

Transcranial Electrical Stimulation and Numerical Cognition

Amar Sarkar and Roi Cohen Kadosh
University of Oxford

The effects of transcranial electrical stimulation (tES) have been documented for a variety of mental functions, including numerical cognition. This article first reviews 2 prominent forms of tES, transcranial direct current stimulation (tDCS) and transcranial random noise stimulation (tRNS). This is followed by an assessment of the applications of this technology in the enhancement of aspects of numerical cognition, including numerosity, magnitude representation, and more complex arithmetic operations. The review concludes with discussions of directions for future research. These include the need to take individual differences into account in experimental designs, extending research to individuals with difficulties and deficits in working with numbers, the need to consider potential cognitive costs that may offset cognitive benefits of tES. A recurring theme in this article is the need to move toward greater ecological validity of experimental findings.

Keywords: transcranial electrical stimulation, transcranial DC stimulation, transcranial random noise stimulation, cognitive enhancement, numerical cognition

Processing, representing, and manipulating numbers and quantities is one of the most advanced cognitive abilities humans possess. This ability is becoming increasingly important with the rising dependence of society on technology, and rising educational and occupational focus on quantitative aptitude. Moreover, deficits in numerical cognition may impair both individual and societal achievement (Beddington et al., 2008; Duncan et al., 2007; Parsons & Bynner, 2005).

Recently, there has been increasing academic and public attention on the applications of transcranial electrical stimulation (tES) for cognitive enhancement. Improvements have been observed in a range of psychological variables in healthy populations, including high-level cognition such as visual short term memory (Tseng et al., 2012), working memory (Fregni et al., 2005; Richmond et al., 2014), planning (Dockery et al., 2009), language learning (Flöel et al., 2008; Meinzer et al., 2014), analogical reasoning (Santarnecchi et al., 2013), and numerical cognition. The application of tES to numerical cognition is the focus of this review.

Research on the use of tES for cognitive enhancement is very new, and within this emerging field, tES for enhancing numerical cognition is itself a nascent field of enquiry. The use of tES is both of scientific importance in understanding numerical cognition, and also of immense practical importance in the enhancement of typical and atypical numerical cognition. There are as yet no reviews on the use of tES for enhancing numerical cognition, though there are several on tES and general cognitive enhancement (e.g., Cohen Kadosh, 2013, in press; Jacobson, Koslowsky, & Lavidor, 2012; Krause & Cohen Kadosh, 2013; Kuo & Nitsche, 2012). An area of

particular interest is the combination of tES and cognitive training, which seems to produce long-lived effects that are apparent even up to 6 months after the last stimulation session (e.g., Cappelletti et al., 2013; Cohen Kadosh et al., 2010; Looi et al., 2015; Reis et al., 2009; Snowball et al., 2013). Cognitive training leads to particular neuroanatomical and neurophysiological changes (Boyke et al., 2008; Draganski et al., 2004; Klingberg, 2010; Slagter et al., 2007). tES is combined with training to facilitate these neural changes, acting as an ingredient to sensitize the neural environment to the effects of training, thereby facilitating the acquisition of the practice effects to a greater degree than training by itself (Cohen Kadosh et al., 2012).

This article attempts to bring together several important findings in this (small) body of research to provide a general picture of this emerging field. The material is divided into three sections: (a) A short overview of two relevant forms of tES; (b) the application of tES in the enhancement of three aspects of numerical cognition: numerosity, magnitude processing, and arithmetic operations; and (c) an agenda for future research.

Principles of tES

The technology is portable, painless, easy to use, and safe when appropriate screening procedures are conducted (e.g., excluding participants with a personal or family history of epilepsy). The impact of the stimulation on neuronal activity depends on the shape of the current, and in this regard, there are several forms of tES that produce different effects based on the nature of the current. All the forms of tES can be accompanied by appropriate placebo conditions, in which the current is simply turned off after a brief period (e.g., 30 s), which serves as an effective placebo by generating physical sensations indistinguishable from real stimulation (Gandiga, Hummel, & Cohen, 2006), but no neural changes (Fritsch et al., 2010).

Two forms of tES have been used in numerical cognition research, transcranial direction current stimulation (tDCS), and

Amar Sarkar and Roi Cohen Kadosh, Department of Experimental Psychology, University of Oxford.

Correspondence concerning this article should be addressed to Roi Cohen Kadosh, Department of Experimental Psychology, University of Oxford, South Parks Road, Oxford, United Kingdom, OX1 3UD. E-mail: roi.cohenkadosh@psy.ox.ac.uk

transcranial random noise stimulation (tRNS), and some of their features are described below.

tDCS

This is the most well-known and most frequently used form of tES. The basis of tDCS is a constant current, whose application produces two types of stimulation. Anodal stimulation occurs where the current enters the brain (at the anode), and cathodal stimulation occurs where the current leaves the brain and reenters the electrode (at the cathode). A number of animal and human investigations has established that the polarity of the current (anodal or cathodal) produces particular types of changes in neural resting membrane potentials (Bindman, Lippold, & Redfearn, 1964; Márquez-Ruiz et al., 2012; Nitsche & Paulus, 2000). Anodal stimulation generally induces depolarization (i.e., bringing resting membrane potential closer to activation) and increasing excitability (Bindman et al., 1964; Fritsch et al., 2010; Nitsche & Paulus, 2000). Cathodal stimulation generally has the opposite effect, resulting in hyperpolarization and decreasing excitability (Bindman et al., 1964; Fritsch et al., 2010; Nitsche & Paulus, 2000). A general pattern of polarity-performance relationships has emerged over the numerous studies that have used tDCS. In particular, the majority of published work shows that anodal stimulation enhances performance, while cathodal stimulation produces impairments (Jacobson, Koslowsky, & Lavidor, 2012; Kuo & Nitsche, 2012). Please note, however, that this is not axiomatic, but rather a rule of thumb. In fact, some studies show the opposite pattern, with anodal stimulation impairing performance and cathodal stimulation enhancing it (e.g., Antal et al., 2004; Terhune, Tai, Cowey, Popescu, & Cohen Kadosh, 2011). Such differences may depend on several factors, such as the region being stimulated, or baseline activity in the stimulated region (Krause et al., 2013; Sarkar, Dowker, & Kadosh, 2014).

The electrical signal cannot directly penetrate further than the cortex, and can therefore only be used to modulate the activity of cortical regions directly beneath the scalp. However, while studies have found that the tDCS-effects are largely localised to the targeted brain region (Holland et al., 2011), more recent work is revealing that it also affects distributed networks functionally linked to the stimulation target, rather than being restricted to it (Keeser et al., 2011; Meinzer et al., 2012; Meinzer, Lindenbergh, Antonenko, Fleisch, & Flöel, 2013). There is also evidence that stimulating the cortex results in transmission of stimulation into subcortical regions (Bolzoni et al., 2013; Weber et al., 2014).

tRNS

Unlike tDCS, which involves a direct-form current, transcranial random noise stimulation involves the application of alternating currents at random frequencies. tRNS involves the generation of “samples” several hundred times per second, which are randomly assigned current amplitudes and normally distributed with a mean current of 0 mA. The fluctuations of these sample currents between positive and negative amplitudes around 0 is random, producing “noise” in the targeted region.

tRNS has several important features that distinguish it from tDCS. For example, it appears to exert excitatory effects at *both* electrodes, because of its oscillatory rather than direct form, which ensures its effects are independent of the polarity/direction of the

current (Chaieb et al., 2009; Terney et al., 2008). Furthermore, compared with anodal tDCS, high-frequency tRNS (e.g., 100–640 Hz) yields larger effects (Fertonani et al., 2011), potentially adding to the effect sizes of experiments. Finally, tRNS has a much higher cutaneous threshold compared with tDCS (Ambrus et al., 2010), meaning that it is more difficult to perceive the current as physical scalp sensations. Although tDCS is not physically painful, it does frequently produce tingling sensations, which fade quickly as the scalp habituates (Nitsche et al., 2008). However, these sensations are much lower in tRNS compared with tDCS (Ambrus et al., 2010). This makes it easier to maintain participant blindness to their experimental condition.

A note on transcranial magnetic stimulation. This review is structured around tES, though some mention of transcranial magnetic stimulation (TMS) will help to contextualise and distinguish the tES domain from that of TMS, which is a separate class of noninvasive brain stimulation. TMS is an older and better studied form of brain stimulation than tES. tES and TMS differ on several important features. TMS is the application of high-intensity magnetic fields to induce action potentials in relatively localised cortical regions. High-frequency pulses tend to produce cortical excitation, while low frequency pulses tend to produce cortical inhibition (Wagner, Valero-Cabre, & Pascual-Leone, 2007). TMS has been used to modulate cognition in a number of different studies, including numerical cognition (for a review, see Luber & Lisanby, 2014). For instance, Renzi, Vecchi, Silvanto, and Cattaneo, (2011) showed that TMS enhances performance on magnitude estimations, and Snyder, Bahramali, Hawker, and Mitchell, (2006) found that TMS improves numerosity or relative quantity judgments (both magnitude perception and numerosity are discussed in greater detail below).

TMS devices are substantially more expensive than tES devices (the former range from \$20,000 to \$100,000, while the latter range from \$400 to \$15,000; Priori, Hallett, & Rothwell, 2009). Beyond the cost, the portability of tES devices, weighing less than 1 kg, is much greater than that of TMS devices, which are much larger and heavier. Both the cost and the portability of the devices affect how easily they can be acquired by research groups, and also their eventual, more widespread use (note that we are not advocating unsupervised home use of tES, especially given the limited existing research, only that one of the aims of tES research is to make it a technology that, if effective, is accessible).

Over and above such issues, both techniques have important drawbacks. For instance, TMS produces a much more reliable inhibitory effect than cathodal tDCS. To this extent, it has been used to induce virtual lesions (temporary deactivation of specific cortical regions) to study the necessity of brain regions in cognitive functions. Within the realm of numerical cognition, TMS has been used to induce virtual lesions in parietal areas, with subsequent processing impairments in both numerosity (Cappelletti, Barth, Fregni, Spelke, & Pascual-Leone, 2007) and magnitude processing (Cohen Kadosh et al., 2007). Although cathodal tDCS has been shown to be inhibitory in many cases, this is not always so outside of the motor cortex, and the true inhibitory effects of cathodal tDCS remain under debate (Jacobson, Koslowsky, & Lavidor, 2012). In general, TMS produces stronger excitation and inhibition than tES is capable of, but at the same time, the cutaneous sensations perceived by the participants are also much stronger, and may be uncomfortable for some individuals and less optimal

when combined with multiple sessions of cognitive training. The placebo-control sham procedure for tES, described earlier, is also considerably superior to TMS. In TMS, sham stimulation typically produces a loud clicking sound that is easily perceived by the participant (Priori, Hallett, & Rothwell, 2009), making adequate participant blinding a major cause for concern. Finally, most tES studies apply current through large electrodes, often of size 25 cm² or 35 cm². This means that substantial sections of cortex are stimulated, including regions not of interest to the research. In contrast, TMS is able to target cortical regions with greater focality. However, this poor spatial resolution is a curious advantage for many tES studies. Because of the large electrode size, researchers can have greater confidence that the brain region of interest is receiving stimulation. In contrast, the focality of TMS implies greater error variance and there is a possibility of missing the intended region (Sack et al., 2009), which can only be addressed with larger sample sizes, thus increasing both the time and cost of the project.

