Cognitive enhancement of numerical and arithmetic capabilities: a mini-review of available transcranial electric stimulation studies

Cognitive enhancement of numerical and arithmetic capabilities: A short review of available transcranial electric stimulation studies

Schroeder, P. A.[a,b*], Dresler, T.[a,d], Bahnmueller, J.[b,c], Artemenko, C.[b,d], Cohen Kadosh, R.[e], Nuerk, H.-C.[b,c,d]

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Address:
a Department of Psychiatry and Psychotherapy, University of Tübingen, Calwerstr. 14, 72076 Tübingen, Germany
b Department of Psychology, University of Tübingen, Schleichstr. 4, 72076 Tübingen, Germany
c Leibniz-Institut für Wissensmedien, Schleichstr. 4, 72076, Tübingen, Germany
d LEAD Graduate School & Research Network, University of Tübingen, Gartenstr. 29, 72074 Tübingen, Germany
e Department of Experimental Psychology, University of Oxford, Oxford 0X1 3UD, United Kingdom

Corresponding author
Dipl.-Psych. Philipp A. Schroeder
Department of Psychiatry & Psychotherapy
Neurophysiology & Interventional Neuropsychiatry
University of Tübingen
Calwerstraße 14
D-72076 Tübingen, Germany
Tel: +49 7071-29-8 0815
Fax: +49 7071-29-59 04
E-Mail: philipp.schroeder@uni-tuebingen.de

Abstract

Arithmetic capabilities are complex cognitive skills essential for handling requirements of the modern world. At the same time, educational institutions are challenged with math-related problems, e.g., developmental dyscalculia, math anxiety, and also with less severe difficulties of arithmetic understanding. Thus, non-invasive techniques for cognitive enhancement have attracted researchers' and practitioners' interest in the fields of education, psychology, and neuroscience. Particularly, studies employing transcranial electric stimulation (tES) in arithmetic learning, problem solving, and performance in numerical tasks and operations have shaped an optimistic perspective of cognitive enhancement in these domains, building on the fronto-parietal correlates of healthy and deficient arithmetic performance and learning. However, the heterogeneity of stimulation approaches in numerical cognition research – with different electrode montages, stimulation protocols, tasks, outcomes, and combinations thereof – may also showcase a variety of parameters relevant more generally to the cognitive domain. Here we present a short overview of the different tES approaches to enhance arithmetic capabilities within the general framework of cognitive enhancement. We conclude that performance and training gains can be obtained from different strategical tES configurations, but more standardization, better translation between neurodevelopmental perspectives and tES principles, and controlled studies in critical populations are needed.

Keywords: transcranial direct current stimulation, transcranial random noise stimulation, cognitive enhancement, numerical cognition, educational neuroscience

Basic arithmetic abilities are critical for numerous activities and societal functioning. Yet, a substantial amount of the general population (e.g., up to 22% in the UK) shows mathematical deficits which are often specified in developmental trajectories, cognitive disabilities, or comorbidities (Kaufmann et al. 2013) and which can result in occupational and economic disadvantages (Bynner and Parsons 1997). Both domain-general and domain-specific functions supplement the successful operation on numerical quantities in everyday life. These cognitive functions include magnitude representation, retrieval of, and operation on arithmetic facts on the domain-specific side, and working memory, executive functions, and attention on the domain-general side. The variety of involved domain-general and domain-specific cognitive functions thus also increases the dimensionalities of possible mathematics training strategies (Looi and Cohen Kadosh 2016).

Arithmetic processing is mainly subserved by the fronto-parietal network of the brain (Klein et al. 2014; Matejko and Ansari 2015; Nieder 2016): Different parietal circuits are particularly relevant for magnitude representations (Dehaene et al. 2003) and arithmetic operations often produce additional prefrontal activations (Arsalidou and Taylor 2011). By modulating activity in these brain areas, arithmetic performance could be changed. Accordingly, investigations with transcranial brain stimulation can causally bolster the correlational evidence from neuroimaging, because brain activity becomes an independent manipulated variable rather than a dependent, measurable variable. Going beyond causal reasoning, neuromodulation has also been proposed as effective strategy to improve arithmetic capabilities over and above behavioral cognitive training.

In particular, transcranial electric stimulation (tES) has been administered repeatedly in recent studies using various arithmetic tasks and trainings. However, the complex neurocognitive functions required in different arithmetic tasks have sparked different approaches within tES studies. Moreover, the neuromodulatory technique itself also allows for different implementations with critical consequences for assumed neurophysiological and behavioral effects. Thus, heterogeneity (anatomically, parametrically, and content-wise) is the norm and it is hard to get a conclusive overview even on this small field. Therefore, we present a short review of studies employing transcranial electric stimulation (tES) on numerical processing and learning disentangling above factors. Our particular focus is to discuss basic methodological and translational aspects of tES approaches in the general framework of cognitive enhancement that may contribute to the current heterogeneity.

