

Cognitive enhancement of numerical and arithmetic capabilities:

A mini-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}

Abbreviated title:

The cognitive enhancement of arithmetic capabilities

Word Count: 3297 words

Number of Tables: 1

Number of Figures: 0

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 OX1 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 numerical and arithmetic capabilities in performance and training 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, as well as pre-registered and controlled studies in critical populations are needed.

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

1 Basic numerical and arithmetic abilities are critical for numerous activities and
2 societal functioning. Yet, a substantial amount of the general population (e.g., up to
3 22% in the UK) shows mathematical deficits which are often specified in
4 developmental trajectories, cognitive disabilities, or comorbidities (Kaufmann et al.
5 2013) and which can result in occupational and economic disadvantages (Bynner
6 and Parsons 1997). Both domain-general and domain-specific functions supplement
7 the successful operation on numerical quantities in everyday life. These cognitive
8 functions include magnitude representation, retrieval of, and operation on arithmetic
9 facts on the domain-specific side, and working memory, executive functions, and
10 attention on the domain-general side. The variety of involved domain-general and
11 domain-specific cognitive functions thus also increases the dimensionalities of
12 possible mathematics training strategies (Looi and Cohen Kadosh 2016).

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

24 In particular, transcranial electric stimulation (tES) has become a promising tool to
25 enhance various arithmetic tasks and trainings. However, the complex neurocognitive
26 functions required in different arithmetic tasks have sparked different approaches
27 within recent tES studies. Moreover, the neuromodulatory technique itself also allows
28 for different implementations with critical consequences for assumed
29 neurophysiological and behavioral effects. Thus, heterogeneity (anatomically,
30 parametrically, and content-wise) is the norm and it is hard to get a conclusive
31 overview even on this small field. In this mini-review, we provide an overview of
32 studies employing tES on numerical processing and learning disentangling above
33 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) examining the causal structure-function relations underlying arithmetic skills with high focality (Salillas and Semenza 2015) or the mechanisms underlying place-value integration in multi-digit number processing (Knops et al., 2006). 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 conditions with indistinguishable sensory artifacts, portability, economic efficiency, and easy implementation in outpatient interventions (Priori et al. 2009; see also: Duecker and Sack 2015).

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; see also: Jacobson et al. 2012). In contrast to TMS, these subtle neuromodulatory shifts are not capable to induce action potentials on their own. However, tES can emphasize or attenuate inherent neural activity and thus also produce cross-cortical network responses (Pope and Miall 2012). 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 electrode) 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). Furthermore, tRNS can facilitate subthreshold detection processes according to stochastic resonance principles (Antal and Herrmann 2016; van der Groen and Wenderoth 2016). Note that tRNS mechanisms are likely to 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 and some studies report on the lack of performance modulations in working memory tasks (Mulquiney et al. 2011; Holmes et al. 2016). However, numerous studies also report on effective performance and learning modulations by tRNS in numerical tasks and trainings (Cappelletti et al. 2013; Snowball et al. 2013; Pasqualotto 2016; Popescu et al. 2016). Little direct behavioral outcome comparisons between the two techniques exist to date. Yet, their different characteristics could imply better targeted implementations: For instance, the after-effects 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 training effects.

----- PLEASE INSERT TABLE 1 ABOUT HERE -----

Short overview of reviewed studies

Acknowledging the involvement and relevance of different domain-specific and domain-general functions, associated brain areas, and networks in numerical and arithmetic processes exceeds the scope of this mini-review, 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. Table 1 presents an overview of the reviewed studies¹.

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. For comparing the magnitudes of two-digit numbers, unilateral left-side parietal anodal tDCS generally led to more accurate responses (Hauser et al. 2013). Conversely, a bipolar oppositional placement with right anodal, left cathodal parietal stimulation impaired response times for single-digits close to the comparison referent (Li et al. 2015). Thus, the bipolar stimulation modulated the increasing difficulty to distinguish closer digits, termed 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 for magnitude representations 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, but also for processing multi-digit numbers could encompass more task-induced activity ready for neuromodulation. NDE in multi-digit comparisons was unaffected by several tDCS

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.