This review focusses on tES for a number of reasons. For example, tES, because it is more easily used and owing to its effective placebo-control, allows for a large number of research questions to be investigated with relative ease. Indeed, there are many more tES studies of numerical cognition than TMS ones. Furthermore, given the different in cutaneous sensations, tES may also be more appropriate for use in children, a population in which stimulation-induced enhancements of numerical cognition are of particular value.

Evidence of tES-Induced Enhancement of Numerical Cognition

The Choice of the Brain Region

Previous neuroimaging research and meta-analyses often yield reliable targets for brain stimulation by indicating where activation occurs during particular types of tasks or experiences. For numerical cognition, two brain regions that have consistently been implicated in the execution of numerical tasks across a large number of studies are the parietal lobes and their subregions (Cantlon et al., 2006; Cohen Kadosh et al., 2008; Dehaene et al., 2003; Izard et al., 2009; Piazza et al., 2004; Zamarian et al., 2009) and the dorsolateral prefrontal cortex (Arsalidou et al., 2011; Zamarian et al., 2009).

Numerosity

Numerosity is proposed to play a critical role in numerical cognition. This evolved mechanism allows for an approximate representation of the number of objects in auditory or visual arrays, and is present both in humans and a variety of animals (Barth et al., 2003; Brannon & Terrace, 1998; Cordes et al., 2001; Dehaene et al., 1998; Gordon, 2004; Meck & Church, 1983; Nieder & Miller, 2003; Pica et al., 2004; Xu & Spelke, 2000). Numerosity can be measured through eliciting larger/smaller judgments in arrays of differing size. Larger approximations are processed without the need for object-by-object counting, and appear to be based on fast perceptual evaluations rather than more effortful verbal ones. Numerosity also appears to be closely associated with the parietal

lobes (Hubbard et al., 2005; Piazza & Izard, 2009; Piazza et al., 2007).

Previous research has indicated that more advanced forms of mathematical attainment are also linked to numerosity. For example, Halberda, Mazzocco, and Feigenson (2008) showed that numerosity is highly variable with considerable interindividual difference in the fineness of larger/smaller discriminations. They also explored the relationship between explicit, symbolic mathematics (as taught in schools) and the quality of individual numerosity, finding that finer larger or smaller judgments are related to greater mathematical achievement (Halberda, Mazzocco, & Feigenson, 2008; Libertus, Feigenson, & Halberda, 2011; Libertus, Odic, & Halberda, 2012).

Recently, a study by Cappelletti et al. (2013) examined the possibility of enhancing numerosity using brain stimulation across four experimental conditions. One of these combined numerosity training with brain stimulation, and the other three served to rule out possible confounds and alternative explanations. Transcranial random noise stimulation was applied (high frequency, 0–250 Hz) for 20 min (or 20 s, in sham stimulation) concurrently with the training sessions (see Figure 1 for the complete study design). In this study, 40 healthy adults were split into four groups: numerosity training with tRNS applied bilaterally to the parietal lobes, numerosity training with tRNS applied bilaterally to the motor cortex (a control region), numerosity training with placebo or sham stimulation, and parietal lobe tRNS in the absence of any training. Numerosity training lasted for five days, between pre- and posttest sessions. Numerosity ability is quantified with the Weber fraction (wf). Larger wfs indicate lower acuity in relative quantity judgments (for more detailed discussions on the wf, see Halberda et al., 2008, 2012).

Difference in wf from pre- to posttest was calculated as a percentage change, following a $[(\text{post-pre})/\text{pre}] \times 100$ rule. The authors found training without stimulation substantially improved numerosity performance (approximately 18%). However, the largest enhancement was noted in participants who received training combined with tRNS to the parietal lobes, (approximately 33%). This effect was also long-lived: at a follow-up 16 weeks later, only participants who received numerosity training combined with stimulation to the parietal lobes maintained the learning effects, suggesting that stimulation facilitated the cortical neuroplasticity associated with learning, improving both the initial acquisition and its subsequent duration.

The experiment also evaluated possible transfer effects to other cognitive variables, and found evidence transfer to two constructs that, like numerosity, involve processing quantity: time and space discrimination (i.e., determining if a line appears for a shorter or longer duration of time, or is shorter or longer in length, compared with a reference line). Perceptions of time and space, continuous variables like numerosity, have neural architectures overlapping with those for numerosity in the parietal lobes (Cantlon, 2012; Cantlon et al., 2009; Cohen Kadosh et al., 2008; Walsh, 2003). Therefore, improvements in numerosity may benefit such variables as well. Enhanced space and time discrimination was evident at the end-of-training posttests for only those participants who completed numerosity training combined with parietal tRNS (see Figure 2). However, the transfer effects were not long-lived, and were not maintained at follow-up. It is still important to acknowledge that

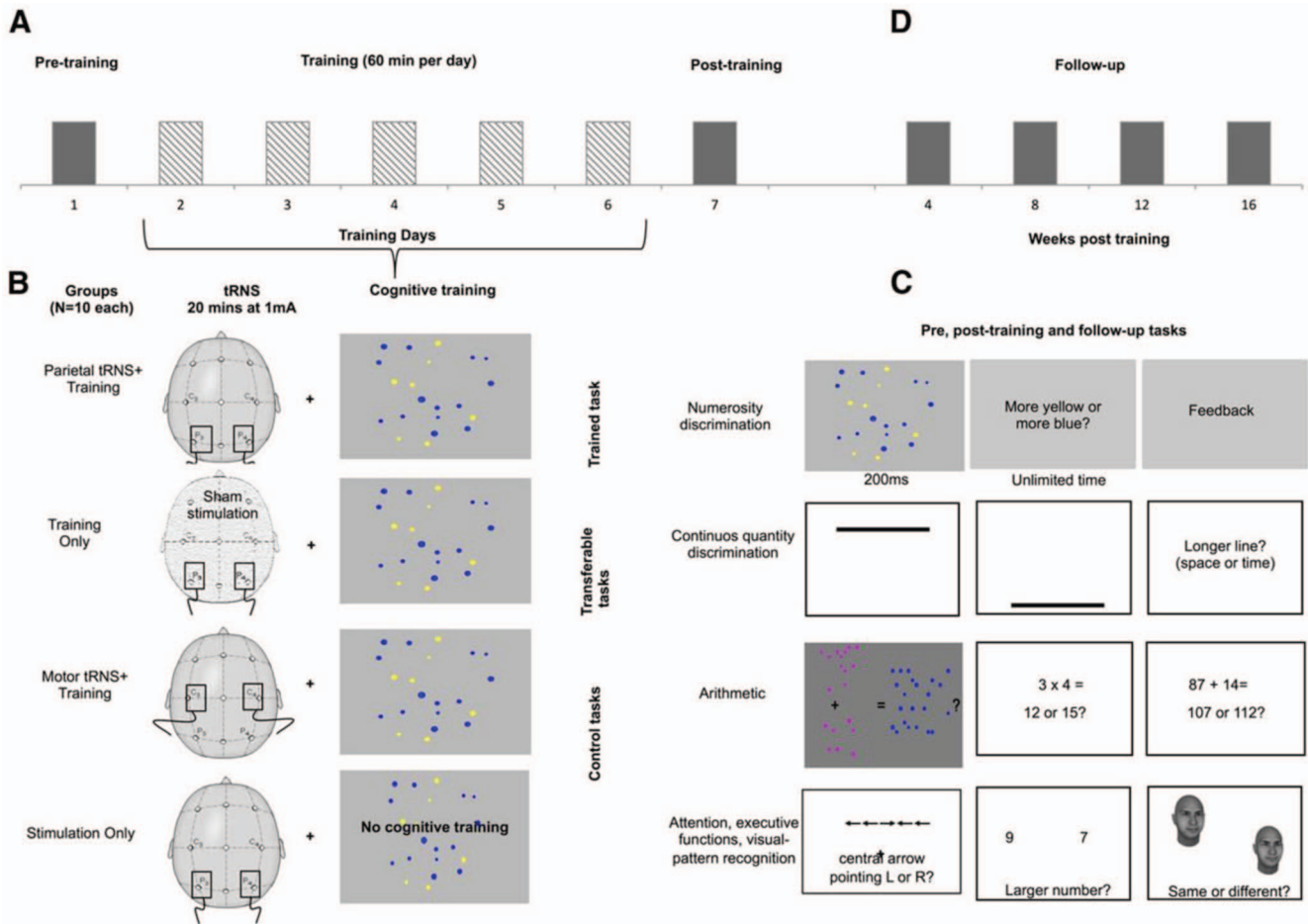


Figure 1. The training paradigm and the tasks used. (A) Participants in the parietal or motor tRNS + Training and in the Training Only groups were trained intensively (560 trials per day) on a numerosity discrimination task for five consecutive days, that is, Day 2–6 while (B) receiving real or sham stimulation to the parietal or motor areas. Participants on the Stimulation Only group received no training. Before the training (Day 1, pretraining), all participants were tested with (C) the numerosity discrimination task in addition to other continuous quantity-based tasks (time and space discrimination), arithmetic and control tasks. The same cognitive tasks were repeated at the end of the training (Day 7, posttraining) to test for any training-induced change, and (D) in the parietal tRNS + Training and Training Only groups again at Week 4, 8, 12, and 16 posttraining to test for any long-term effect of the training. Taken from [Cappelletti et al. \(2013\)](#). See the online article for the color version of this figure.

even this brief transfer could only be facilitated by tES, because the other groups given training showed no such transfer to time and space discrimination. This is indicative of the role of tES in enabling transfer effects from training regimes. There was no transfer to functions that were not as closely linked to numerosity, such as perception and attention.

The experiment also assessed performance on simple and complex arithmetic problems. For example, a simple problem would involve choosing the correct result for 3×4 from the two options 12 and 15. A more complex arithmetic operation would involve choosing the response *closer* to the correct response in an equation such as $87 + 14 = 104$ or 112, where the correct response is 104, which is closer to the true solution 101. An interesting finding was the *absence* of transfer to performance on either simple or complex problems, especially

given the suggested connection between numerosity and arithmetic performance in young children ([Halberda et al., 2008](#)). Therefore, though such findings are of considerable scientific interest, their ecological validity, in terms of improved mathematical performance, remains untested. There are both methodological and conceptual explanations for this lack of transfer.