Stimulation for enhancing arithmetic capabilities

The current review focuses on tES methods, but numerical cognition research is also informed by extensive previous work with transcranial magnetic stimulation (TMS) essentially testing the causal structure-function relations underlying arithmetic skills with high focality (Salillas and Semenza 2015). Some advantages of administering weak currents through scalp electrodes with tES over active interference with electromagnetic TMS pulses are the possibility of modulating brain activity online (that is: concurrent to a behavioral task or training) without auditory and sensory distraction, the establishment of sham and active control stimulation with indistinguishable sensory artifacts (see also Duecker and Sack 2015), portability, economic efficiency, and easy implementation in outpatient interventions (Priori et al. 2009).

Within tES applications for the enhancement of numerical cognition, the most prominently investigated methods are transcranial direct current stimulation (tDCS) and transcranial random noise stimulation (tRNS). For both techniques, two (or more) surface electrodes are fixed over brain regions and a weak current is applied (mostly 1-2 mA). Using direct currents in tDCS, cathode and anode electrodes differ in their neurophysiological effect. It is assumed that in the human brain underneath the anode, depolarization mostly produces excitatory shifts of resting membrane potentials whereas underneath the cathode, hyperpolarization mostly modulates neuronal activity in inhibitory ways (Nitsche and Paulus 2000; but see Jacobson et al. 2012 for review of polarity effects). In contrast to TMS, these subtle neuromodulatory shifts are not capable to induce action potentials on their own, but tES can emphasize or attenuate inherent neural activity and thus also produce cross-cortical network responses. Any modulation of behavioral effects thus rests on the current network activity (state-dependency) and on neural activations as induced by a task (Silvanto and Pascual-Leone 2008; Bikson and Rahman 2013).

Often, only the effect under one ‘target’ electrode is desirable. However, ‘return’ electrode placement (typically of the cathode) is highly relevant, because its placement also affects current flow and current fields underneath the target electrode, e.g., due to target-return distance and direction, shunting over the scalp, or network dynamics (Bikson et al. 2010; Moliadze et al. 2010). In addition, regions between the electrodes are flooded by tangential current, which can modulate additional synaptic efficiency of some neuronal populations (Rahman et al. 2013). This is a particular problem in numerical cognition, because – as outlined above – domain-general functions also contribute to numerical functioning. It is not sufficient to avoid number-related brain areas for the placement of the return electrode, because a domain-general function underlying the overall current flow may also exert its influence on numerical processing. Furthermore, an opposite polarization in another brain region may be of theoretical interest (e.g., in oppositional placements). However, in most cases of unilateral placement with one theoretically motivated target electrode, the return and intermediate area activity is neglected and accordingly, large return pads are used that produce less dense current fields or return electrodes are placed on extracephalic locations.

In contrast, alternating currents are used in tRNS with (high) frequencies randomly picked from a normally distributed range of predefined oscillations. What is known about tRNS mechanisms is that its intensity- and frequency-dependent administration can enhance cortical excitability underneath both surface electrodes (Terney et al. 2008) and tRNS can facilitate subthreshold detection processes according to stochastic resonance principles (Antal and Herrmann 2016; van der Groen and Wenderoth 2016). Note that tRNS working mechanisms differ from the fixed application of a single oscillation in transcranial alternating current stimulation (tACS), which is thought to act by entrainment and phase-locking (Ozen et al. 2010; Battleday et al. 2014). The excitatory effect of tRNS tended to be larger, yet shorter, compared to anodal tDCS, in motor cortex evaluations (Moliadze et al. 2014). In cognitive tasks, mixed results were obtained with effective modulations in numerical tasks and trainings (Cappelletti et al. 2013; Snowball et al. 2013; Pasqualotto 2016; Popescu et al. 2016), steeper learning rates – as opposed to anodal tDCS – in visual discrimination (Fertonani et al. 2011), but no performance modulations in working memory tasks (Mulquiney et al. 2011). Little direct behavioral outcome comparisons between the two techniques exist to date. Yet, their different characteristics could imply better targeted implementations: For instance, the aftereffects of tRNS appear NMDA receptor independent, in contrast to anodal tDCS (Chaieb et al. 2015). Thus, different neuroplastic (long-term) consequences of tRNS and tDCS could further augment and specify future training effects in different conditions.

