block* was significant ($F(4.58, 338.75) = 10.59$, $p \leq .001$, $\eta p^2 = .125$). The performance of the first experimental block over all groups differed significantly from the performance in all other blocks ($p \leq .001$) except from the third and fourth block. Furthermore, performance differed between block 2 and 4 ($p = .025$), 3 and 2 ($p = .017$) as well as block 3 and 6 ($p = .014$). Detailed information about the performance (in %correct) within the experimental blocks for each group can be found in supplementary table 2.

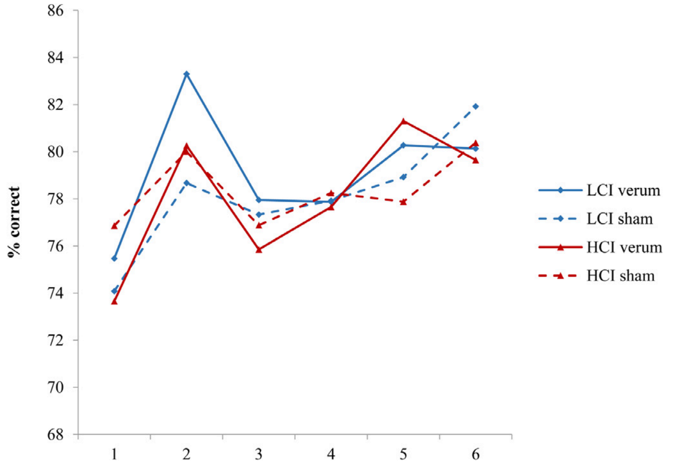

Fig. 5. Performance patterns in experimental blocks of the single-session DIIN training. For reasons of clarity, the error bars are not depicted.

3.2. Transfer effects on working memory

A significant three-fold interaction between the factors *time* x *stimulation* x *WM capacity* was found for %correct in WM overall ($F(1, 74) = 7.10$, $p = .009$, $\eta p^2 = .088$; fig. 6A). The four experimental groups improved their performance differently over time. Whereas HCI in the verum group highly enhanced from pre (77.51%) to post (82.87%), LCI of the verum group showed the smallest change in performance from pre (75.97%) to post (77.50%). LCI_{sham} (pre = 76.07%, post = 80.42%) and HCI_{sham} (pre = 77.04%, post = 79.99%) enhanced similarly to $\text{HCI}_{\text{verum}}$.

On the basis of the significant interaction, we ran additional analyses for the sub conditions WM- and WM+ and found that the three-fold interaction did not survive in WM-. Only the main effect *time* could be shown ($F(1, 74) = 32.93$, $p \leq .001$, $\eta p^2 = .308$), indicating a significant performance difference between pre and post (fig. 6B). In WM+, however, the three-fold interaction was significant ($F(1, 74) = 8.89$, $p = .004$, $\eta p^2 = .107$; fig. 6C and *supplementary table 3*). The performance increase from pre (74.28%) to post (80.04%) in $\text{HCI}_{\text{verum}}$ was considerably higher than in $\text{LCI}_{\text{verum}}$ (pre = 72.59%, post = 73.32%). Similar to $\text{HCI}_{\text{verum}}$, LCI_{sham} increased performance from pre (72.68%) to post (77.71%). We observed the lowest increase in HCI_{sham} from pre (75.78%) to post (76.04%).

There was no significant three-fold interaction *time* x *stimulation* x *WM capacity* on RT in WM overall. Only the main effect *time* reached significance ($F(1, 74) = 8.88$, $p = .004$, $\eta_p{}^2 = .107$; *supplementary table 4*).

3.3. Performance gains in working memory

For further analyses, we examined if the performance gains differed significantly between the four groups (*see also supplementary table 5*). Performance gains were defined as the difference between post performance and pre performance (Δ performance). We found a significant effect of groups on the WM overall performance gain ($F(3,74) = 2.82$, $p = .045$, $\eta p^2 = .103$). Hereby, the performance gains between $\text{HCI}_{\text{verum}}$ and $\text{LCI}_{\text{verum}}$ differed significantly (*mean difference* = 3.84, $p = .04$; fig. 7A).