Methodologically, there is the possibility of dose-dependence of effects. [Jaeggi et al. \(2008\)](#) showed that the transfer of working memory training (an adaptive *n*-back task) to measures of fluid intelligence (matrix reasoning) was sensitive to the number of weeks of working memory training, with larger training doses predicting greater performance on the matrix tasks. It is possible that transfer to other variables would have been observed with larger doses. From a conceptual standpoint, one possibility for the absence of transfer to arithmetic performance is that such an effect

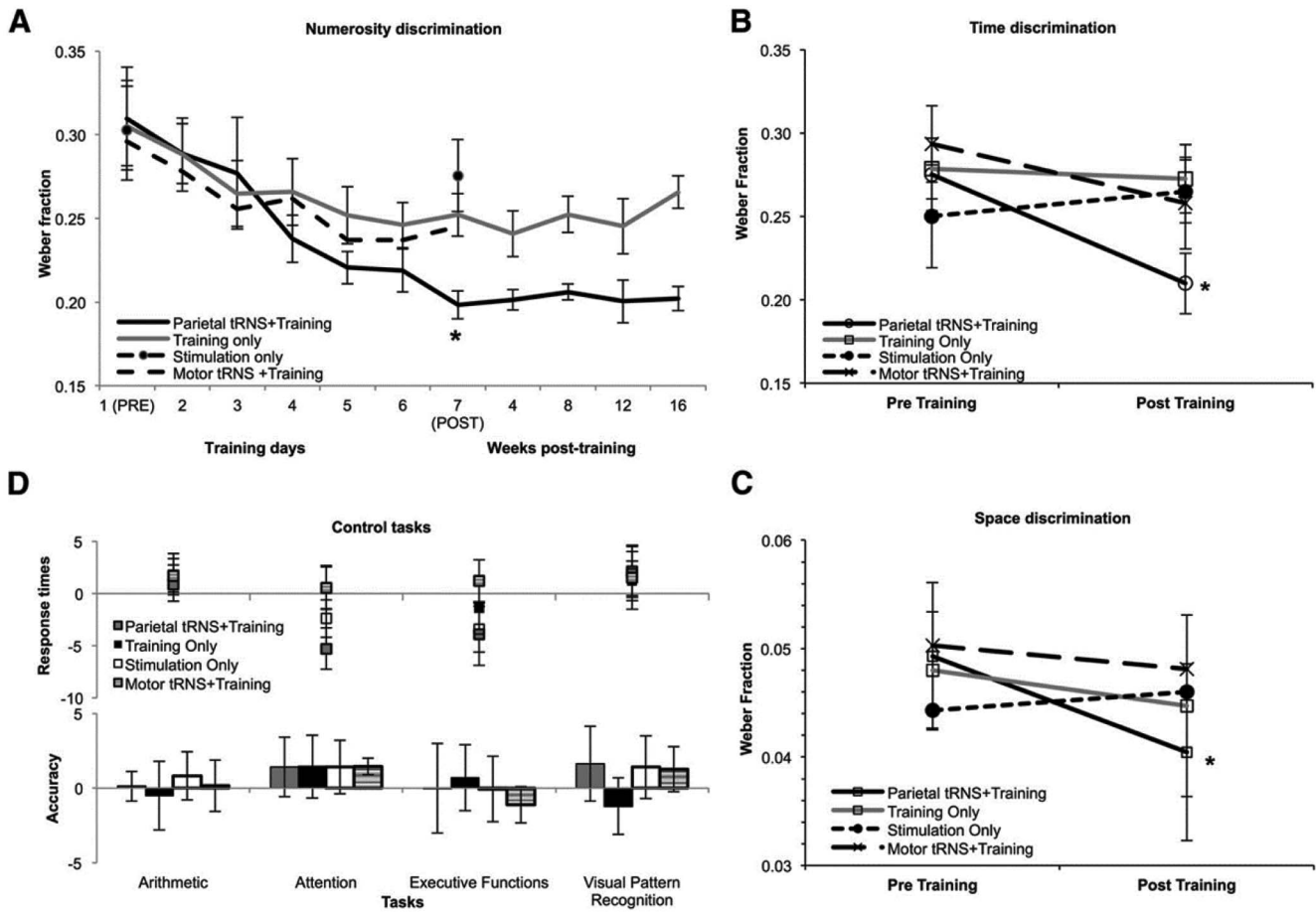


Figure 2. Results. Performance in the four groups expressed as Weber fraction in (A) the numerosity discrimination task at pretraining and at posttraining, during each of the training days, and at Week 4, 8, 12, and 16 after training; in the transfer tasks, that is, time (B) and space (C) discrimination at pretraining and posttraining; and (D) in tasks measuring arithmetic, attention, executive functions, and visual pattern recognition showing no training-induced changes in accuracy (correct answers) or reaction times (RTs) measured as percentage change from pretraining. Smaller *wf* indicates better performance. Taken from [Cappelletti et al. \(2013\)](#). In (A), the graph may give the impression of a missing data curve for the stimulation-only group. The curve is not missing, but instead shows that numerosity data were only collected at pre- and posttest, with no training or numerosity engagement provided during the intervening sessions. Data curves in the other conditions represent changes in numerosity as a function of training.

may require simultaneous stimulation of regions where more complex operations are carried out and which implement higher level cognition, such as working memory (e.g., the dIPFC). Another possibility is that the connection between numerosity and mathematical achievement may be closer or stronger in the developing brain compared to adult brains ([Price, Palmer, Battista, & Ansari, 2012](#)). This would explain both how [Halberda et al. \(2008\)](#) found a relationship between numerosity and arithmetic performance in children, and the absence of transfer of numerosity training to arithmetic performance observed by [Cappelletti et al. \(2013\)](#) in adults. Alternatively, numerosity might itself be based on purely sensory information, rather than true numerical processing ([Gebuis, Gevers, & Cohen Kadosh, 2014](#); [Gebuis & Reynvoet, 2012](#)), and an improvement in numerosity may, therefore, not translate to enhanced mathematical performance.

Perceiving Magnitudes

A prominent aspect of numerical cognition in humans is the association of magnitude with symbols (e.g., 1 and 9 each represents a different magnitude in Western culture). A technique for evaluating basic numerical competence is to present these numbers side-by-side in an alternative form of the Stroop task ([MacLeod, 1991](#); [Stroop, 1935](#)). In the traditional format, participants must name the colour of the ink a word is printed in, rather than what the word actually reads as. When the word is the name of a colour (printed in another colour, which the participant has to identify), the semantic and physical properties of the stimulus are in competition, and the resultant increase in response latencies is the Stroop effect. One variation of the Stroop task involves the presentation of numbers side-by-side, with participants determining

which number is larger *in print*. There are two main types of trials in this task. For a pair of numbers on a congruent trial (e.g., 1 and 9), 9 is physically larger than 1, and there is no competition between perceptual semantic and processing. On an incongruent trial (e.g., 1 and 9), 1 is physically larger than 9, resulting in competition between the semantic and physical features of the stimuli. It is on incongruent trials that basic numerical competence can be assessed. If a Stroop effect appears (slower RTs on the incongruent trials), it is interpreted as evidence of a well-developed, automatised symbolic magnitude system (Girelli et al., 2000; Rubinsten et al., 2002; Schwarz & Ischebeck, 2003; Tzelgov et al., 2000). In contrast, difficulties in this capability is a behavioural signature of numerical deficits, as the semantic features of numbers are unable to assert themselves over more basic perceptual features, suggesting that the system is impaired or poorly developed (Cohen Kadosh et al., 2007; Rubinsten & Henik, 2005). This is a behavioural marker of a poorly developed magnitude system in young children in whom such expertise has not yet emerged (Girelli et al., 2000; Rubinsten et al., 2002), and adults with dyscalculia (Rubinsten & Henik, 2005, 2006).

Cohen Kadosh et al. (2010) applied this task in assessing the effects of tES on the acquisition of a *novel* system of symbols. In the task, the digits 1–9 were substituted with symbols developed in Gibson et al. (1962), and later used by Tzelgov et al. (2000), creating, in effect, a new number set (see Figure 3). In Cohen

Kadosh et al. (2010), participants received 20 min of tDCS over 6 days of training. Participants were divided into three groups, each with a different stimulation configuration. One group received cathodal stimulation to the left parietal lobe and anodal tDCS to the right parietal lobe (the right-anodal, left-cathodal, or RA-LC group). The second group received anodal stimulation to the left parietal lobe and cathodal tDCS to the right parietal lobe (RC-LA group). The third group was a sham condition to rule out placebo effects. The training sessions entailed developing the association between the new digits and their magnitudes. At posttest, participants given cathodal stimulation to the left parietal lobe and anodal stimulation to the right parietal lobe showed that the greatest numerical Stroop effect (measured in RTs), interpreted as the emergence of a sense of familiarity with these new symbols. The group given cathodal stimulation to the right parietal lobe and anodal stimulation to the left parietal lobe showed the opposite effect, underperforming on this task, suggesting poor familiarity with the new symbols, similar to individuals with numerical difficulties. The performance of the group given sham stimulation fell in between these two points (see Figure 4). Notably, the performance on a version of this task that presented everyday digits was not modulated by tDCS, indicating that the effect was not because of general cognitive control and conflict resolution.

Cohen Kadosh et al. (2010) also examined the effects of tDCS with a second task, number-to-space maps. If a system of numbers is well-learned and familiar to the individual, pointing out these numbers on a horizontal number line result in a linear pattern (e.g., if indicating positions 1–9 on a number line, digits are placed at roughly equal distances from the neighbouring digits). Participants were provided with a number line anchored by the smallest and largest of the arbitrary symbols, corresponding to 1 and 9, and had to place the digits they had learnt on that number line (see Figure 5). As with greater interference on incongruent trials of the modified Stroop task, linear number-to-space maps are a marker of intact numerical skill (Booth & Siegler, 2008; Geary et al., 2008; Siegler & Opfer, 2003). In contrast, an indicator of poorer or less-developed numerical skill is a logarithmic number-to-space map, characteristic of young children or tribal communities with minimal, if any, explicit mathematical education (Booth & Siegler, 2008; Dehaene et al., 2008). An example is placing 7 further away from 6 than 6 from 5. In Cohen Kadosh et al. (2010), all number-to-space maps for everyday numbers were linear. However, the only participants who produced linear number-to-space maps for the arbitrary learned symbols were those given cathodal stimulation to the left parietal lobe and anodal stimulation to the right parietal lobe. The other groups generated logarithmic maps (see Figure 6). These findings indicate that tDCS (with cathodal stimulation applied to the left parietal lobe and anodal stimulation to the right parietal lobe) enhanced the emergence and maintenance of a new system of symbolic magnitudes. Moreover, the effects were long-lived, and were apparent at a 6-month follow-up.

Although it is easy to conclude that anodal tDCS to the right parietal lobe produced the improvement, the electrode montage does not, in fact, allow this interpretation. Because bilateral tDCS requires another region, cephalic or noncephalic, be stimulated simultaneously with the opposite polarity, the cathodal stimulation applied to the left parietal lobe suggests that the improvement may derive from either the anodal stimulation, or the cathodal stimulation, or both.