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Short overview of reviewed studies

Acknowledging the involvement and relevance of different domain-specific and domain-general functions, associated brain areas, and networks in numeracy and arithmetic processes exceeds the scope of this mini-review, but good and elaborated descriptions are available elsewhere (Arsalidou and Taylor 2011; Looi et al. 2016b). So far, various combinations of tasks, study designs, and electrode configurations have been investigated using tES methods in single studies. Table 1 presents a systematic overview of the reviewed studies[1]. Here, we discuss the heterogeneity of approaches towards interactions between stimulation parameters and tasks assessing numerosity and arithmetic performance and learning.

Numerical performance modulations

The available study results corroborate the importance of bilateral parietal brain regions for numerical processing, but active control stimulations and tasks also indicate distinct lateralization and state-dependency.

In number magnitude comparison tasks, unilateral left-side parietal anodal tDCS generally increased accuracy with two-digit number symbols (Hauser et al. 2013). Conversely, a bipolar oppositional placement with right anodal, left cathodal parietal stimulation impaired single-digit comparison latencies (Li et al. 2015) for digits close to the referent. Thus, the bipolar stimulation modulated the increasing difficulty to distinguish digits closer to the comparison referent (numerical distance effect (NDE); Moyer and Landauer 1967). Considering the state-dependency principle of tES effects, this modulation of NDE could be either domain-specific or it could be driven by the higher level of task difficulty and neural activation in critical trials. In other words, higher demands for discriminating close targets and for processing multi-digits could encompass more task-induced activity ready for neuromodulation. NDE was

[1] A PubMed search (tDCS/tRNS AND arithmetic/numerical cognition) identified 34 papers that were manually screened for original results and new cross-referenced studies.

unaffected by several tDCS configurations of Hauser et al. (2013) in multi-digit comparisons, but the distractor-distance effect for selecting correct two-digit addition results was monotonically modulated by a bilateral-bicephalic parietal stimulation (Klein et al. 2013). Both single-digit accuracy rates and latencies as well as NDE were unaffected by prefrontal cathodal tDCS, but spatial-numerical associations were eliminated (Schroeder et al. 2016).

Arithmetic performance modulations

Performing even on simple operations requires domain-general working memory and executive functions involvement to maintain operation components, yet to different extents depending on the exact task. Most studies employed supraorbital or prefrontal return cathodes without necessarily highlighting potential effects on such domain-general functions. Interestingly, for novel and complex subtractions, left-parietal tDCS prevented characteristic prefrontal deactivations below the right-prefrontal cathode as captured with simultaneous fMRI (Hauser et al. 2016), whereas a behavioral effect for subtraction problems was only found in a preceding study (Hauser et al. 2013). Similarly, left-parietal performance enhancements in a complex statistical procedure were observed with temporal (Houser et al. 2015), but not with prefrontal cathode placement (Houser et al. 2014). Also considering neurodevelopmental studies, the accumulation of arithmetic proficiency may be accompanied by a shift from broad prefrontal to precise parietal activations (Zamarian et al. 2009). In this line, both frontal and parietal excitatory tRNS generated greater speed improvements over the course of an experiment in subtraction verifications, but not in word classifications (Pasqualotto 2016). Furthermore, tDCS to one area can lead to altered activations over wide-spread networks in the brain and to effects on cognitive functions related to areas distant from the stimulated area. For example, two studies report improvements in paced auditory serial subtraction tasks from cathodal stimulation of the cerebellum, thought to disinhibit prefrontal activity (Pope and Miall 2012), and comparable results were obtained with prefrontal anodal tDCS (Pope et al. 2015). In clinical research, a variant of the serial addition WM task is often used in conjunction with tDCS to enhance domain-general functions and emotional processing in depressive patients (Vanderhasselt et al. 2015). Solving repeated additions with adaptive speed increases is frustrating and elicits negative affect, but anodal prefrontal tDCS can concurrently improve emotional responses and arithmetic performance (Plewnia et al. 2015). Highlighting individual differences, low- and high-math anxiety individuals responded differentially with decreased and increased arithmetic performance to prefrontal tDCS (Sarkar et al. 2014). These finding also highlight the importance of emotion for math-related cognitive processing, for which behavioral correlations have often been reported (Suárez-Pellicioni, Macarena, Núñez-Peña, María Isabel, & Colomé 2016).

Also domain-specific effects in multi-digit processing could be modulated: Left-parietal anodal tDCS with 1.5 mA was beneficial for solving problems with larger operands (problem size effect; sums exceeding 10 and including carries), but decreased accuracy in small problems (Rütsche et al. 2015). Whereas the latter result is counterintuitive, system noise injection by anodal tDCS (see also Fertonani and Miniussi 2016) could skew arithmetic retrieval precisions and this conception was corroborated by concurrent EEG theta measurement results (Rütsche et al. 2015). Regarding place-value effects (e.g., carrying unit-digits), right-side anodal vs. cathodal parietal tDCS prolonged latency increases for carry operations in a two-digit addition task out of a series of unilateral placements (Artemenko et al. 2015).