1 configurations of Hauser et al. (2013), but the distractor-distance effect for selecting
2 correct two-digit addition results was monotonically modulated by a bilateral-
3 bicephalic parietal stimulation (Klein et al. 2013). In contrast to the effect of tDCS on
4 the parietal lobe, when the prefrontal cortex was stimulated both NDE and single-digit
5 accuracy rates were unaffected. Instead, spatial-numerical associations were blocked
6 by cathodal tDCS (Schroeder et al. 2016).

8 ***Arithmetic performance modulations***

9 Performing even on simple arithmetic operations requires domain-general working
10 memory and executive functions involvement to maintain operation components, yet
11 to different extents depending on the exact task. Most studies employed supraorbital
12 or prefrontal return cathodes without necessarily highlighting potential effects on such
13 domain-general functions. Interestingly, for novel and complex subtractions, left-
14 parietal tDCS prevented characteristic prefrontal deactivations below the right-
15 prefrontal cathode as captured with simultaneous fMRI (Hauser et al. 2016) and this
16 configuration improved reaction times (Hauser et al. 2013). In another paradigm, after
17 viewing an instructional video, administering a complex statistical procedure was
18 enhanced from left-parietal anodal tDCS with temporal cathode (Houser et al. 2015),
19 but not with prefrontal cathode placement (Houser et al. 2014). Also considering
20 neurodevelopmental studies, the accumulation of arithmetic proficiency may be
21 accompanied by a shift from broad prefrontal to precise parietal activations
22 (Zamarian et al. 2009). In this line, both frontal and parietal excitatory tRNS
23 generated greater speed improvements over the course of an experiment in
24 subtraction verifications, but not in word classifications (Pasqualotto 2016).
25 Furthermore, tDCS to one area can lead to altered activations over wide-spread
26 networks in the brain and to effects on cognitive functions related to areas distant
27 from the stimulated area. For example, cathodal stimulation of the cerebellum led to
28 improvements in paced auditory serial subtraction by disinhibition of prefrontal activity
29 (Pope and Miall 2012), and comparable results were obtained with prefrontal anodal
30 tDCS (Pope et al. 2015). In clinical research, a variant of the serial addition WM task
31 is often used in conjunction with tDCS to enhance domain-general functions and
32 emotional processing in depressive patients (Vanderhasselt et al. 2015): Repetitively
33 solving additions at increasing speed frustrates participants and elicits negative
34 affect, but anodal prefrontal tDCS can concurrently improve emotional responses and

1 arithmetic performance (Plewnia et al. 2015). Correspondingly, low- and high-math
2 anxiety individuals show impaired and improved arithmetic performance, respectively,
3 following tDCS above the prefrontal cortex (Sarkar et al. 2014). These results also
4 highlight the importance of emotion for math-related cognitive processing, for which
5 behavioral correlations have often been reported (Suárez-Pellicioni, Macarena,
6 Núñez-Peña, María Isabel, & Colomé 2016).

7 Also domain-specific effects in multi-digit processing could be modulated: Left-
8 parietal anodal tDCS with 1.5 mA was beneficial for solving problems with larger
9 operands (problem size effect; sums exceeding 10 and including carries), but
10 decreased accuracy in small problems (Rütsche et al. 2015). These differential
11 (beneficial and detrimental) effects seem to be incompatible with a simple domain-
12 general explanation, such as attention, working memory or response preparation
13 processes. Furthermore, whereas the latter result of impaired accuracy from anodal
14 tDCS is counterintuitive, system noise injection by anodal tDCS could skew
15 arithmetic retrieval precisions and this conception was corroborated by concurrent
16 EEG theta measurements (Rütsche et al. 2015; see also Fertonani and Miniussi
17 2016). Regarding place-value effects (e.g., carrying unit-digits), right-side anodal vs.
18 cathodal parietal tDCS prolonged latency increases for carry operations in a two-digit
19 addition task out of a series of unilateral placements (Artemenko et al. 2015).

21 ***Numerical training modulations***

22 Whereas tRNS was used only selectively in studies on performance, the technique
23 appears more appealing for numerical and arithmetic training. Highlighting the role of
24 concurrent ('online') stimulation during cognitive training, Cappelletti et al. (2013)
25 assembled comparisons between the combinations of training with parietal, motor,
26 and sham tRNS over five days, but also with a parietal tRNS during rest. Number
27 acuity in dot-array discrimination improved most from the parietal stimulation
28 combined with training, but no transfer to arithmetic tasks was observed.