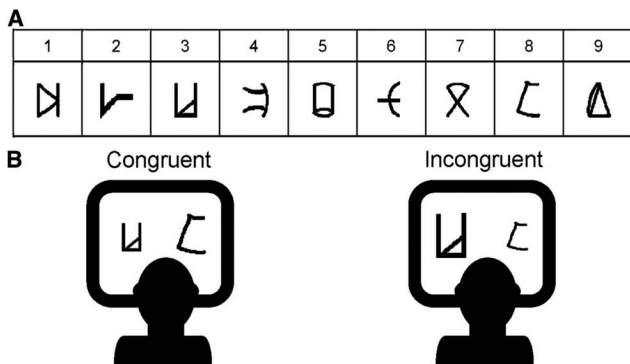


Figure 3. Example of stimuli and the numerical Stroop task. (A) Everyday digits and their corresponding artificial digits that were used to create the new numerical system. Each everyday digit appears above its corresponding artificial digit. Over 6 days of training, participants were instructed to refer to the artificial digits as representing various magnitudes and to decide on each learning trial which one of the two stimuli has a larger magnitude, while receiving visual feedback for their decision. Only adjacent pairs have been presented during this phase. (B) An example for congruent and incongruent trials with artificial digits from the numerical Stroop task. In the current example, the symbols corresponding to the Arabic digits 3 and 8 appear on the left and right sides of a congruent and an incongruent trial, respectively. Participants were asked to compare the stimuli according to their physical size while ignoring their numerical meaning. On congruent trials, the larger number appeared in larger font, whereas on incongruent trials the larger number appeared in smaller font. The numerical Stroop effect (incongruent vs. congruent) indicates the slowing in the decision time when numbers are irrelevant to the task and are therefore processed automatically (Henik & Tzelgov, 1982). Nonadjacent pairs have been presented in this task to examine transitive inference from the learned material (Tzelgov et al., 2000). Taken from Iuculano and Cohen Kadosh (2013).

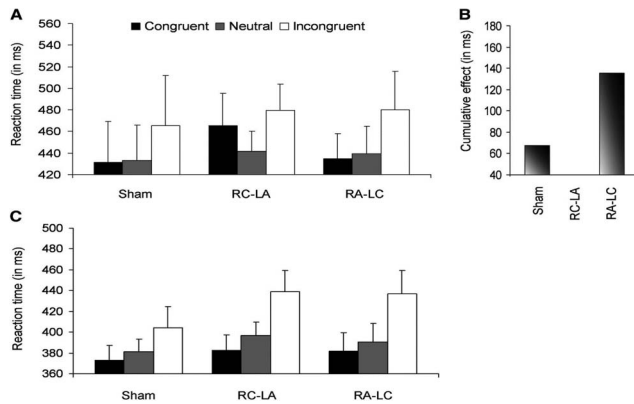


Figure 4. The congruity effect for the artificial digits, the cumulative congruity effect over training, and the congruity effect for everyday digits for the sham, RC-LA, and RA-LC groups in the numerical Stroop task. The data of the artificial digits for each group are averaged across the sessions that showed a significant congruity effect (three sessions for the RA-LC group, two sessions for the sham group, and five sessions for the RC-LA group; note that the latter group showed an abnormal congruity effect that was not changed as a function of learning). (A) Whereas the RA-LC group and the sham group showed a typical congruity effect, the RC-LA group showed an abnormal effect that mirrored the performance of children at the age of 6 years and might reflect perceptual rather than semantic interference (Girelli et al., 2000). (B) The cumulative congruity effect demonstrates the emergence of a consistent automatic numerical processing already from the fourth day for the RA-LC group ($p = .005$, Supplemental Material Table 1), whereas it occurred only later for the sham group ($p = .049$, Table S1) and did not appear for the RC-LA group. (C) All groups showed a consistent and typical congruity effect for everyday digits ($p = .00009$; group \times congruity interaction, $p = .46$), as reflected by slower RTs for the incongruent condition versus the congruent condition. Data are mean \pm SE of the mean. Note the different scaling in each panel. Taken from Cohen Kadosh et al. (2010).

Using multiple electrodes. A technique to increase the number of stimulation sites with tDCS is to use *four* electrodes (two anodal and two cathodal, using, e.g., two tDCS devices simultaneously, or a single multichannel device; Ruffini et al., 2014), to provide stimulation of the same polarity to both sides of a lateralised structure. The experiments described here have all used bilateral, two-electrode setups. However, with tDCS, a bilateral



Figure 5. Artificial digits. Symbols used as stimuli during the learning phase and the numerical Stroop task and their equivalent as everyday digits—adapted from Tzelgov et al., 2000. Taken from Iuculano & Cohen Kadosh (2014).

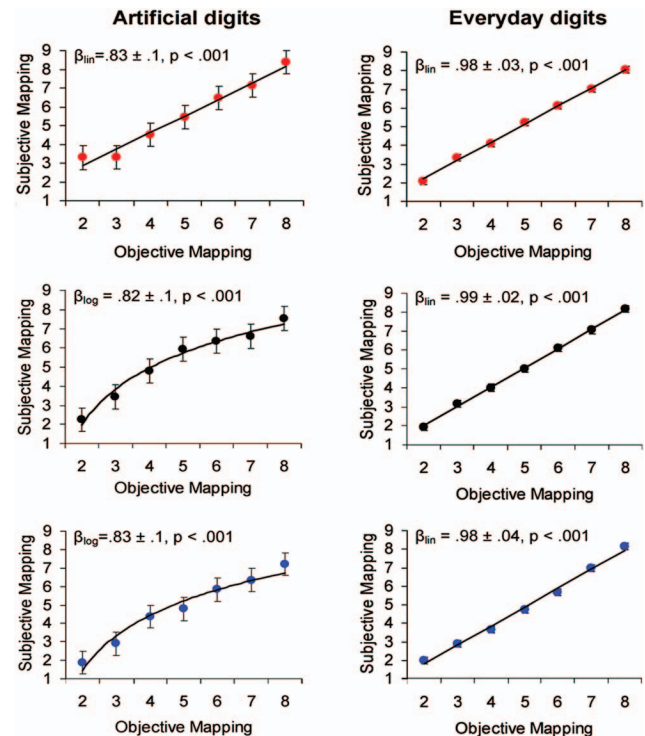


Figure 6. Average location of artificial digits on the horizontal segment, shown separately for artificial digits in the left column, everyday digits in the right column, and type of stimulation. β represents the selection of the best weight, whether it was logarithmic (β_{log}) or linear (β_{lin}), in stepwise regression analysis with linear and logarithmic predictors. Data are mean \pm SE of the mean. The first row reflects the performance of the RA-LC group (red circles), the middle row reflects the performance of the sham group (black circles), and the bottom row presents the performance of the RC-LA group (blue circles). Whereas the performance with artificial digits was affected by the type of brain stimulation and showed a linear fit only for the RA-LC group, the performance with everyday digits was independent of the type of brain stimulation and showed a linear fit for all the groups. Taken from Cohen Kadosh et al. (2010). See the online article for the color version of this figure.

montage ensures that one of the areas will be downregulated while the contralateral area is upregulated. With four electrodes, both the left and right regions can be given the same form of tDCS. In such cases, the reference electrodes can be placed over putatively inactive sites, such as the supraorbital regions (but see Truong, Magerowski, Blackburn, Bikson, & Alonso-Alonso, 2013). Anodal tDCS, cathodal tDCS, or sham stimulation are then applied bilaterally. One way around the use of multiple stimulators is to apply bihemispheric tRNS to both sites of interest (e.g., Cappelletti et al., 2013; Snowball et al., 2013). However, the limitation with tRNS is that this only allows for an assessment of upregulatory effects. Downregulation through tRNS is not as well understood as cathodal tDCS, and is therefore more difficult to examine.

Hauser, Rotzer, Grabner, Méritat, and Jäncke (2013) used a four-electrode montage (in all cases, the reference electrode was placed over the supraorbital areas). In addition to sham stimulation, participants received anodal stimulation to either the left parietal lobe, anodal stimulation over both the left and right pari-

etal lobe, or cathodal stimulation over both the left and right parietal lobe (for the setup, see Figure 7). The study followed a within-subjects design, so all participants completed the tasks in all conditions (that were counterbalanced). In a second experiment, participants received either sham stimulation or anodal stimulation to the right parietal lobe. Participants completed two numerical tasks. In one, they had to judge whether a number from 31 to 99 was larger in magnitude than 65 (magnitude processing). In the second task, participants had to complete a two-digit subtraction problem (e.g., $63-29$), and choose the response from amongst three options, two of which were distractors (e.g., the solution to $63-29$ is 34, which was presented alongside 44 and 32, which were distractors). The tasks were completed before and after the application of tDCS (25 min, 1 mA).

The central finding was that, compared with sham, only anodal stimulation to the left parietal lobe improved performance in both numerical tasks. For the subtraction task, left-anodal stimulation alone reduced reaction time (RTs), and there were no changes in accuracy. For the magnitude processing task, only the left-anodal stimulation produced improvements in both RT and accuracy.

At first glance, these results are surprising. According to previous studies, both parietal lobes should be involved in the tasks (e.g., [Arsalidou & Taylor, 2011](#)). Therefore, the bilateral anodal stimulation to both parietal lobes would have been expected to yield benefits. The authors conclude that the lack of such a finding is suggestive of more complex interactions between the left and right parietal lobes during numerical processing, and explain this pattern with the principle of interhemispheric inhibition. Briefly, the left parietal lobe, which anodal stimulation revealed was crucially involved in the tasks, may be inhibited by the right parietal lobe, which itself may be less involved in the cognitive functions tested. The present results are in line with the principle of an inhibitory relationship between the hemispheres that exerts an influence on numerical performance. Anodal stimulation to the left parietal lobe would, therefore, help it overcome cross-hemispheric inhibition from the right parietal lobe (hence the improvements in this condition), but bilaterally increasing (or decreasing) excitability would abolish the benefit conferred by anodal stimulation to the left hemisphere (for further discussions on interhemispheric inhi-

bition in the context of numerical cognition, see [Cappelletti, Barth, Fregni, Spelke, & Pascual-Leone, 2007](#); [Cohen Kadosh, et al., 2010](#)).

The [Hauser et al. \(2013\)](#) results also appear contradictory to the findings of [Cohen Kadosh et al. \(2010\)](#). [Hauser et al. \(2013\)](#) did not find evidence for enhanced performance for anodal tDCS applied to the right parietal lobe, which [Cohen Kadosh et al. \(2010\)](#) did. However, both studies differ in several aspects that prevent a direct comparison of their results. First, in [Hauser et al. \(2013\)](#), the participants received real anodal stimulation to the right parietal lobe for only one session (in a two session study). [Cohen Kadosh et al. \(2010\)](#) investigated the development of number-symbol associations over several days, and not the influence of tDCS on arithmetic task performance. Therefore, the number of stimulation sessions and the goal of the two studies were different. Second, the tDCS protocols differed between the two studies. [Hauser et al. \(2013\)](#) used offline tDCS. Participants performed tasks before and after stimulation, and the stimulation itself was provided during a period of inactivity. In contrast, [Cohen Kadosh et al. \(2010\)](#) applied tDCS online, during the symbol learning task. Whether the stimulation is provided before or during the task may bear on the results. When stimulation precedes the task, the task is engaging a neural population whose activity has already been modulated. In contrast, combining stimulation with the task entails modulation of neural activity in tandem with task performance, which may result in the formation of different types of associations and learning effects. In the field of numerical cognition, any discussion on the differences in task performance as a result of stimulation timing is speculative, and a particularly valuable study would be a direct comparison of the timing of the stimulation. Finally, both studies examined different types of numerical cognition. [Hauser et al. \(2013\)](#) investigated mental arithmetic and magnitude processing. [Cohen Kadosh et al. \(2010\)](#) examined the development of associations between symbols and magnitudes, as well as the development of a sense of automaticity and the mapping of these newly learned symbols onto a number line. These methodological differences prevent straightforward comparisons between the findings. At the same time, the findings illustrate that despite originating in different research groups, resulting from different methods, and having different interpretations, tES is able to enhance different aspects of numerical cognition.