Numerical training modulations

Whereas tRNS was used only selectively in studies on performance, the technique appears more appealing for numerical and arithmetic training. Highlighting the role of concurrent (‘online’) activities, Cappeletti et al. (2013) assembled comparisons between the combinations of training with parietal, motor, and sham tRNS over five days, as well as with a resting-state parietal stimulation. Number acuity in dot-array discrimination improved most from the parietal stimulation combined with training, but no transfer to arithmetic tasks was observed.

To investigate numerosity learning, a prominently investigated paradigm is the artificial symbols training where arbitrary, meaningless figures are assigned to numerical magnitudes. Repeated feedback-guided magnitude comparisons with the artificial symbols (training phase) produce automatic numerosity evaluations that interfere with physical size presentations and map onto space (test phase; Tzelgov et al. 2000). An oppositional parietal tDCS placement (right anodal, left cathodal) produced faster automaticity and more linear mapping of artificial symbols in a training over 6 days, with sustainability after 6 months (Cohen Kadosh et al. 2010).

For the opposite placement, an impaired automaticity was detected, but here the bilateral parietal stimulation also produced steeper learning curves superior to prefrontal and sham stimulations (Iuculano and Cohen Kadosh 2013). Interestingly, when the numerical training paradigm was administered in two individuals with severe arithmetic problems, only the left-anodal right-cathodal configuration, which led to impairment in typical participants, led to behavioral improvements (Iuculano and Cohen Kadosh 2014). Although certainly larger samples are required to confirm this pattern, the application of tDCS-combined numerical trainings may provide effective rehabilitation and treatment prospects for numerical deficits.

Arithmetic training modulations

With artifical symbols depicting calculation algorithms for typical Arabic numbers, drill and calculation training combined with prefrontal tRNS improved learning rates and led to sustained calculation performance 6 months later (Snowball et al. 2013). In addition, hemodynamic recordings captured short-term and long-term physiological tRNS effects. More recently, an interesting combination of prefrontal tRNS on days 1-3 and parietal tRNS on days 4-5 was observed to improve performance in difficult math problems and accuracy in new and easy problems (Popescu et al. 2016). But also targeting the left parietal tDCS with 1.5 mA in a single-day training study on multiplication and subtraction facts, polarity-specific and operation-specific subtraction learning improvements were found and performance differences were sustained in 24h follow-up (Grabner et al. 2015).

In combination with an adaptive body-tracking video-game on fractions, prefrontal bipolar-balanced tDCS (left anodal, right cathodal) resulted in improved and sustained task performance and transferred also to domain-general functions (Looi et al. 2016a).

These first training studies demonstrate the potential of tES for enhancing arithmetic training effects in healthy adult subjects. Evaluation numerical training studies with tDCS and tRNS already incorporate assessments of additional informative indices such as learning curves, specific and general transfer to non-trained stimuli and tasks, long-term effects, and neurophysiological profiles, although effects on domain-general functions are less well discriminated. In contrast, studies employing tES-augmented trainings in atypical populations are scarce and potentially restrained by additional physical and cognitive side effects (Krause and Cohen Kadosh 2013).

Different neurophysiological profiles of individuals or groups (e.g., dyscalculia, stroke patients, children) at certain development stages most likely necessitate parametrical and training-related adjustments, e.g., to also consider specific numerical, arithmetic, and domain-general disadvantages such as working memory capacity. Moreover, most conclusions are based on single studies, researchers implement dissimilar tES configurations, and the interdependence of different brain areas and effects in certain tasks is not completely clear. In order to further integrate these partially heterogeneous findings, interpretations of different modulations by tES must also consider and build on the ongoing validation of its very basic principles.

tES Configurations

According to physical arrangements classification (Nasseri et al. 2015), successful modulations of numerical performance utilized unilateral monopolar placements with large return electrodes, bilateral bipolar-balanced and non-balanced, as well as the dual-channel bilateral double-monopolar arrangement by Klein et al. (2013). Most studies focus on parietal placements with 1mA, but also prefrontal placements appear at least partially successful with tRNS (Pasqualotto 2016) and produce significant modulations of spatial-numerical associations (Schroeder et al. 2016) and improvements in arithmetic decisions for high-math anxiety individuals (Sarkar et al. 2014).