In WM-, performance gains from pre to post did not differ significantly between groups (fig. 7B). Comparing the performance gains from pre to post in WM+ between groups, we found a significant main effect

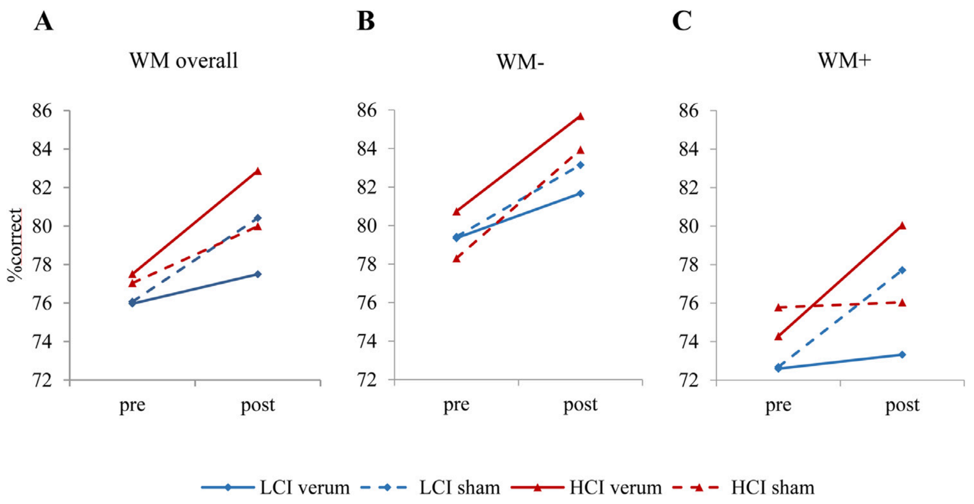

Fig. 6. Performance in WM overall and its sub conditions over time. (A) Performance in WM overall. (B) Performance in WM- condition without distraction. (C) Performance in WM+ condition with distraction. For reasons of clarity, the error bars are not depicted.

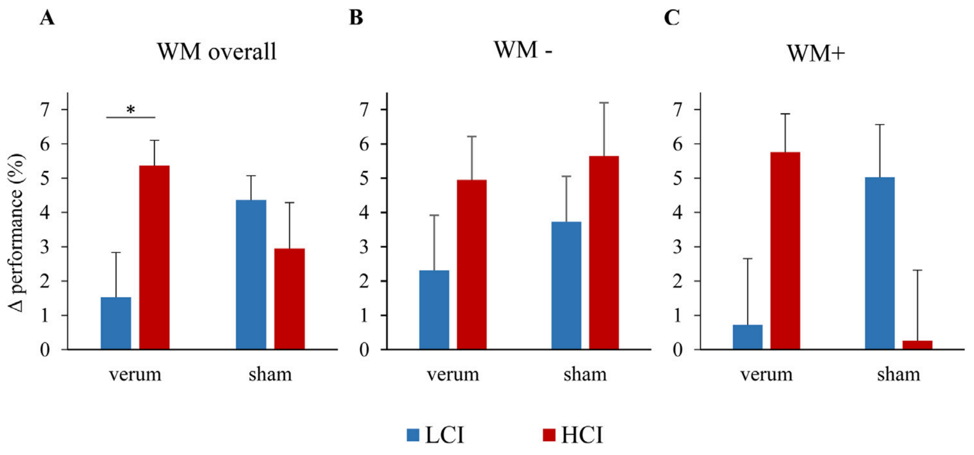

Fig. 7. Performance gain in WM overall and its sub conditions. Performance gain was assessed as change in performance from pre to post. (A) Performance gain in WM overall (B) Performance gain in WM- condition without distraction. (C) Performance in WM+ condition with distraction. Error bars represent 1 standard error.

($F(3, 74) = 3.02$, $p = .035$, $\eta p^2 = .109$; fig. 7C). In the post-hoc comparisons, the difference in performance gain of $\mathrm{HCI}_{\mathrm{verum}}$ and $\mathrm{LCI}_{\mathrm{verum}}$ did not reach significance when corrected (*mean difference* = 5.04, $p = .151$, $p_{uncorrected} = .036$). Interestingly, the mean difference in performance gain of $\mathrm{HCI}_{\mathrm{verum}}$ and $\mathrm{HCI}_{\mathrm{sham}}$ showed a marginal trend for significance (*mean difference* = 5.50, $p = .090$, $p_{uncorrected} = .020$).

We additionally ran a correlation analyses and found that the increase from WM $\mathrm{overall}_{\mathrm{pre}}$ to WM $\mathrm{overall}_{\mathrm{post}}$ correlated significantly with the *WM capacity* only in the verum group ($r_S = .366$, $p = .024$), but not in the sham group ($r_S = -.156$, $p = .337$).