In another study, [Klein et al. \(2013\)](#) used four-electrode tDCS to stimulate both the left and right parietal cortex with the same current polarity. Participants performed two tasks, an addition task, and also a colour-word Stroop task (as a control task to test for possible nonnumerical cognitive effects), while receiving 20 min of anodal tDCS, cathodal tDCS, or sham tDCS at 1 mA. There were two subtasks within the addition task. In one, participants were presented with an addition problem for which they had to choose which of two options was closer to the solution. For example, $25 + 31 = 54$ or 51 . Neither 54 nor 51 is the correct solution (it is 56). However, 54 is closer to the correct solution than 51, and is the correct response. The distance between 51 and 54 was termed the distractor distance. Clearly, larger distractor distances are easier to work with than smaller ones. In the second task, the solution was one of the correct responses (e.g., $25 + 31 = 56$ or 51), and the participant had to identify the correct option.

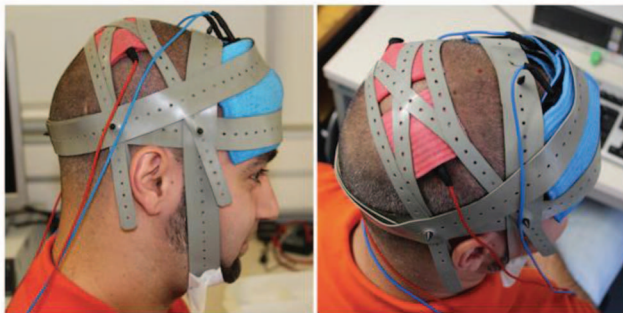


Figure 7. A four-electrode montage. The blue electrodes are the cathodes, the red electrodes are the anodes. Most frequently, just one anode and one cathode are used. The setup displayed above uses four electrodes (e.g., from two stimulators) and allows for tDCS of the same polarity to be given to more than one brain region. Figure taken from [Klein et al. \(2013\)](#). See the online article for the color version of this figure.

Identification of correct responses was not affected by tDCS. However, bilateral anodal stimulation reduced the distractor distance effect, suggesting an improvement in number magnitude processing. In contrast, bilateral cathodal stimulation impaired number magnitude processing, as revealed through increased distractor distance effect. In contrast, tDCS did not affect the performance in the colour-word Stroop task. This design is important for several reasons. For example, by examining two types of numerical processes and finding that tDCS influenced only one, the authors are able to show the specificity of stimulation outcomes to a given mental operation (distractor distance, rather than the identification of the correct response), and also that a brain region, even when associated with a particular function (in this case, the broad area of numerical processing), is not involved to the same extent for all tasks. The inclusion of the Stroop task shows that stimulating a brain region may not produce generalised improvement in nonnumerical processes apparently subserved by the same region.

Arithmetic Operations

tES has also been applied to more challenging, and therefore more ecologically valid, numerical tasks (though even here the ecological validity is poorly developed). For example, [Snowball et al. \(2013\)](#) assessed performance on a more advanced aspect of

numerical performance: arithmetic operations. Participants performed arithmetic operations that are learned via drills or calculations over five days of training. Drilling is based on rote learning, and is the retrieval of arithmetic information from long term memory (e.g., $7 \times 6 = 42$). On the other hand, calculation learning requires the manipulation of numbers according to specific rules or mathematical operations to reach the solution (e.g., $32 - 17 + 5 = 20$; see [Figure 8](#)). While participants performed these tasks, 1 mA tRNS was applied bilaterally to the dorsolateral prefrontal cortex (dlPFC), a brain region closely implicated in arithmetic learning ([Delazer et al., 2005](#); [Rivera et al., 2005](#); [Zamarian, Ischebeck, & Delazer, 2009](#)). Near infrared spectroscopy (NIRS) was applied to assess concomitant physiological changes in the targeted brain regions. NIRS utilises light from the near-infrared zone of the electromagnetic spectrum, which is differentially absorbed by tissue, providing information about changes in haemoglobin concentrations ([Villringer & Chance, 1997](#); [Villringer et al., 1993](#)).

[Snowball et al. \(2013\)](#) found that real tRNS enhanced performance on both drill and calculation tasks. There was also evidence of tRNS-induced differences in the left, but not right, dlPFC with respect to latency and amplitude of deoxygenated and oxygenated haemoglobin. This was interpreted as a stimulation-induced reduction in the quantity of oxygen required by the left-dlPFC as compared to sham stimulation. Enhanced behavioural performance

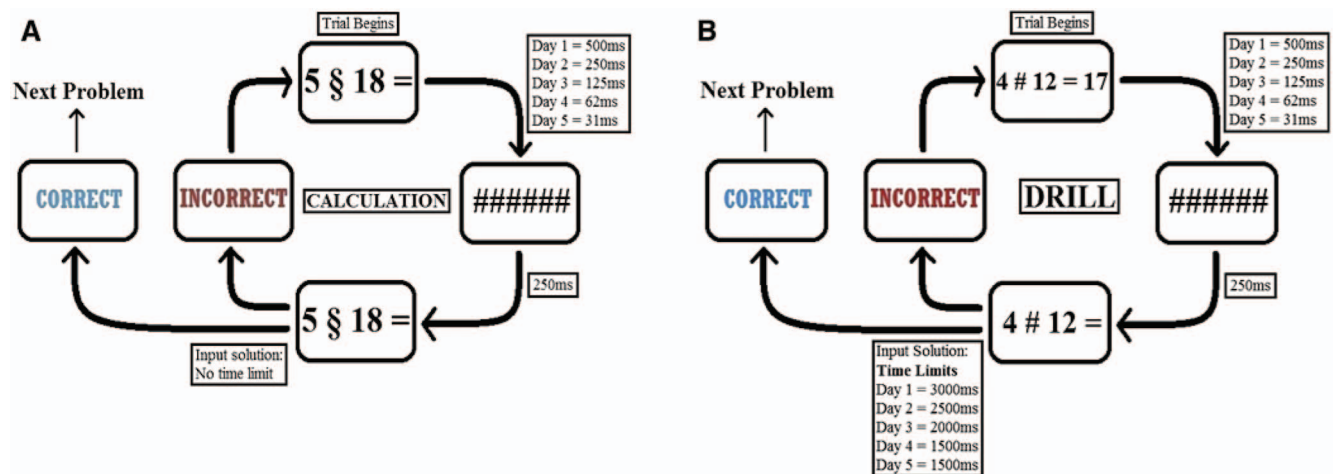


Figure 8. Schematic representation of the arithmetic learning regimes. (A) The calculation task. Answers to each calculation problem were obtained by manipulation of two numerical operands according to a particular algorithm (either [(right number—left number) + 1] + right number or [(right number + left number) - 10] + right number). Participants were instructed to enter their two-digit solution on the number pad of a standard QWERTY keyboard. Positive and negative feedback was provided for each answer (500 ms duration), and participants were only allowed to progress to subsequent problems once they had obtained the correct solution. (B) The drill task. Each trial began with the presentation of two numerical operands accompanied by the problem's answer. After the initial presentation, the problem would disappear from the screen and reappear without the answer, at which point subjects were required to enter their two-digit solution. Positive and negative feedback was provided (500 ms duration), and if participants answered incorrectly, the whole presentation cycle would repeat. Calculation and drill problems were presented in alternating groups of 18, referred to as "blocks." In line with previous studies ([Delazer et al., 2005](#)), the total number of blocks varied according to the day of training: 10 blocks on the first day, 12 on the second, 14 on the third, 16 on the fourth, and 14 on the fifth. The ratio of calculation to drill blocks was the same on each day, at 1:1. For both tasks, the round-edged boxes represent the individual presentation screens, and the square-edged boxes the time delays between each presentation screen [Snowball et al. \(2013\)](#). See the online article for the color version of this figure.

co-occurring with decreased oxygen consumption is suggestive of greater efficiency in neurophysiological activity following stimulation (see Figures 9, 10, and 11).

Both the physiological and behavioural effects were long-lived, being apparent at a 6-month follow-up. The behavioural improvement was limited to performing calculations, and was not apparent for drilling, indicating that the nature of the learning process affects the duration of the outcome. There was also some evidence of transfer, with enhanced performance on calculation problems at the follow-up that were not part of the original training. This transfer was restricted to the participants who were given tRNS (see Figure 8). Transfer beyond the original stimuli is fairly uncommon in cognitive training research (Green & Bavelier, 2003; Owen et al., 2010). These results, like Cappelletti et al. (2013), are suggestive of the potential of tES to enable transfer. It should be acknowledged that only half the original 25 participants returned for the follow-up. However, these findings remain important ones that supply evidence of enhancement of numerical cognition on a more advanced level than numerosity, as well key physiological insight on how brain stimulation may exert its effects.

Another study (Looi et al., 2015) combined training on fractions with brain stimulation. Proficiency in working with fractions predicts mathematical achievement (Siegler & Booth, 2004; Bailey et al., 2012). For example, ease in handling fractions is indicative of sophisticated part-to-whole magnitude relations. The fractions training was provided in the form of an adaptive videogame in which participants mapped fractions onto number lines. This has the advantage of being more entertaining for participants. Based on ideas of embodied learning of numerical infor-

mation (see Link et al., 2013), participants physically stepped from side to side, movements that were captured by a motion detector. These physical movements place an onscreen marker, which represents a fraction, onto the number line. The videogame was programed to increase in difficulty as participants improved, thus requiring greater and greater finesse in placing the marker on the number line.

Participants received two 30-min sessions of tDCS at 1 mA. Based on previous research (Iuculano & Cohen Kadosh, 2013), cathodal stimulation was applied to the left-dIPFC and anodal stimulation was applied to the right-dIPFC. Thirty participants were assigned to one of three groups (real tDCS + nonnumerical training, sham tDCS + numerical training, real tDCS + numerical training). The group given real tDCS and numerical training substantially outperformed the sham tDCS group in terms of response speed. The difference was particularly pronounced in the higher difficulty items, where the sham group displayed a typical decline in performance which the real stimulation group did not, with no evidence of a speed-accuracy trade-off. One explanation for these findings is that real tDCS facilitated a more efficient implementation of neuronal resources, while training by itself (sham tDCS) could not. After just two training sessions, participants who received real tDCS were approximately 13% faster in mapping fractions onto number lines than those who were given sham tDCS.