All studies with tRNS used a bilateral bipolar-balanced placement with electrodes either targeting left and right prefrontal areas (e.g., F3 and F4) or parietal areas (e.g., P3 and P4). We wish to highlight once more that these placements are taken to increase excitability over both targeted areas and there is no need of an additional return electrode. Thus, in contrast to tDCS, but similar to placements with two pairs of tDCS electrodes (cf. Klein et al., 2013), the bipolar-balanced placement in tRNS is less likely to modulate hemispheric activity dominance and may prove useful for bilateral magnitude processing. Yet, its exact neurophysiological principles are different from (anodal) tDCS and currently not completely understood (Antal and Herrmann 2016).

An interesting concept is the modulation of distinct learning phases over different cortex regions as implemented by Popescu et al. (2016). Future research needs to validate this approach by closed-loop tDCS or by comparing different configuration changes directly (e.g., switching from prefrontal to parietal stimulation after 2, 3, or 4 days). The potential of an augmentative effect and better targeting of stimulation by considering training phase is also confirmed by the finding that a specific tDCS polarity sequence can lead to more effective modulations with long-term sustainability (Dockery et al. 2009). Thus, basic research can also inform interventional administrations, although generalizations from healthy volunteers to different clinical populations (e.g., developmental dyscalculia or acalculia after a stroke) should consider all translational aspects (e.g., functional, structural, and behavioral differences) in corresponding models before selecting tES configuration parameters. Technical tES parameters have important connotations for behavioral effects. In the literature, prominently debated tES parameters are electrode configuration and sizes, current intensity and duration, and timing of stimulation (online vs. offline). These and other parameters do not work linearly (e.g., higher intensities can exceed optimal stimulation ranges; Batsikadze et al. 2013) and their combination outcomes might critically depend on task and individual characteristics. Eventually, this variety of possibilities will allow for broad-ranging applications and fine-grained targeting from underlying theoretical models. Currently, however, simplification or even standardization of certain parameters would facilitate effectivity estimations, and the ongoing development of electric field modelling tools can already be used for selecting stimulation targets (Truong et al. 2014). Regarding numerical processes, stimulations should be administered concurrent to a task and could then achieve neurostructural precision following task-selective recruitment (Clemens et al. 2013; Bikson and Rahman 2013), but effectivity can vary according to individual differences. Based on the available literature so far, electrode sizes do not appear to produce remarkable effectivity differences in this domain. However, since the anti-proportional relationship between current density and electrode size (at fixed current strength) does not linearly scale for respective distances from the electrode (e.g., scalp-brain distance) and smaller electrodes may not reach deeper regions(Miranda et al. 2009), this observation will require systematic evaluation in the future. Furthermore, publication biases can impede the development of better stimulation models, because nonsignificant results are dismissed, theories are elaborated post-hoc, and results could lack reproducibility. In this vein, preregistration of according studies and protocols (e.g., aspredicted.org or www.osf.io) could facilitate scientific communication and rigorous evaluation of tES methods.

Conclusion

Both tDCS and tRNS can enhance arithmetic capabilities in adult populations and could be promising tools for deviant performance populations. The current literature is coined by heterogeneity already in standard technical parameters such as montage, but effectivity estimation requires better standardization. Studies with (sub-)clinical populations and children are needed to examine the usefulness of stimulation for at-risk groups. However, having said that, future research must consider their potentially different neurofunctional signatures, potential additional side effects, and neuroethical questions (Cohen Kadosh et al. 2012; Davis 2014). Documentation of (individualized) task-specific brain activity will potentially allow for predictive adjustment of tES configurations and better evaluation thereof, i.e., using fMRI (Clemens et al. 2013), EEG (Grabner et al. 2015), or NIRS (Snowball et al. 2013). Further tES precision could be obtained from considering a neurodevelopmental perspective, concurrent (individualized) imaging, relevant domain-related states, and theoretical optimization of task-related brain-structure correspondence in experimental and training studies.