29 To investigate numerical learning in adults, a prominently investigated paradigm is
30 the artificial symbols training where arbitrary, meaningless figures are assigned to
31 numerical magnitudes. Repeated feedback-guided magnitude comparisons with the
32 artificial symbols (training phase) produce automatic number evaluations that
33 interfere with physical size presentations and map onto space (test phase; Tzelgov et
34 al. 2000). In this paradigm, oppositional parietal tDCS (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 (Luculano 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 (Luculano and Cohen Kadosh 2014). Although certainly larger samples are required to confirm this pattern, the application of tDCS-combined trainings may provide effective rehabilitation and treatment prospects for numerical deficits.

Arithmetic training modulations

With artificial symbols depicting calculation algorithms for arithmetic operations, drill and calculation training combined with prefrontal tRNS improved learning rates, led to sustained calculation performance 6 months later, and generalized to untrained calculation problems (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 cortex 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 (verbal working memory span) (Looi et al. 2016a). These first studies demonstrate the potential of tES for enhancing arithmetic training effects in healthy adult subjects and they 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

1 potentially restrained by unknown physical and cognitive side effects (Krause and
2 Cohen Kadosh 2013). Different neurophysiological profiles of individuals or groups at
3 certain development stages (e.g., dyscalculia, stroke patients, children) most likely
4 necessitate tailored parametrical and training-related adjustments, e.g., to also
5 consider specific numerical, arithmetic, and/or domain-general impairments such as
6 working memory capacity. In this respect, tES research is still in its infancy.
7 Moreover, most conclusions are based on single studies, researchers implement
8 dissimilar tES configurations, and the interdependence of different brain areas and
9 effects in certain tasks is not completely clear. In order to further integrate these
10 partially heterogeneous findings, interpretations of different modulations by tES must
11 also consider and build on the ongoing validation of its very basic principles.

13 **tES Configurations**

14 According to physical arrangements classification (Nasseri et al. 2015), successful
15 modulations of numerical performance utilized unilateral monopolar placements with
16 large return electrodes, bilateral bipolar-balanced and non-balanced, as well as the
17 dual-channel bilateral double-monopolar arrangement by Klein et al. (2013). Most
18 studies focus on parietal placements with 1mA, but also prefrontal placements
19 appear effective with tRNS (Pasqualotto 2016) and produce significant modulations
20 of spatial-numerical associations (Schroeder et al. 2016) and of math-related
21 emotional processing (Sarkar et al. 2014; Plewnia et al. 2015).

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

31 An interesting concept is the modulation of distinct learning phases over different
32 cortex regions as implemented by Popescu et al. (2016). Future research needs to
33 validate this approach by individualized transcranial stimulation or by comparing
34 different configuration changes directly (e.g., switching from prefrontal to parietal

1 stimulation after 2, 3, or 4 days). The potential of an augmentative effect and better
2 targeting of stimulation by considering training phase is also confirmed by the finding
3 that specific tDCS polarity sequences can lead to more effective modulations with
4 long-term sustainability (Dockery et al. 2009). Thus, fundamental research can also
5 inform interventional administrations, although generalizations from healthy
6 volunteers to different clinical populations (e.g., developmental dyscalculia or
7 acalculia after a stroke) should consider all translational aspects (e.g., functional,
8 structural, strategical compensation, and behavioral differences) in corresponding
9 models before selecting tES configuration parameters.

10 In the literature, prominently debated tES parameters are electrode configuration and
11 sizes, current intensity and duration, and timing of stimulation compared to task
12 performance (online vs. offline). These and other parameters do not seem to work
13 linearly (e.g., higher intensities can exceed optimal stimulation ranges; Batsikadze et
14 al. 2013) and their combination outcomes might critically depend on task and
15 individual characteristics as well as return electrode effects (Schroeder and Plewnia,
16 in press). Eventually, this variety of possibilities will allow for broad-ranging
17 applications and fine-grained targeting from underlying theoretical models. Currently,
18 however, simplification or even standardization of certain parameters would facilitate
19 cumulative research, and the ongoing development of electric field modelling tools
20 can already be used for selecting stimulation targets (Truong et al. 2014). Regarding
21 numerical processes, stimulations should be administered concurrent to a task and
22 could then achieve neurostructural precision following task-selective recruitment
23 (Clemens et al. 2013; Bikson and Rahman 2013), but effectivity can vary according to
24 individual differences. Based on the available literature, so far, electrode sizes do not
25 appear to produce remarkable effectivity differences in this domain. However, since
26 the anti-proportional relationship between current density and electrode size (at fixed
27 current strength) does not linearly scale for respective distances from the electrode
28 (e.g., scalp-brain distance) and smaller electrodes may not produce as dense fields
29 in deeper regions (Miranda et al. 2009; see also: Ho et al., 2016), this observation will
30 require systematic evaluation in the future. Furthermore, publication biases can
31 impede the development of better stimulation models, because nonsignificant results
32 are dismissed, theories are elaborated post-hoc, and results could lack
33 reproducibility. In this vein, preregistration of according studies and protocols (e.g.,