4. Discussion

This study aimed to modulate transfer effects of a single-session DIIN training on WM performance by tDCS. A theory-driven, network-oriented approach was expected to shift neural activity from posterior parietal to prefrontal regions, thereby improving the trained ability to inhibit distractors. We found that the degree of transfer under tDCS depended on the individual WM capacity. As such, high WM capacity individuals (HCI) displayed larger training-induced transfer benefits in terms of performance gain from pre to post under tDCS, while such benefits were scarce in low WM capacity individuals (LCI) after tDCS application. Without tDCS, however, LCI showed a transfer effect that was comparable to the one in HCIs who received verum tDCS.

4.1. Stimulation effects within the trained task

All subjects improved within the single-session of the DIIN training. Neither stimulation nor WM capacity had an influence on this improvement. Stimulation effects might be covered by practice effects of the 45 minutes lasting DIIN training. On a descriptive level, we observed a larger performance increase from the first to the second block in the verum groups. This may imply that the stimulation indeed impacted the inhibition process given the temporal overlap these experimental blocks with the application of verum tDCS. Yet, these differences did not reach significance.

4.2. General stimulation effects on working memory

Irrespective of tDCS, WM performance improved from the first to the second session, a finding we had previously observed (Schmicker et al., 2016). No general stimulation effect was found, assumingly due to the expected interindividual variance of WM network accentuation in participants (Gray et al., 2003; Klingberg, 2006; Kwon et al., 2002).

4.3. Capacity-dependent stimulation effects on working memory

We observed that tDCS had a supportive effect on transfer to WM in HCI but a detrimental effect in LCI. The non-significant comparison of transfer gains in the WM+ sub condition between the verum groups can be explained by the high variance. However, the descriptive trends and the significant overall effect of group speak for substantial differences in tDCS response with regard to WM capacity in the distractor condition. This result contradicts the intuitive assumption that LCI would benefit more from tDCS (Gözenman and Berryhill, 2016; Habich et al., 2017; Heinen et al., 2016; Hsu et al., 2014; Ruf et al., 2017; Wu et al., 2014). One difference between our experimental protocol and other studies was the outcome task. Whereas most previous studies assessed pre-post differences in a task that was similar or identical to the modulated one, we focused on pre-post differences in a task that was never performed under tDCS. Furthermore, it has been suggested that individual differences take considerably more effect in single-session tDCS application compared to longitudinal trainings under tDCS application (Cerreta et al., 2020). As such, other studies, more comparable to our single-session design, found that high performing individuals can benefit from tDCS, too (Arciniega et al., 2018; Berryhill and Jones, 2012; Grieder et al., 2019; Jones and Berryhill, 2012). WM improvements after parietal tDCS (anodal as well as cathodal) in HCI compared to LCI reflect that this region might be differently involved in network processes that depend on WM capacity (Jones and Berryhill, 2012).

In fact, it has been suggested that there are two pathways which are specifically engaged during different task-demands (Ekman et al., 2016). A direct corticocortical pathway between the prefrontal and posterior parietal cortex is involved in simple WM maintenance tasks. On the other hand, an indirect frontostriatal pathway via the thalamus and basal ganglia is recruited in more complex WM tasks that demand manipulation of information such as inhibition of distractors. The basal ganglia herein function as the gate-keeper for WM by hindering irrelevant information from entering the posterior parietal storage node (Gruber et al., 2006; McNab and Klingberg, 2008). Interestingly, connectivity of the pathways positively correlates with WM capacity (Darki and Klingberg, 2015; Ekman et al., 2016; Klingberg, 2006) and storage of irrelevant information was found to negatively correlate with WM capacity (McNab and Klingberg, 2008).

We propose that HCI efficiently engage the frontostriatal pathway as they are superior at inhibiting distractors and display high network connectivity. Our network stimulation might have optimally supported this pathway by emphasizing frontal distractor inhibition and additionally suppressing unnecessary parietal storage. We suggest that the tDCS-induced parietal modulation could have additionally acted as a noise filter in HCI (Filmer et al., 2014; Weiss and Lavidor, 2012). Shifting neural activity towards prefrontal regions potentially enhanced the top-down processes of HCI (Brass et al., 2005; Bressler et al., 2008; Edin et al., 2009; Oliveri et al., 2001).