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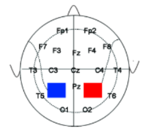
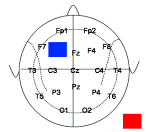
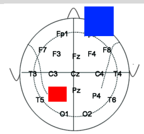
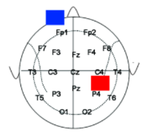
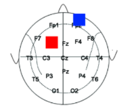
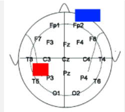
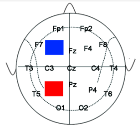
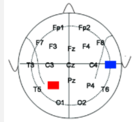
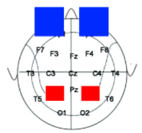
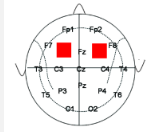
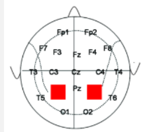
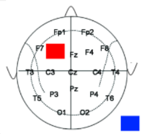
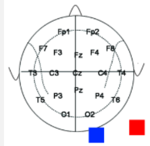
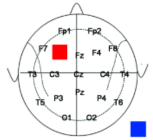
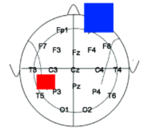
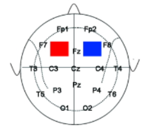
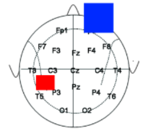
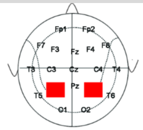
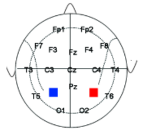
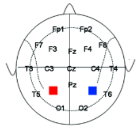
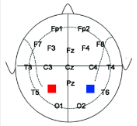
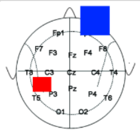
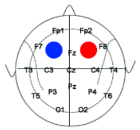
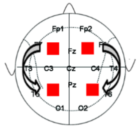
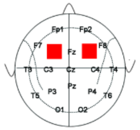
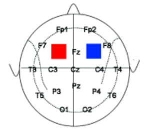
Table 1. Overview of original tES studies on numerosity and arithmetic performance, learning, and training. The majority of studies administered tES online to the behavioral task, in healthy student populations (mixed-sex aged 18-42 y) and deviations from these parameters are explicitly stated below. Anode and cathode target regions refer to the international 10-20 system for electrode placements. For tRNS, both anode and cathode deliver current (reported: peak-to-peak intensity) in negative and positive direction and are assigned randomly (no study employed DC offset).

Study	**tES Method** (group), anode, cathode, current *Duration, electrode size, AC range*	**Sample & Design**	**Task**	**Result** + physiological effects # transfer, additional measures	**Effect Size**	**Successful Montage**
1. Cognitive Enhancement of Performance **1.1. Numerosity**						
Li et al., 2015	**tDCS** online (LA-RC) P3, P4, 2mA (RA-LC) P4, P3, 2mA (S) sham *30 min, 5x5 cm*	N=18 cross-over	number comparison spatial attention (modified Posner task) continuous attention, vigilance level	(S)>(RA-LC) [RT] no modulation of spatial attention (RC-LA)>(RA-LC) [RT in final CRT block)	d=0.61 d=0.83	
Schroeder, Pfister, Kunde, Nuerk, & Plewnia, 2016	**tDCS** online (1) extracephalic, F3, 1 mA and sham (2) F3, extracephalic, 1 mA and sham *25 min, 5x7 cm*	N_1=24, N_{rep}=24, N_2=24 separate cross-over	number-space representation (SNARC) stimulus-response conflict	(1) reduces representation: prefrontal areas direct implicit number-space link no effect on explicit conflict no modulation of NDE [RTs] #conceptual replication	d=0.49 d=0.56	
1.2. Arithmetic						
Artemenko, Moeller, Huber, & Klein, 2015	**tDCS** online (LA) P3, SO, 1mA (RA) P4, SO, 1mA (LC) SO, P3, 1mA (RC) SO, P4, 1mA (S) sham *20 min, 5x5 parietal & 10x10 cm SO*	N=25 cross-over	addition 2AFC color-word stroop (offline control)	carry effect: RA > RC no effect on stroop place-value lateralized in right IPS	d=0.36	
Clemens, Jung, Zvyagintsev, Domahs, & Willmes, 2013	**tDCS** online (1) CP4, SO, 2mA and sham *20 min, 5x7 cm*	N=10 male within (pre-post)	simple multiplication verification	no behavioral effect [RT/PE] +pre- and post fMRI: +AG activity increase	 d=1.85-2.94[1]	
Gill, Shah-Basak, Hamilton, 2015	**tDCS** offline (1) F3, SO, 2 mA and sham *20 min, 5x5 cm*	N=22 (collapsed) cross-over	PASAT addition Preceding easy or difficult verbal WM task with tDCS	better accuracy for fast additions if preceded by difficult WM task (3-Back)	d=1.82	