1 <https://aspredicted.org> or <https://osf.io>) could facilitate scientific communication and
2 rigorous evaluation of tES methods.

4 **Conclusion**

5 Both tDCS and tRNS can enhance arithmetic capabilities in adult populations and
6 could be promising tools for deviant performance populations. The current literature
7 is coined by heterogeneity in variable parameters such as montage, but effectivity
8 estimation requires better standardization. Studies with (sub-) clinical populations and
9 children are needed to examine the usefulness of tES for at-risk groups. However,
10 having said that, future research must consider their potentially different
11 neurofunctional signatures, examine potential side effects, and discuss neuroethical
12 questions (Cohen Kadosh et al. 2012; Davis 2014). Documentation of (individualized)
13 task-specific brain activity will potentially allow for predictive adjustment of tES
14 configurations and better evaluation thereof, i.e., using fMRI (Clemens et al. 2013),
15 EEG (Grabner et al. 2015), or fNIRS (Snowball et al. 2013). Further tES precision
16 could be obtained from considering a neurodevelopmental perspective, relevant
17 domain-related states, concurrent neuroimaging, and theoretical optimization of task-
18 related brain-structure correspondence in experimental and training studies to
19 improve efficacy and replication (Harty, Sella, & Cohen Kadosh, in press).

21 **Acknowledgements**

22 Christina Artemenko and Thomas Dresler were funded by the LEAD Graduate School
23 & Research Network [GSC1028], a project of the Excellence Initiative of the German
24 federal and state governments, where Hans-Christoph Nuerk is a principal
25 investigator. Hans-Christoph Nuerk's work was funded by the ScienceCampus
26 Tübingen (Cluster 8).

28 **References**

- 29 Antal A, Herrmann CS (2016) Transcranial Alternating Current and Random Noise
30 Stimulation: Possible Mechanisms. *Neural Plast.* doi: 10.1155/2016/3616807
31 Arsalidou M, Taylor MJ (2011) Is $2+2=4$? Meta-analyses of brain areas needed for
32 numbers and calculations. *Neuroimage* 54:2382–93. doi:

1 10.1016/j.neuroimage.2010.10.009

2 Artemenko C, Moeller K, Huber S, Klein E (2015) Differential influences of unilateral
3 tDCS over the intraparietal cortex on numerical cognition. *Front Hum Neurosci*
4 9:110. doi: 10.3389/fnhum.2015.00110

5 Batsikadze G, Moliadze V, Paulus W, et al (2013) Partially non-linear stimulation
6 intensity-dependent effects of direct current stimulation on motor cortex
7 excitability in humans. *J Physiol* 591:1987–2000. doi:
8 10.1113/jphysiol.2012.249730

9 Battleday RM, Muller T, Clayton MS, Kadosh RC (2014) Mapping the mechanisms of
10 transcranial alternating current stimulation: A pathway from network effects to
11 cognition. *Front Psychiatry* 5:162. doi: 10.3389/fpsyt.2014.00162

12 Bikson M, Datta A, Rahman A, Scaturro J (2010) Electrode montages for tDCS and
13 weak transcranial electrical stimulation: Role of “return” electrode’s position and
14 size. *Clin Neurophysiol* 121:1-1976–1978. doi:
15 10.1097/MPG.0b013e3181a15ae8.Screening

16 Bikson M, Rahman A (2013) Origins of specificity during tDCS: anatomical, activity-
17 selective, and input-bias mechanisms. *Front Hum Neurosci* 7:688. doi:
18 10.3389/fnhum.2013.00688