Another interesting and important result in Looi et al. (2015) was an enhancement in verbal working memory span, which was assessed at pre- and posttraining and was not explicitly part of the numerical training, suggesting successful transfer. Be-

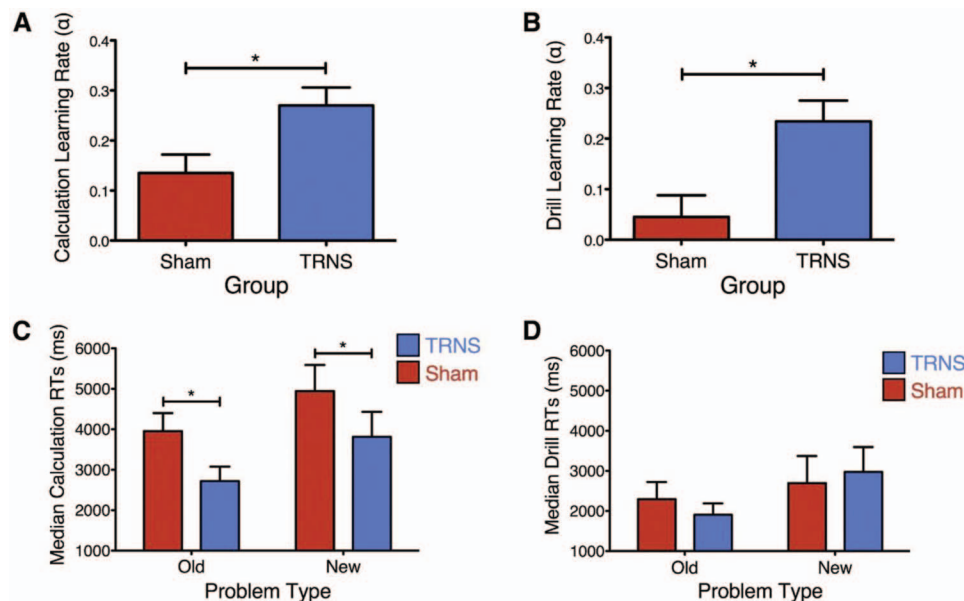


Figure 9. The effect of TRNS on arithmetic performance. (A) Calculation learning rates during training were significantly higher in the TRNS group relative to sham controls. (B) Drill learning rates during training were significantly higher in the TRNS group relative to sham controls. (C) Calculation reaction times (RTs) during testing were significantly faster in the TRNS group relative to sham controls for both old and new problems. (D) Drill RTs during testing did not differ between TRNS and sham groups for either old or new problems. Error bars indicate 1 SEM. Significant differences are marked with asterisks. Taken from Snowball et al. (2013). See the online article for the color version of this figure.

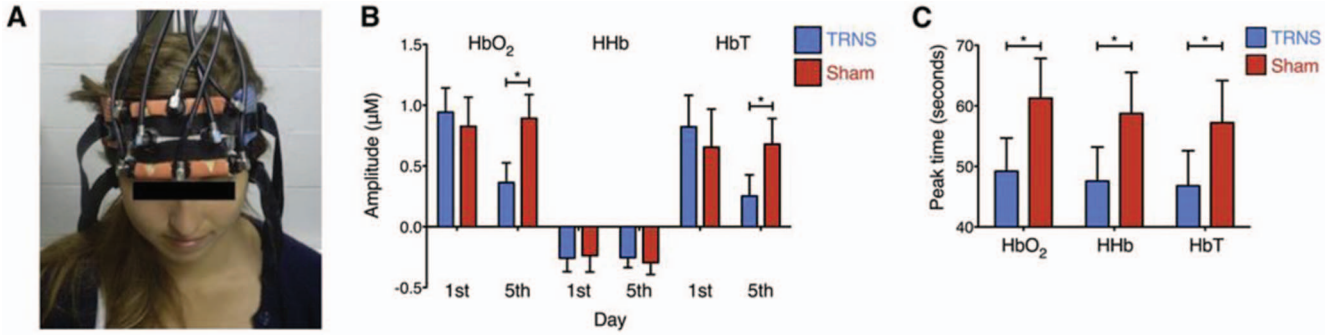


Figure 10. NIRS: The effect of TRNS on hemodynamic response amplitudes and latencies within the left LPFC during training. (A) Combined TRNS-NIRS setup. The NIRS plate (orange) is embedded with two transmitting and six receiving optodes and secured to the forehead: transmitting optodes are capped with blue labels, and receiving optodes are unmarked. Recordings were taken during the training phase on the first day and the fifth (last) day, as well as during the testing phase 6 months later. The fiber optic cables connecting the optodes to the NIRS device can be seen emanating from the top of the image. TRNS electrodes are positioned over the bilateral DLPFC and encased in blue and red saline-soaked sponges, as shown. This innovative TES-NIRS combination allowed us to quantify the hemodynamic response to functional activation and to assess how it varied as a function of brain stimulation and arithmetic training. (B) TRNS reduced the amplitude of HbO₂ and HbT responses by the end of training. A significant three-way interaction between hemodynamic measure, day, and group in the left LPFC indicates a significant decrease in peak amplitude for HbO₂ and HbT at the end of the training (fifth day) in the TRNS group relative to sham controls. (C) Reduced peak latencies emerged in the TRNS group compared to sham controls, for HbO₂, HHb, and HbT responses, independent of day. Both these effects were restricted to the left LPFC. Error bars indicate 1 SEM. Significant differences are marked with asterisks. Taken from [Snowball et al. \(2013\)](#). See the online article for the color version of this figure.

havioural training studies have succeeded in producing similar capacity improvements (an expansion in capacity of about one item) with up to 100 hr of training ([Schmiedek et al., 2010](#)). Similar to [Cappelletti et al. \(2013\)](#) and [Snowball et al. \(2013\)](#), only those participants who received real stimulation demonstrated this improvement. Furthermore, the improvements in fraction performance and verbal working memory capacity were maintained at a 2-month follow-up, suggesting that the

effects are both achievable in short timeframes and sustainable over large timeframes.

Future Research on the Role of Individual Differences

The use of tES has offered several important insights into the neurocognitive aspects of processing numerical information, as well as in the enhancement of numerical cognition. There are a

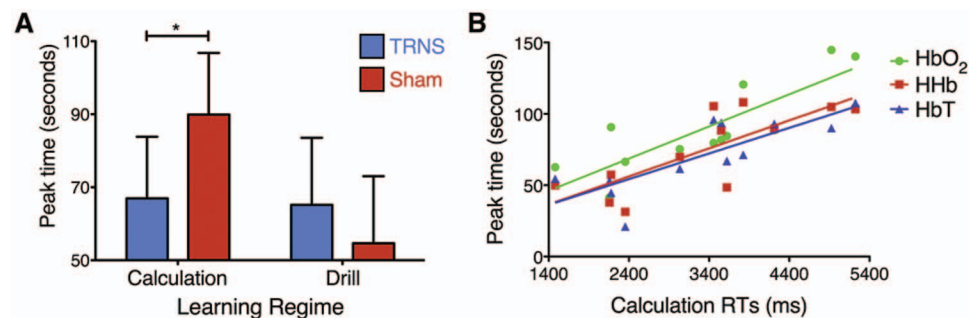


Figure 11. The effect of TRNS on hemodynamic response latencies during testing: relationship with behavioural performance. (A) A significant two-way interaction existed between learning regime and group for peak latency in the left LPFC, 6 months after the end of training. Although the TRNS and sham groups did not differ for drill problems, the TRNS group showed a significant decrease in peak latency compared to sham controls for calculation problems. Error bars indicate 1 SEM. Significant differences are marked with asterisks. (B) Significant correlations existed between calculation RTs and the peak time of changes in HbO₂, HHb, and HbT concentrations 6 months after the completion of training. Taken from [Snowball et al. \(2013\)](#). See the online article for the color version of this figure.

number of avenues future investigations must take up to both solve many of the existing puzzles and explore emerging possibilities in the brain stimulation literature.

It is important to acknowledge the substantial variability in the published work on the enhancement of numerical cognition through tES. Indeed, there are some studies that have been unable to elicit a behavioural effect with brain stimulation. For example, [Clemens, Jung, Zvyagintsev, Domahs, and Willmes, \(2013\)](#) attempted to enhance arithmetic fact retrieval by applying tDCS to the angular gyrus, a region in the posterior parietal cortex, in a single session of stimulation. Performance on the task was not significantly better in real compared to sham stimulation. However, the authors also included functional magnetic resonance imaging (fMRI) before and after the application of tDCS, and found changes in brain activation post-tDCS. These results are in line with those of [Snowball et al. \(2013\)](#), who also showed that neurophysiological effects of tES can appear even immediately after a single session, without a concomitant behavioural effect, which may emerge after multiple sessions of tES. In the case of [Clemens et al. \(2013\)](#), it is possible that a behavioural effect would have become apparent if stimulation had been continued for more than one session. This is a particularly important illustration of tES effects: though they may not be immediately apparent on the behavioural level, there may be underlying neurophysiological changes that would be beyond detection unless they were being assessed as well (as through fMRI or NIRS). Null results with respect to behavioural output (e.g., RT, accuracy) need not imply there were no effects.

All of the aforementioned studies have yielded valuable insights. The study by [Clemens et al. \(2013\)](#) is especially useful in revealing evidence of neural changes in the absence of behavioural ones. However, as with other interventions, a one-size-fits-all with tES is useful when little is known about the effects, but the approach is unsustainable in the long-term. This is especially true in the context of enhancement, where the enhancement itself is likely dependent on the technique's sensitivity to individual differences. Indeed, there is a growing interest in the modulation of tES outcomes by individual differences. Of course, "individual differences" represents an enormous category of variables, but there is increasing evidence that tES exerts differential effects based on precisely such differences. Indeed, these range from catechol-O-methyl transferase polymorphisms ([Plewnia et al., 2013](#); [Nieratschker, Kiefer, Giel, Krüger, & Plewnia, 2015](#)), educational attainment ([Berryhill & Jones, 2012](#)) and level of training in a skill or ability ([Waters-Metenier et al., 2014](#)). The developmental stage of the participant is also likely to influence the relative role a brain region plays in a cognitive function. For example, arithmetic and numerical processing in a child's brain appears to engage greater frontal activity than parietal ones, while in the brain of the adult, such processes appear to engage parietal regions more strongly ([Kaufmann et al., 2011](#); [Rivera, Reiss, Eckert, & Menon, 2005](#)). Gender and cultural background are potentially relevant to stimulation outcomes as well. For instance, variation in the sex hormones estradiol and progesterone over the different phases of the menstrual cycle for female participants may affect cortical excitability, which are very likely to interact with stimulation ([Krause & Cohen Kadosh, 2014](#)). The design of the experiment and the stimulation paradigms will need to account for these differences as carefully as possible.

Two studies have also examined the role of individual differences with respect to modulating numerical cognition with tES. [Kasahara et al. \(2013\)](#) first examined parietal activity using fMRI while participants performed calculation tasks. Following this, participants performed these calculation tasks while receiving tDCS. The participants who benefitted the most (i.e., faster RTs) from a left-anodal, right-cathodal montage were those who showed greater left-dominance in performing the calculations during the fMRI. This effect was not observed for individuals who did not show such left-dominance during the task, suggesting that functional lateralisation of brain regions plays a role in determining the efficacy of stimulation. [Sarkar et al. \(2014\)](#) applied tDCS bilaterally to the dorsolateral prefrontal cortex (left-anodal, right-cathodal) to 45 participants with high or low mathematics anxiety while they performed a simple arithmetic task. Mathematics anxiety is the automatic negative emotional reaction, primarily fear, an individual experiences when dealing with numerical situations ([Richardson & Suinn, 1972](#)). Participants with high mathematics anxiety improved on the task in real compared with sham tDCS (i.e., faster RTs), while participants with low mathematics anxiety performed worse in real compared with sham stimulation (i.e., slower RTs). Because individuals with mathematics anxiety find mathematical situations stressful, the authors also examined a physiological measure of stress: salivary cortisol, collected before and after each stimulation session. The cortisol findings were parallel to the RT results. Cortisol concentrations dropped from pre- to posttest samples in individuals with high mathematics anxiety in real, but not sham, stimulation. However, for the low mathematics anxiety participants, cortisol dropped in sham stimulation, but not in real stimulation. In other words, individual traits, such as mathematics anxiety, can exert marked effects on brain stimulation outcomes (see [Figure 12](#)).