Hauser et al., 2016	**tDCS** online→offline (1) P5-CP5, SO, 1 mA or (2) sham *first 30 min of task, 5x7 cm anode & 5x10 cm cathode*	N_1=20, N_2=20 between	subtraction 3AFC repeated vs. novel problems	no group differences in learning and problem solving (ceiling effect) +tDCS nullified novelty- +related right prefrontal +deactivation [fMRI]	d=2.01	
Houser, Thoma, & Stanton, 2014	**tDCS** offline (1) P3, F3, sham, (2) 1mA, or (3) 2mA *20 min, 5x7 cm*	N_1=14, N_2=15, N_3=13 between	statistical problem (calculation of non-parametric-Kruskal-Wallis)	sham = 1mA, 1mA > 2mA Instruction and calculation time covary with task success; possible 2mA effect of prefrontal cathode	d=0.4	
Houser, Thoma, Fonseca, O'Connor, & Stanton, 2015	**tDCS** offline (1) P3, T4, sham, (2) 1mA, or (3) 2mA *20 min, 3x5 cm*	N_1=13, N_2=10, N_3=9 between	statistical problem (calculation of non-parametric-Kruskal-Wallis)	1mA & 2mA > sham	d=1.51-1.28[1]	
Klein et al., 2013	**Bi-tDCS** online (1) P3+P4, SO+SO, 1mA (2) SO+SO, P3+P4, 1mA (3) sham *20 min, 5x5 parietal & 10x10 cm SO*	N24 cross-over	addition 2AFC color-word Stroop (control)	(1)<(2) (distractor distance) no effect on stroop bilateral IPS for number magnitude processing	d=0.46[1]	
Pasqualotto, 2016	**tRNS** online (F) F4, F3, 1mA (P) P4, P3, 1mA (S) sham *20 min, 5x5 cm, AC: 100-600 Hz*	N_F=18, N_P=18, N_S=18 within-between	subtraction verification word categorisation	(F)=(P)>(S) Improvement [RT block 4-1] 1w follow-up: (F)=(P)>S [PE trained and novel problems] no effect on categorisation	- -	 
Plewnia et al., 2015	**tDCS** online (1) F3, extracephalic, 1 mA and sham *20 min, 5x7 cm*	N=28 male between	PASAT addition	Improved performance Decreased negative affect	d=0.94 d=1.37	
Pope et al., 2012	**tDCS** offline (A) cerebellum, extracephalic, 2mA (C) extracephalic, cerebellum, 2mA (S) sham *20 min, 5x5 cm*	N_A=22, N_C=22, N_S=22 between (pre-post)	PASAT addition and subtraction; verb generation	(C)>(S)=(A) for subtraction and verb generation	-	

Pope et al., 2015	**tDCS** offline (A) F3, extracephalic, 2mA (C) extracephalic, F3, 2mA (S) sham *20 min, 5x5 cm*	N_A=20, N_C=20, N_S=19 between (pre-post)	PASAT addition and subtraction	(A)>(S)=(C) for subtraction and verb generation	-	
Rütsche, Hauser, Jäncke, & Grabner, 2015	**tDCS** offline (1) P5-CP5, SO, 1.5 mA and sham *30 min, 5x7 parietal & 10x10 cm SO*	N=23 cross-over	small arithmetic problems large arithmetic problems (verbal production)	decreased performance PE increased performance RT differential involvement of LPPC in arithmetic problems; state dependency +EEG during task: +alpha & theta modulations	d=0.51 d=0.45 d=0.47-0.72	
Sarkar, Dowker, & Kadosh, 2014	**tDCS** online (1) F3, F4, 1mA and sham *30 min, 5x5 cm*	$N_{high\ math\ anxiety}$ =25, $N_{low\ math\ anxiety}$=20 mixed cross-over	affective priming+ arithmetic verification, attention (ANT)	RT benefit for high anxiety, RT impaired for low anxiety and executive control score +modulation of salivary +cortisol (pre-post)	d=5.69[1] d=4.13[1] d=1.03[1]	
1.3. Numerosity & Arithmetic						
Hauser, Rotzer, Grabner, Mérillat, & Jäncke, 2013: Exp. 1	**(Bi-)tDCS** offline (1) P3, SO, 1mA (2) P3+P4, SO, 1mA (3) SO, P3+P4, 1mA (4) sham *25 min, 5x7 target & 10x10 cm return electrodes*	N=21 cross-over	number comparison, subtraction 3AFC	P3 > sham [PE] P3 > sham [RT] unilateral left parietal tDCS enhanced performance no modulation of NDE	d=0.76 d=0.51	
Hauser, Rotzer, Grabner, Mérillat, & Jäncke, 2013: Exp. 2	**tDCS** offline (1) P4, SO, 1mA and sham *25 min, 5x7 target & 10x10 cm return electrodes*	N=16 cross-over	number comparison, subtraction 3AFC	no effects (control experiment; laterality specificity)		
2. Cognitive Enhancement of Training and Learning **2.1. Numerosity**						
Cappelletti et al., 2013	**tRNS** online → offline (P) P3, P4, 1mA (PNT) P3, P4, 1mA, no training (M) C3, C4, 1mA (ST) sham & training *20 min for 5 d, 5x7 cm, AC: 0-250 Hz*	N_P=10, N_{PNT}=10, N_M=10, N_{ST}=10 between	dot-array numerosity discrimination training (5d) transfer: continuous magnitudes discrimination, arithmetic, attention, executive, Stroop (control)	number acuity: P>M=ST>PNT (P) improved continuous magnitude discrimination no effects on arithmetic & control tasks +(P) displayed sustained +discrimination acuity after +16 weeks	d=1.12-1.25[1]	