19 Bynner J, Parsons S (1997) Does Numeracy Matter? Evidence from the National
20 Child Development Study on the Impact of Poor Numeracy on Adult Life. Basic
21 Skills Agency, Commonwealth House, London WC1A 1NU, London, United
22 Kingdom

23 Cappelletti M, Gessaroli E, Hithersay R, et al (2013) Transfer of Cognitive Training
24 across Magnitude Dimensions Achieved with Concurrent Brain Stimulation of the
25 Parietal Lobe. *J Neurosci* 33:14899–14907. doi: 10.1523/JNEUROSCI.1692-
26 13.2013

- 1 Chaieb L, Antal A, Paulus W (2015) Transcranial random noise stimulation-induced
- 2 plasticity is NMDA-receptor independent but sodium-channel blocker and
- 3 benzodiazepines sensitive. *Front Neurosci* 9:125. doi: 10.3389/fnins.2015.00125
- 4 Clemens B, Jung S, Zvyagintsev M, et al (2013) Modulating arithmetic fact retrieval: A
- 5 single-blind, sham-controlled tDCS study with repeated fMRI measurements.
- 6 *Neuropsychologia* 51:1279–1286. doi: 10.1016/j.neuropsychologia.2013.03.023
- 7 Cohen J (1988) *Statistical Power analysis for the Behavioral Sciences*, 2nd ed.
- 8 Lawrence Erlbaum Associates, Inc., New Jersey
- 9 Cohen Kadosh R, Levy N, O’Shea J, et al (2012) The neuroethics of non-invasive
- 10 brain stimulation. *Curr Biol* 22:R108-11. doi: 10.1016/j.cub.2012.01.013
- 11 Cohen Kadosh R, Soskic S, Luculano T, et al (2010) Modulating neuronal activity
- 12 produces specific and long-lasting changes in numerical competence. *Curr Biol*
- 13 20:2016–2020. doi: 10.1016/j.cub.2010.10.007
- 14 Davis NJ (2014) Transcranial stimulation of the developing brain: a plea for extreme
- 15 caution. *Front Hum Neurosci* 8:8–11. doi: 10.3389/fnhum.2014.00600
- 16 Dehaene S, Piazza M, Pinel P, Cohen L (2003) Three parietal circuits for number
- 17 processing. *Cogn Neuropsychol* 20:487–506. doi: 10.1080/02643290244000239
- 18 Dockery CA, Hueckel-Weng R, Birbaumer N, Plewnia C (2009) Enhancement of
- 19 planning ability by transcranial direct current stimulation. *J Neurosci* 29:7271–7.
- 20 doi: 10.1523/JNEUROSCI.0065-09.2009
- 21 Duecker F, Sack AT (2015) Rethinking the role of sham TMS. *Front Psychol* 6:1–5.
- 22 doi: 10.3389/fpsyg.2015.00210
- 23 Fertonani A, Miniussi C (2016) Transcranial Electrical Stimulation: What We Know
- 24 and Do Not Know About Mechanisms. *Neurosci*. doi:
- 25 10.1177/1073858416631966
- 26 Fertonani A, Pirulli C, Miniussi C (2011) Random noise stimulation improves

- 1 neuroplasticity in perceptual learning. *J Neurosci* 31:15416–23. doi:
2 10.1523/JNEUROSCI.2002-11.2011
- 3 Gill J, Shah-basak PP, Hamilton R (2015) It's the Thought That Counts: Examining
4 the Task-dependent Effects of Transcranial Direct Current Stimulation on
5 Executive Function. *Brain Stimul* 8:253–259. doi: 10.1016/j.brs.2014.10.018
- 6 Grabner RH, Rüttsche B, Ruff CC, Hauser TU (2015) Transcranial direct current
7 stimulation of the posterior parietal cortex modulates arithmetic learning. *Eur J*
8 *Neurosci* 42:1667–1674. doi: 10.1111/ejn.12947
- 9 Harty S, Sella F, Cohen Kadosh R. (in press). Mind the Brain: The mediating and
10 moderating role of neurophysiology. *Trends Cogn Sci*
- 11 Hauser TU, Rotzer S, Grabner RH, et al (2013) Enhancing performance in numerical
12 magnitude processing and mental arithmetic using transcranial Direct Current
13 Stimulation (tDCS). *Front Hum Neurosci* 7:244. doi: 10.3389/fnhum.2013.00244
- 14 Hauser TU, Rüttsche B, Wurmitzer K, et al (2016) Neurocognitive Effects of
15 Transcranial Direct Current Stimulation in Arithmetic Learning and Performance:
16 a Simultaneous tDCS-fMRI Study. *Brain Stimul*. doi: 10.1016/j.brs.2016.07.007
- 17 Ho KA, Taylor JL, Chew T, et al (2016) The Effect of Transcranial Direct Current
18 Stimulation (tDCS) Electrode Size and Current Intensity on Motor Cortical
19 Excitability: Evidence from Single and Repeated Sessions. *Brain Stimul* 9:1–7.
20 doi: 10.1016/j.brs.2015.08.003
- 21 Holmes J, Byrne EM, Gathercole SE, et al (2016) Transcranial Random Noise
22 Stimulation Does Not Enhance the Effects of Working Memory Training. *J Cogn*
23 *Neurosci* 28:1471-1483. doi:10.1162/jocn_a_00993
- 24 Houser R, Thoma S, Fonseca D, et al (2015) Enhancing statistical calculation with
25 transcranial direct current stimulation (tDCS) to the left intra-parietal sulcus
26 (IPS). *Trends Neurosci Educ* 4:98–101. doi: 10.1016/j.tine.2015.07.002