[Sarkar et al. \(2014\)](#) also examined performance on a flanker task ([Fan et al., 2002](#)), which measured executive control, and found that executive control (RT on incongruent trials minus RT on congruent trials) for both high and low mathematics anxiety participants was lower following real compared with sham stimulation. This finding is central to the issue of cognitive costs of tES. The brain is supplied with a relatively fixed quantity of oxygen and nutrients. Altering excitability in one region could potentially affect other brain regions and cognitive domains (for further experimental support see [Iuculano & Cohen Kadosh \(2013\)](#); for theoretical perspectives see [Brem et al., 2014](#); [Krause et al., 2013](#); [Pascual-Leone et al., 2012](#)).

[Sarkar et al. \(2014\)](#) is also one of two studies to examine numerical performance in individuals with identifiable difficulties in dealing with numbers. The potential for tES to mitigate numerical difficulties is an especially important theme in research with large translational significance, given that quantitative proficiency is becoming ever more important. Low mathematical attainment at 7 years is associated with poorer educational and socioeconomic achievement at 42 years ([Ritchie & Bates, 2013](#)). Furthermore, individuals with numerical deficits are more than twice times as likely as individuals with regular numeracy to be unemployed ([Parsons & Bynner, 2005](#)). Some estimates suggest that as many as 15–20% of the population experiences generalised numerical difficulties ([Bynner & Parsons, 1997](#); [Parsons & Bynner, 2005](#)). Within the population of individuals facing numerical difficulties, approximately 3–7% have dyscalculia, a severe difficulty in work-

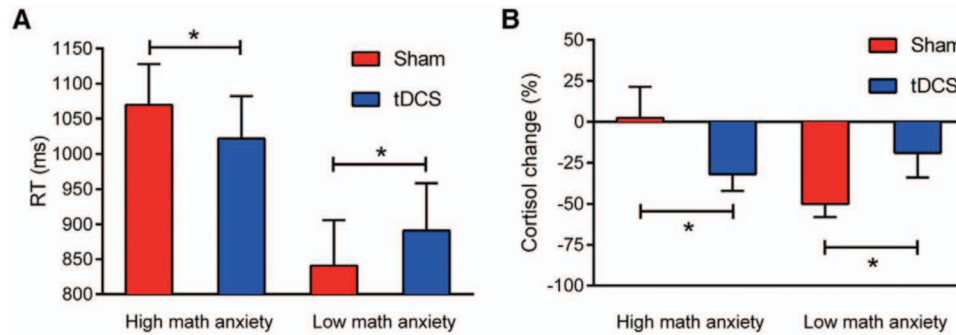


Figure 12. Mathematics anxiety-dependent effects of tDCS. (A) Behavioural double-dissociation between high and low mathematics anxiety groups. For the high mathematics anxiety group ($n = 25$), tDCS produced faster arithmetic decisions compared to sham stimulation. For the low mathematics anxiety group ($n = 20$), tDCS impaired arithmetic decision reaction times (RTs) compared with sham (both $ps < .001$). (B) Double-dissociation in salivary cortisol concentration between high and low mathematics anxiety. Negative cortisol change indicates lower cortisol concentrations at posttest compared to pretest. High mathematics anxiety participants showed greater cortisol reductions after real stimulation, while low mathematics anxiety participants showed greater cortisol reductions after sham stimulation (both $ps < .05$). Error bars represent 1 SEM. Taken from Sarkar et al. (2014). See the online article for the color version of this figure.

ing with even the most basic numerical processes (Butterworth, Varma, & Laurillard, 2011; Reigosa-Crespo et al., 2012; Shalev, 2007).

Recently, Iuculano and Cohen Kadosh (2014) applied tDCS bilaterally to the parietal lobes of two participants with developmental dyscalculia. One participant received anodal stimulation to the left parietal lobe and cathodal stimulation to the right parietal lobe, while the other was given cathodal stimulation to the left parietal lobe and anodal stimulation to the right parietal lobe. Participants were trained on the novel symbolic magnitude system described above for Cohen Kadosh et al. (2010). For the participant given anodal stimulation to the left parietal lobe and cathodal stimulation to the right parietal lobe, there was a clear emergence of the Stroop effect associated with basic numerical competence. The data for the number-space mapping performance (see Figure 7) were best modelled by a linear function, which, as mentioned above, is a behavioural marker of intact numerical capabilities. The other participant, who was given the reverse stimulation montage, did not show any evidence of familiarity with the new symbols, and there was no particular pattern in the number-space mapping. For this participant, the montage had no effect, demonstrating the need to choose lateralised regions of the cortex with care. These results are the opposite of those in Cohen Kadosh et al. (2010), and suggest that developmental dyscalculia might involve differential recruitment of cortical structure and function, possibly because of compensation and the usage of different strategies, which might in turn lead to different responses to brain stimulation. However, the possibility of ameliorating dyscalculia through tES is extremely promising, and undertaking larger studies should be a research priority.

Conclusions

Evidence of the applications of tES in numerical and other forms of cognition continues to accumulate, and despite the variability, the technique is promising. Part of this promise will be realised through increasing the internal validity of methods. To

some extent, this is inevitable as a field gains in width and depth. Technological progress and the innovative combination of neuroimaging methods (e.g., smaller and more focal electrodes, combining tES with EEG, NIRS, or fMRI), as well as stricter criteria for assessing findings (e.g., taking the placebo effect into account, maintaining regional and task specificity, appropriate blinding), will bolster the internal validity of tES findings. The remainder of this promise of tES must be realised through greater ecological validity, through furthering applications and testing in the real world. For example, there is now strong evidence that tES can be applied to enhance numerical cognition in individuals with both adequate and impaired numerical competence, as has been discussed in this review. Some headway has already been made in terms of ecological validity with respect to longevity of findings (Cappelletti et al., 2013; Looi et al., 2015; Snowball et al., 2013). However, the problem lies in taking these benefits beyond the laboratory, and making them appreciable in everyday life, a considerably challenging task that is all too easy to ignore. Part of the difficulty of translating tES into ecologically valid settings lies in the effective operationalisation and extension of laboratory constructs. Indeed, for many of the studies reported here, the improvements are in the range of milliseconds to, at most, a couple of seconds. While scientifically intriguing in their own right, the utility of such improvement falls far short of the media hype surrounding cognitive enhancement. For example, Dockery et al. (2009) have shown that tDCS is able to produce long-lasting improvements in planning performance. Planning is an extremely advanced form of cognition that allows the individual to frame ongoing behaviour in the service of distal goals, and is, in many ways, a hallmark of human cognition (Miller & Cohen, 2001). A reliable and well-validated laboratory measure of planning is the Tower of London task (Peretti et al., 2002; Shallice, 1982), which Dockery et al. (2009) used as the response variable in their study. However, does tDCS-induced improvement on a Tower of London task suggest that planning in everyday life has actually been improved? If so, what kind of planning? Scheduling, goal setting, financial planning, and others are all subforms of planning

that may have been affected. However, the variation and dynamism implicit in these processes is so great that is difficult to measure how any of them may have been improved by tDCS. Equally, there may have been no translation to any planning processes. In the case of planning, one possibility may be the implementation of virtual reality technology. Virtual reality has already been used in the study of planning in combination with fMRI (Campbell et al., 2009). This allows for a more ecologically valid test of tDCS-induced changes in planning ability, while also providing neural-level information. Though this would only be a first step, and would not be applicable to many other abilities, it is an experimentally feasible technique that could be implemented with existing technology. But the enhancement of numerical cognition remains a challenge, with no reported benefits on performance variables that would suggest greater quantitative ability (e.g., exam scores). To a very broad extent, the accurate mapping of laboratory constructs to their daily life counterparts remains an important and contentious issue in psychological science. However, in the case of tES, many of the claims are directly in terms of cognitive enhancement, and therefore, these translations cannot be ignored. As of yet, there are no studies confirming the ecological validity of tES, and this must become an important goal in the research agenda.

Résumé

Les effets de l'électrostimulation crânienne (ETC) ont été documentés pour diverses fonctions mentales, dont la cognition numérique. Dans un premier temps, cet article passe en revue deux formes fréquentes d'ECT, la stimulation transcrânienne à courant continu et la stimulation transcrânienne par bruit aléatoire. Dans un deuxième temps, il évalue les applications de cette technologie pour l'amélioration d'aspects de la cognition numérique, y compris la numérosité, la représentation de la magnitude et diverses opérations arithmétiques complexes. La revue se termine par la discussion des orientations possibles de la recherche future. Celles-ci incluent la nécessité de tenir compte des différences individuelles dans la conception expérimentale, d'élargir la recherche pour inclure les individus ayant des difficultés et des déficits quant à l'utilisation des chiffres, et de prendre en compte les coûts cognitifs éventuels qui pourraient contrebalancer les avantages de l'ETC pour la cognition. Un thème récurrent de cet article est le besoin de s'orienter vers une plus grande validité écologique des résultats de recherches expérimentales.

Mots-clés : électrostimulation crânienne, stimulation transcrânienne à courant continu (STCC), stimulation transcrânienne par bruit aléatoire, amélioration cognitive, cognition numérique.