Cohen Kadosh, Soskic, Iuculano, Kanai, & Walsh, 2010	**tDCS** online → offline (LA-RC) P3, P4, 1mA (RA-LC) P4, P3, 1mA (S) sham *20 min for 6 d, 3x3 cm*	N_{LA-RC}=5, N_{RA-LC}=5, N_S=5 between	training with artificial numerical symbols (6d) numerical Stroop number-to-space (MNL)	RA-LC>S>LA-RC: faster automaticity RA-LC: linear MNL +sustained automaticity +(RA-LC) after 6 months	-	
Iuculano & Cohen Kadosh, 2013	**tDCS** online → offline (PPC) P3, P4, 1mA (DLPFC) F4, F3, 1mA (S) sham *20 min, 3x3cm*	N_{TOTAL}=19 between	training with artificial numerical symbols (6d) numerical stroop digit stroop	Slope: PPC>S>DLPFC Automaticity: DLPFC>S>PPC digit stroop: no transfer Dissociation of learning and automaticity	d=2.0[1] d=1.45[1]	
Iuculano & Cohen Kadosh, 2014	**tDCS** online→ offline (LA-RC) P3, P4, 1mA (RA-LC) P4, P3, 1mA *20 min, 3x3 cm*	2 patients with developmental dyscalculia between single-case	training with artificial numerical symbols (6d) numerical stroop number-to-space	LA-RC>RA-LC: automaticity, but no linear number-to-space mapping	-	
2.2. Arithmetic						
Grabner, Rütsche, Ruff, & Hauser, 2015	**tDCS** online → offline (PA) P5-CP5, SO, 1.5 mA (PC) SO, P5-CP5, 1.5 mA (S) sham *30 min for 1 d, 5x7 cm*	N_{PA}=20, N_{PC}=20, N_S=20 between	multiplication and subtraction facts (1d)	slope: PA=S>PC [RT] slope: PA>S=PC [PE subtractions] +PA=S>PC for trained +problems after 1 day [RT]	d=0.85 d=0.71 d=0.55	
Looi et al., 2016	**tDCS** online (FT) F4, F3, 1mA (FNT) F4, F3, 1mA+placebo training (S) sham *30 min, 25cm² electrodes*	N_{FT}=10, N_{FNT}=10, N_S=10 between	adaptive body-tracking video-game on fractions (2d)	better performance (sham+placebo training) transfer to verbal WM better tES effect for lower baseline ability +long-term effects and +sustained transfer after 2 +months	- - d=0.63-0.72	
Popescu et al., 2016	**tRNS** online (tRNS) F3, F4, 1mA (days 1-3) (tRNS) P3, P4, 1mA (days 4-5) (S) sham (days 1-5) *20 min, 4x4cm, AC: 100-640 Hz*	N_{tRNS}=16, N_S=16 between	training (5d): calculation and (time-pressured) drill, old & new problems (d5) attention (ANT)	tRNS>S in difficult problems [RT, training+test] tRNS>S in new & easy problems [PE] no effect on ANT	d=1.39 d=1.16 d=1.46	
Snowball et al., 2013	**tRNS** online (tRNS) F3, F4, 1mA or (S) sham *20 min, 5x5cm, AC: 100-600 Hz*	N_{tRNS}=13, N_S=12 between	training on arithmetic problems (6d): calculation and (time-pressured) drill mental rotation, attention (ANT)	steeper calculation learning rates and drill learning rates no effects on mental rotation and ANT	- d=1.09	

				+sustained calculation +performance after 6 +months #pre-post NIRS: prefrontal #hemodynamic response #mirrors behavioral results		
Vanderhasselt et al., 2015	**tDCS,** online (1) F3, F4, 2mA or (S) sham *30 min, 5x5cm*	N_1=19, N_s=14 depressed patients between	Training (5d) on the PASAT task	performance pre/post training effects effects on depression	NS d=0.70	

Notes: 2AFC=two alternatives forced choiceAC=alternating current, AG=angular gyrus, IPS=intraparietal sulcus, NDE=numerical distance effect, PASAT=Paced Auditory Serial Addition Task, PE=percentage of errors, PFC=prefrontal cortex, RT=response times, SO=(contralateral) supraorbital region. Cross-over design refers to repeated measurement of different stimulation conditions in counterbalanced order. Cohen's d: 0.2=small effect, 0.5=medium effect, 0.8=large effect. [1] Effect sizes are transformed following Cohen (1988) for two means and for more than two means with a significant linear trend.