- 1 Houser R, Thoma S, Stanton M (2014) The effect of transcranial direct current
2 stimulation (tDCS) on learning and performing statistical calculations. J Artic
3 Support Null Hypothesis 11:1–10.
- 4 Iuculano T, Cohen Kadosh R (2013) The Mental Cost of Cognitive Enhancement. J
5 Neurosci 33:4482–4486. doi: 10.1523/JNEUROSCI.4927-12.2013
- 6 Iuculano T, Cohen Kadosh R (2014) Preliminary evidence for performance
7 enhancement following parietal lobe stimulation in Developmental Dyscalculia.
8 Front Hum Neurosci 8:38. doi: 10.3389/fnhum.2014.00038
- 9 Jacobson L, Koslowsky M, Lavidor M (2012) tDCS polarity effects in motor and
10 cognitive domains: a meta-analytical review. Exp brain Res 216:1–10. doi:
11 10.1007/s00221-011-2891-9
- 12 Kaufmann L, Mazzocco MM, Dowker A, et al (2013) Dyscalculia from a
13 developmental and differential perspective. Front Psychol 4:1–5. doi:
14 10.3389/fpsyg.2013.00516
- 15 Klein E, Mann A, Huber S, et al (2013) Bilateral Bi-Cephalic tDCS with Two Active
16 Electrodes of the Same Polarity Modulates Bilateral Cognitive Processes
17 Differentially [corrected]. PLoS One 8:e71607. doi:
18 10.1371/journal.pone.0071607
- 19 Klein E, Suchan J, Moeller K, et al (2014) Considering structural connectivity in the
20 triple code model of numerical cognition: differential connectivity for magnitude
21 processing and arithmetic facts. Brain Struct Funct 1–17. doi: 10.1007/s00429-
22 014-0951-1
- 23 Knops A, Nuerk H-C, Sparing R, et al (2006) On the Functional Role of Human
24 Parietal Cortex in Number Processing: How Gender Mediates the Impact of a
25 Virtual Lesion Induced by rTMS. Neuropsychologia 44:2270-2283.Krause B,
26 Cohen Kadosh R (2013) Can transcranial electrical stimulation improve learning