On the contrary, as LCI store unnecessary distractors and reach their capacity limit earlier (Vogel et al., 2005), we assume that they recruit the frontostriatal pathway inefficiently and thus rely more on the corticocortical pathway. The finding that our tDCS protocol hindered LCI in their WM transfer led us to assume that LCI might compensate poor DIIN by keeping items in posterior storage available for late filtering processes (Jones and Berryhill, 2012; Lavie, 2010). As a result, the posterior parietal cortex might play a more important role in attentional processes for LCI than for HCI. In line with that, parietal regions were also found to be associated with selective attention as well as attentional load, not only with storage processes (Corbetta and Shulman, 2002; Culham et al., 2001; Filmer et al., 2015; Molenberghs et al., 2007; Moos et al., 2012; Roe et al., 2016). Berryhill, Chein and Olson (Berryhill et al., 2011) argued, that the posterior parietal cortex is involved in the direction of attention on maintained information. In this regard, possible supportive effects of frontal anodal stimulation might have been annihilated since parietal cathodal tDCS disturbed compensational processes in LCI.

Eventually, the missing differences in performance changes from pre to post between the groups in WM- could be explained by lower attentional control demands in this task. Firstly, as WM- did not require distractor inhibition and thus no possible parietal compensational mechanisms by LCI, tDCS probably did not have a strong impact on task performance. Secondly, several studies have shown that tDCS-effects become especially apparent in complex tasks, possibly because higher demands are posed on the involved networks (Gill et al., 2015; Pope and Miall, 2012; Wu et al., 2014).

4.4. *Frontoparietal network connectivity alterations*

We here stimulated two network nodes simultaneously. As described above, we had assumed that this stimulation protocol would modulate the functional connectivity and activity within the frontoparietal network as shown before (Keeser et al., 2011; Li et al., 2019; Mencarelli et al., 2020). Connectivity seems to be especially supported when network-targeted tDCS is applied online (Pisoni et al., 2018; Trumbo et al., 2016), thereby enhancing the “natural” activity associated with executing the demanded task. Sandrini and colleagues (Sandrini et al., 2020) found that even a single-session application of frontal anodal tDCS improved response inhibition and strengthened cortical as well as subcortical nodes of the network. With regard to the frontoparietal network and its involvement in working memory tasks, there is evidence from electrophysiological studies that tDCS over prefrontal and parietal areas causes oscillatory alterations within the network (Hill et al., 2018; Jones et al., 2020). Jones, Johnson and Berryhill (Jones et al., 2020) conducted a four-day WM training and found that tDCS targeting the relevant network nodes of the prefrontal cortex and the posterior parietal cortex had a positive effect on frontoparietal network oscillations. These changes also accounted for WM improvements. Besides, also the baseline connectivity of the default mode network appeared to be predictive of training improvement over the course of a multi-day WM training under tDCS (Cerreta et al., 2020). Consistent with these findings, our results support the notion, that individual differences in network- and cognitive processes could predetermine beneficial effects of tDCS, even after single-session application. HCI gained from a very short single-session cognitive training under concurrent tDCS and LCI benefitted from an isolated cognitive single-session training without electrical stimulation. In order to identify connectivity modulations within the entire cortical and subcortical network behavioral effects should be confirmed by functional imaging data.

4.5. *Limitations*

Using tDCS as a between-subject factor made it difficult to account for intraindividual variance. We nevertheless voted for this option, as we expected strong training effects to mask the stimulation outcome, which was confirmed by the current results.

Furthermore, the study did not include a passive control group that neither received the DIIN training nor tDCS alone. However, we have already compared the five-day DIIN training to a pure maintenance training (Schmicker et al., 2016). Besides, we need to stress, that the primary goal of this study was to investigate the tDCS induced modulation of transfer effects of the single-session DIIN training.

Another limitation is that the division of subjects into high and low capacity individuals was only possible after data collection due to the experimental procedure. This division resulted, however, in an uneven distribution of HCI and LCI across stimulation groups. Although the ANOVA and the adjustments in the square sum calculations are considered to be fairly robust against unbalanced data (Shaw and Mitchell-Olds, 1993), we would recommend an *a priori* assessment of subjects' WM capacity, in order to assign them equally to either stimulation group and would treat working memory capacity as a continuous variable in future analysis. In order to validate the hypotheses of the neuromodulation by the specific stimulation protocol, a comparison to different tDCS set-ups is necessary, using the same transfer design as reported. As the current study used one specific electrode montage, relating the effects to only one electrode or circumscribed neuronal mechanism is hardly possible. Therefore, switching the electrode's positions or the comparison to a common tDCS set-up seem pivotal. We would recommend the montage of an isolated anode over the prefrontal cortex and placing the cathode over an extracephalic region. Using this set-up only distractor inhibition related activity would be enhanced, while the assumed compensational posterior processes in LCI would be left unimpeded. Moreover, more multimethodal studies are needed, combining tDCS e.g. with electrophysiological or neuroimaging measures, in order to expand the knowledge about the neuronal process nudged by the modulation. Especially the role of the basal ganglia in the frontoparietal WM-attention network is of special interest for the current study. Connectivity analyses could also shed more light onto the neuronal characteristics of LCI and HCI and their significance for the responsiveness to the tDCS.