- 1 difficulties in atypical brain development? A future possibility for cognitive
- 2 training. *Dev Cogn Neurosci* 6:176–194. doi: 10.1016/j.dcn.2013.04.001
- 3 Li LM, Leech R, Scott G, et al (2015) The effect of oppositional parietal transcranial
- 4 direct current stimulation on lateralized brain functions. *Eur J Neurosci* 42:2904–
- 5 2914. doi: 10.1111/ejn.13086
- 6 Looi CY, Cohen Kadosh R (2016) Brain stimulation, mathematical and numerical
- 7 training : Contribution of core and non-core skills. In: *Progress in brain research*.
- 8 pp 353–88
- 9 Looi CY, Duta M, Brem A-K, et al (2016a) Combining brain stimulation and video
- 10 game to promote long-term transfer of learning and cognitive enhancement. *Sci*
- 11 *Rep* 6:22003. doi: 10.1038/srep22003
- 12 Looi CY, Thompson J, Krause B, Cohen Kadosh R (2016b) *The Neuroscience of*
- 13 *Mathematical Cognition and Learning*. Paris
- 14 Matejko AA, Ansari D (2015) Drawing connections between white matter and
- 15 numerical and mathematical cognition: A literature review. *Neurosci Biobehav*
- 16 *Rev* 48:35–52. doi: 10.1016/j.neubiorev.2014.11.006
- 17 Miranda PC, Faria P, Hallett M (2009) What does the ratio of injected current to
- 18 electrode area tell us about current density in the brain during tDCS? *Clin*
- 19 *Neurophysiol* 120:1183–1187. doi: 10.1016/j.clinph.2009.03.023
- 20 Moliadze V, Antal A, Paulus W (2010) Electrode-distance dependent after-effects of
- 21 transcranial direct and random noise stimulation with extracephalic reference
- 22 electrodes. *Clin Neurophysiol* 121:2165–71. doi: 10.1016/j.clinph.2010.04.033
- 23 Moliadze V, Fritzsche G, Antal A (2014) Comparing the efficacy of excitatory
- 24 transcranial stimulation methods measuring motor evoked potentials. *Neural*
- 25 *Plast* 2014:Article ID 837141. doi: 10.1155/2014/837141
- 26 Moyer RS, Landauer TK (1967) Time required for Judgements of Numerical

- 1 Inequality. *Nature* 215:1519–1520. doi: 10.1038/2151519a0
- 2 Mulquiney PG, Hoy KE, Daskalakis ZJ, Fitzgerald PB (2011) Improving working
3 memory: Exploring the effect of transcranial random noise stimulation and
4 transcranial direct current stimulation on the dorsolateral prefrontal cortex. *Clin*
5 *Neurophysiol* 122:2384–2389. doi: 10.1016/j.clinph.2011.05.009
- 6 Nasser P, Nitsche MA, Ekhtiari H (2015) A framework for categorizing electrode
7 montages in transcranial direct current stimulation. *Front Hum Neurosci* 9:1–5.
8 doi: 10.3389/fnhum.2015.00054
- 9 Nieder A (2016) The neuronal code for number. *Nat Rev Neurosci*. doi:
10 10.1038/nrn.2016.40
- 11 Nitsche MA, Paulus W (2000) Excitability changes induced in the human motor
12 cortex by weak transcranial direct current stimulation. *J Physiol* 527 Pt 3:633–9.
- 13 Ozen S, Sirota A, Belluscio MA, et al (2010) Transcranial Electric Stimulation Entrain
14 Cortical Neuronal Populations in Rats. *J Neurosci* 30:11476–11485. doi:
15 10.1523/JNEUROSCI.5252-09.2010
- 16 Pasqualotto A (2016) Transcranial random noise stimulation benefits arithmetic skills.
17 *Neurobiol Learn Mem* 133:7–12. doi: 10.1016/j.nlm.2016.05.004
- 18 Plewnia C, Schroeder PA, Kunze R, et al (2015) Keep Calm and Carry On: Improved
19 Frustration Tolerance and Processing Speed by Transcranial Direct Current
20 Stimulation (tDCS). *PLoS One* 10:e0122578. doi: 10.1371/journal.pone.0122578
- 21 Pope PA, Brenton JW, Miall RC (2015) Task-Specific Facilitation of Cognition by
22 Anodal Transcranial Direct Current Stimulation of the Prefrontal Cortex. *Cereb*
23 *Cortex* 1–8. doi: 10.1093/cercor/bhv094
- 24 Pope PA, Miall RC (2012) Task-specific facilitation of cognition by cathodal
25 transcranial direct current stimulation of the cerebellum. *Brain Stimul* 5:84–94.
26 doi: 10.1016/j.brs.2012.03.006

- 1 Popescu T, Krause B, Terhune DB, et al (2016) Transcranial random noise
- 2 stimulation mitigates increased difficulty in an arithmetic learning task.
- 3 Neuropsychologia 81:255–264. doi: 10.1016/j.neuropsychologia.2015.12.028
- 4 Priori A, Hallett M, Rothwell JC (2009) Repetitive transcranial magnetic stimulation or
- 5 transcranial direct current stimulation? Brain Stimul 2:241–245. doi:
- 6 10.1016/j.brs.2009.02.004
- 7 Rahman A, Reato D, Arlotti M, et al (2013) Cellular effects of acute direct current
- 8 stimulation: somatic and synaptic terminal effects. J Physiol 591:2563–78. doi:
- 9 10.1113/jphysiol.2012.247171
- 10 Rütsche B, Hauser TU, Jäncke L, Grabner RH (2015) When problem size matters:
- 11 Differential effects of brain stimulation on arithmetic problem solving and neural
- 12 oscillations. PLoS One 10:1–17. doi: 10.1371/journal.pone.0120665
- 13 Salillas E, Semenza C (2015) Mapping the Brain for Math: Reversible inactivation by
- 14 direct cortical electrostimulation and transcranial magnetic stimulation. In: Cohen
- 15 Kadosh R, Dowker A (eds) The Oxford Handbook of Numerical Cognition. Oxford
- 16 University Press, New York, USA, pp 583–611
- 17 Sarkar A, Dowker A, Kadosh RC (2014) Cognitive Enhancement or Cognitive Cost:
- 18 Trait-Specific Outcomes of Brain Stimulation in the Case of Mathematics Anxiety.
- 19 J Neurosci 34:16605–16610. doi: 10.1523/JNEUROSCI.3129-14.2014
- 20 Schroeder PA, Pfister R, Kunde W, et al (2016) Counteracting implicit conflicts by
- 21 Electrical Inhibition of the Prefrontal Cortex. J Cogn Neurosci 28:1737–1748. doi:
- 22 10.1162/jocn
- 23 Schroeder PA, Plewnia C (in press) Beneficial effects of cathodal transcranial direct
- 24 current stimulation (tDCS) on cognitive performance *J Cogn Enhancement*.
- 25 Silvanto J, Pascual-Leone A (2008) State-dependency of transcranial magnetic
- 26 stimulation. Brain Topogr 21:1–10. doi: 10.1007/s10548-008-0067-0

- 1 Snowball A, Tachtsidis I, Popescu T, et al (2013) Long-term enhancement of brain
- 2 function and cognition using cognitive training and brain stimulation. *Curr Biol*
- 3 23:987–992. doi: 10.1016/j.cub.2013.04.045
- 4 Suárez-Pellicioni M, Núñez-Peña MI, Colomé À (2016) Math anxiety: A review of its
- 5 cognitive consequences, psychophysiological correlates, and brain bases. *Cogn*
- 6 *Affect Behav Neurosci* 16:3–22. doi: 10.3758/s13415-015-0370-7
- 7 Terney D, Chaieb L, Moliadze V, et al (2008) Increasing human brain excitability by
- 8 transcranial high-frequency random noise stimulation. *J Neurosci* 28:14147–
- 9 14155. doi: 10.1523/JNEUROSCI.4248-08.2008
- 10 Truong DQ, Hüber M, Xie X, et al (2014) Clinician accessible tools for GUI
- 11 computational models of transcranial electrical stimulation: BONSAI and
- 12 SPHERES. *Brain Stimul* 7:521–524. doi: 10.1016/j.brs.2014.03.009.Clinician
- 13 Tzelgov J, Yehene V, Kotler L, Alon A (2000) Automatic comparisons of artificial digits
- 14 never compared: learning linear ordering relations. *J Exp Psychol Learn Mem*
- 15 *Cogn* 26:103–120. doi: 10.1037/0278-7393.26.1.103
- 16 van der Groen O, Wenderoth N (2016) Transcranial Random Noise Stimulation of
- 17 Visual Cortex: Stochastic Resonance Enhances Central Mechanisms of
- 18 Perception. *J Neurosci* 36:5289–98. doi: 10.1523/JNEUROSCI.4519-15.2016
- 19 Vanderhasselt M-A, De Raedt R, Namur V, et al (2015) Transcranial electric
- 20 stimulation and neurocognitive training in clinically depressed patients: A pilot
- 21 study of the effects on rumination. *Prog Neuro-Psychopharmacology Biol*
- 22 *Psychiatry* 57:93–99. doi: 10.1016/j.pnpbp.2014.09.015
- 23 Zamarian L, Ischebeck A, Delazer M (2009) Neuroscience of learning arithmetic-
- 24 Evidence from brain imaging studies. *Neurosci Biobehav Rev* 33:909–925. doi:
- 25 10.1016/j.neubiorev.2009.03.005