4.6. Future perspectives

This study indicates that single-session tDCS might modulate cognitive transfer depending on the specific neuronal pathways which an individual usually recruits in the task at hand and could therefore be considered for personalized cognitive enhancement. On the one hand, our results thus indicate that efficient network mechanisms can be further bolstered by the application of tDCS resulting in improving the "best". On the other hand, they suggest that WM capacity might be a suitable proxy for specific frontoparietal network processes. However, future research in this field needs to further unravel how tDCS affects functional network connectivity and synchronization and under which circumstances these modulations can be controlled in the most effective as well as efficient manner.

Beyond single-session application, tDCS has been considered a promising addition to usual cognitive training paradigms by boosting training effects and producing successful long-term modulation of transfer effects on other cognitive functions. In this regard different studies have already shown the positive effects of longitudinal tDCS application on the trained task (Au et al., 2016; Elmasry et al., 2015; Filmer et al., 2017b; Jones et al., 2015; Trumbo et al., 2016) and on the connectivity of involved networks (Jones et al., 2020; Nissim et al., 2019). As long-term cognitive training under tDCS seems to also enhance transfer effects to other, non-trained cognitive functions (Brem et al., 2018; Filmer et al., 2017b, 2017a; Jones et al., 2015; Richmond et al., 2014; Stephens and Berryhill, 2016) and WM training results in modulations of the frontoparietal network (Olesen et al., 2004), it should be encouraged to further investigate network-oriented tDCS in WM training paradigms, where it can be assumed to induce additional training benefits (Brem et al., 2018; Jones et al., 2020). Training as well as transfer effects of a multi-session WM training under tDCS could be compared to a longitudinal training of distractor inhibition, as suggested in the current study. Since individual differences were still found to play a role in long-term cognitive training under tDCS (Berryhill, 2017; Katz et al., 2017; Ruf et al., 2017), our findings and previous results once again underline the importance of analyzing individual differences, applied stimulation methods and their interactions with regard to neuronal processes associated with the executed task to paint the whole picture of tDCS effects.

5. Conclusion

To our knowledge, this is the first study that investigated individualized effects of a network-oriented electrode montage in the context of transfer effects. The results reinforce the notion that effects of tDCS, especially in single-sessions, are dependent on inter-individual factors, task demands and their interplay. They cannot be interpreted one-dimensionally but must be regarded as a neuromodulation that is always interacting with initial neuronal activity and internal behavioral patterns (Cerreta et al., 2020; Krause and Cohen Kadosh, 2014; Li et al., 2015; Miniussi and Vallar, 2011). Here we showed, that WM capacity is such a contributing factor as it correlates with different underlying neurophysiological processes. In this respect, our results might imply different frontostriatal and corticocortical mechanisms in individuals with high and low working memory capacity.

All in all, the presented results hint to the promising use of network-oriented tDCS as a personalized stimulation approach. Hereby, tDCS might function as a "catalyst" for specific network activity. By taking advantage of the interplay of both electrodes, more individualized, purposeful interventions might be possible, also in clinical contexts. At the same time, our findings raise awareness for the thoughtful application of tDCS, as not all individuals will benefit from the same stimulation protocol. For future studies, we would therefore recommend assessing within data of different tDCS protocols to evaluate individual responsiveness so as to examine network connectivity and communication. As a consequence, tDCS could prospectively function as a transfer modulator when combined with cognitive training. These are also important indications for future tDCS research and the neuro-rehabilitation context.

Author contributions

MS and IM developed the idea for this experiment and designed the tasks. IM, CS and MS collected and analyzed the data. MS and IM drafted the article. MS, IM, CS, MT, TZ and NM contributed to the discussion of content-related issues and to the critical revision of the article.

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Research data

Data, protocols and more detailed methodological procedures and material can be shared in case of acceptance for publication.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.neuroimage.2021.118438.

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