References

- Ambrus, G. G., Paulus, W., & Antal, A. (2010). Cutaneous perception thresholds of electrical stimulation methods: Comparison of tDCS and tRNS. *Clinical Neurophysiology*, 121, 1908–1914. <http://dx.doi.org/10.1016/j.clinph.2010.04.020>
- Antal, A., Nitsche, M. A., Kruse, W., Kincses, T. Z., Hoffmann, K.-P., & Paulus, W. (2004). Direct current stimulation over V5 enhances visuo-motor coordination by improving motion perception in humans. *Journal of Cognitive Neuroscience*, 16, 521–527. <http://dx.doi.org/10.1162/089892904323057263>
- Arsalidou, M., & Taylor, M. J. (2011). Is $2+2=4$? Meta-analyses of brain areas needed for numbers and calculations. *NeuroImage*, 54, 2382–2393. <http://dx.doi.org/10.1016/j.neuroimage.2010.10.009>
- Bailey, D. H., Hoard, M. K., Nugent, L., & Geary, D. C. (2012). Competence with fractions predicts gains in mathematics achievement. *Journal of Experimental Child Psychology*, 113, 447–455. <http://dx.doi.org/10.1016/j.jecp.2012.06.004>
- Barth, H., Kanwisher, N., & Spelke, E. (2003). The construction of large number representations in adults. *Cognition*, 86, 201–221. [http://dx.doi.org/10.1016/S0010-0277\(02\)00178-6](http://dx.doi.org/10.1016/S0010-0277(02)00178-6)
- Beddington, J., Cooper, C. L., Field, J., Goswami, U., Huppert, F. A., Jenkins, R., . . . Thomas, S. M. (2008). The mental wealth of nations. *Nature*, 455, 1057–1060. <http://dx.doi.org/10.1038/4551057a>
- Berryhill, M. E., & Jones, K. T. (2012). tDCS selectively improves working memory in older adults with more education. *Neuroscience Letters*, 521, 148–151.
- Bindman, L. J., Lippold, O. C. J., & Redfearn, J. W. (1964). The action of brief polarizing currents on the cerebral cortex of the rat (1) during current flow and (2) in the production of long-lasting after-effects. *The Journal of Physiology*, 172, 369–382. <http://dx.doi.org/10.1113/jphysiol.1964.sp007425>
- Bolzoni, F., Bącznyk, M., & Jankowska, E. (2013). Subcortical effects of transcranial direct current stimulation in the rat. *The Journal of Physiology*, 591, 4027–4042.
- Booth, J. L., & Siegler, R. S. (2008). Numerical magnitude representations influence arithmetic learning. *Child Development*, 79, 1016–1031. <http://dx.doi.org/10.1111/j.1467-8624.2008.01173.x>
- Boyke, J., Driemeyer, J., Gaser, C., Büchel, C., & May, A. (2008). Training-induced brain structure changes in the elderly. *The Journal of Neuroscience*, 28, 7031–7035. <http://dx.doi.org/10.1523/JNEUROSCI.0742-08.2008>
- Brannon, E. M., & Terrace, H. S. (1998). Ordering of the numerosities 1 to 9 by monkeys. *Science*, 282, 746–749. <http://dx.doi.org/10.1126/science.282.5389.746>
- Brem, A. K., Fried, P. J., Horvath, J. C., Robertson, E. M., & Pascual-Leone, A. (2014). Is neuroenhancement by noninvasive brain stimulation a net zero-sum proposition? *NeuroImage*, 85, 1058–1068.
- Butterworth, B., Varma, S., & Laurillard, D. (2011). Dyscalculia: From brain to education. *Science*, 332, 1049–1053. <http://dx.doi.org/10.1126/science.1201536>
- Bynner, J., & Parsons, S. (1997). *Does numeracy matter?* London: The Basic Skills Agency.
- Campbell, Z., Zakzanis, K. K., Jovanovski, D., Joordens, S., Mraz, R., & Graham, S. J. (2009). Utilizing virtual reality to improve the ecological validity of clinical neuropsychology: An FMRI case study elucidating the neural basis of planning by comparing the Tower of London with a three-dimensional navigation task. *Applied Neuropsychology*, 16, 295–306. <http://dx.doi.org/10.1080/09084280903297891>
- Cantlon, J. F. (2012). Math, monkeys, and the developing brain. *Proceedings of the National Academy of Sciences of the United States of America*, 109(Suppl. 1), 10725–10732. <http://dx.doi.org/10.1073/pnas.1201893109>
- Cantlon, J. F., Brannon, E. M., Carter, E. J., & Pelphrey, K. A. (2006). Functional imaging of numerical processing in adults and 4-y-old children. *PLoS Biology*, 4, e125. <http://dx.doi.org/10.1371/journal.pbio.0040125>
- Cantlon, J. F., Platt, M. L., & Brannon, E. M. (2009). Beyond the number domain. *Trends in Cognitive Sciences*, 13, 83–91. <http://dx.doi.org/10.1016/j.tics.2008.11.007>
- Cappelletti, M., Barth, H., Fregni, F., Spelke, E. S., & Pascual-Leone, A. (2007). rTMS over the intraparietal sulcus disrupts numerosity processing. *Experimental Brain Research*, 179, 631–642. <http://dx.doi.org/10.1007/s00221-006-0820-0>

- Cappelletti, M., Gessaroli, E., Hithersay, R., Mitolo, M., Didino, D., Kanai, R., . . . Walsh, V. (2013). Transfer of cognitive training across magnitude dimensions achieved with concurrent brain stimulation of the parietal lobe. *The Journal of Neuroscience*, 33, 14899–14907. <http://dx.doi.org/10.1523/JNEUROSCI.1692-13.2013>
- Chaieb, L., Kovacs, G., Cziraki, C., Greenlee, M., Paulus, W., & Antal, A. (2009). Short-duration transcranial random noise stimulation induces blood oxygenation level dependent response attenuation in the human motor cortex. *Experimental Brain Research*, 198, 439–444. <http://dx.doi.org/10.1007/s00221-009-1938-7>
- Clemens, B., Jung, S., Zvyagintsev, M., Domahs, F., & Willmes, K. (2013). Modulating arithmetic fact retrieval: A single-blind, sham-controlled tDCS study with repeated fMRI measurements. *Neuropsychologia*, 51, 1279–1286. <http://dx.doi.org/10.1016/j.neuropsychologia.2013.03.023>
- Cohen Kadosh, R. (2013). Using transcranial electrical stimulation to enhance cognitive functions in the typical and atypical brain. *Translational Neuroscience*, 4, 20–33.
- Cohen Kadosh, R. (in press). Modulating and enhancing cognition using brain stimulation: Science and fiction. *Journal of Cognitive Psychology*.
- Cohen Kadosh, R., Cohen Kadosh, K., Schuhmann, T., Kaas, A., Goebel, R., Henik, A., & Sack, A. T. (2007). Virtual dyscalculia induced by parietal-lobe TMS impairs automatic magnitude processing. *Current Biology*, 17, 689–693. <http://dx.doi.org/10.1016/j.cub.2007.02.056>
- Cohen Kadosh, R., Lammertyn, J., & Izard, V. (2008). Are numbers special? An overview of chronometric, neuroimaging, developmental and comparative studies of magnitude representation. *Progress in Neurobiology*, 84, 132–147. <http://dx.doi.org/10.1016/j.pneurobio.2007.11.001>
- Cohen Kadosh, R., Levy, N., O'Shea, J., Shea, N., & Savulescu, J. (2012). The neuroethics of non-invasive brain stimulation. *Current Biology*, 22, R108–R111. <http://dx.doi.org/10.1016/j.cub.2012.01.013>
- Cohen Kadosh, R., Soskic, S., Iuculano, T., Kanai, R., & Walsh, V. (2010). Modulating neuronal activity produces specific and long-lasting changes in numerical competence. *Current Biology*, 20, 2016–2020. <http://dx.doi.org/10.1016/j.cub.2010.10.007>
- Cordes, S., Gelman, R., Gallistel, C. R., & Whalen, J. (2001). Variability signatures distinguish verbal from nonverbal counting for both large and small numbers. *Psychonomic Bulletin & Review*, 8, 698–707. <http://dx.doi.org/10.3758/BF03196206>
- Dehaene, S., Dehaene-Lambertz, G., & Cohen, L. (1998). Abstract representations of numbers in the animal and human brain. *Trends in Neurosciences*, 21, 355–361. [http://dx.doi.org/10.1016/S0166-2236\(98\)01263-6](http://dx.doi.org/10.1016/S0166-2236(98)01263-6)
- Dehaene, S., Izard, V., Spelke, E., & Pica, P. (2008). Log or linear? Distinct intuitions of the number scale in Western and Amazonian indigene cultures. *Science*, 320, 1217–1220. <http://dx.doi.org/10.1126/science.1156540>
- Dehaene, S., Piazza, M., Pinel, P., & Cohen, L. (2003). Three parietal circuits for number processing. *Cognitive Neuropsychology*, 20, 487–506. <http://dx.doi.org/10.1080/02643290244000239>
- Delazer, M., Ischebeck, A., Domahs, F., Zamarian, L., Koppelstaetter, F., Siedentopf, C. M., . . . Felber, S. (2005). Learning by strategies and learning by drill—Evidence from an fMRI study. *NeuroImage*, 25, 838–849. <http://dx.doi.org/10.1016/j.neuroimage.2004.12.009>
- Dockery, C. A., Hueckel-Weng, R., Birbaumer, N., & Plewnia, C. (2009). Enhancement of planning ability by transcranial direct current stimulation. *The Journal of Neuroscience*, 29, 7271–7277. <http://dx.doi.org/10.1523/JNEUROSCI.0065-09.2009>
- Draganski, B., Gaser, C., Busch, V., Schuierer, G., Bogdahn, U., & May, A. (2004). Neuroplasticity: Changes in grey matter induced by training. *Nature*, 427, 311–312. <http://dx.doi.org/10.1038/427311a>
- Duncan, G. J., Dowsett, C. J., Claessens, A., Magnuson, K., Huston, A. C., Klebanov, P., . . . Japel, C. (2007). School readiness and later achievement. *Developmental Psychology*, 43, 1428–1446. <http://dx.doi.org/10.1037/0012-1649.43.6.1428>
- Fan, J., McCandliss, B. D., Sommer, T., Raz, A., & Posner, M. I. (2002). Testing the efficiency and independence of attentional networks. *Journal of Cognitive Neuroscience*, 14, 340–347. <http://dx.doi.org/10.1162/089892902317361886>
- Fertonani, A., Pirulli, C., & Miniussi, C. (2011). Random noise stimulation improves neuroplasticity in perceptual learning. *The Journal of Neuroscience*, 31, 15416–15423. <http://dx.doi.org/10.1523/JNEUROSCI.2002-11.2011>
- Flöel, A., Rösler, N., Michka, O., Knecht, S., & Breitenstein, C. (2008). Noninvasive brain stimulation improves language learning. *Journal of Cognitive Neuroscience*, 20, 1415–1422. <http://dx.doi.org/10.1162/jocn.2008.20098>
- Fregni, F., Boggio, P. S., Nitsche, M., Berman, F., Antal, A., Feredoes, E., . . . Pascual-Leone, A. (2005). Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Experimental Brain Research*, 166, 23–30.
- Fritsch, B., Reis, J., Martinowich, K., Schambra, H. M., Ji, Y., Cohen, L. G., & Lu, B. (2010). Direct current stimulation promotes BDNF-dependent synaptic plasticity: Potential implications for motor learning. *Neuron*, 66, 198–204.
- Gandiga, P. C., Hummel, F. C., & Cohen, L. G. (2006). Transcranial DC stimulation (tDCS): A tool for double-blind sham-controlled clinical studies in brain stimulation. *Clinical Neurophysiology*, 117, 845–850.
- Geary, D. C., Hoard, M. K., Nugent, L., & Byrd-Craven, J. (2008). Development of number line representations in children with mathematical learning disability. *Developmental Neuropsychology*, 33, 277–299. <http://dx.doi.org/10.1080/87565640801982361>
- Gebuis, T., Gevers, W., & Cohen Kadosh, R. (2014). Topographic representation of high-level cognition: Numerosity or sensory processing? *Trends in Cognitive Sciences*, 18, 1–3. <http://dx.doi.org/10.1016/j.tics.2013.10.002>
- Gebuis, T., & Reynvoet, B. (2012). The interplay between nonsymbolic number and its continuous visual properties. *Journal of Experimental Psychology: General*, 141, 642–648. <http://dx.doi.org/10.1037/a0026218>
- Gibson, E. J., Gibson, J. J., Pick, A. D., & Osser, H. (1962). A developmental study of the discrimination of letter-like forms. *Journal of Comparative and Physiological Psychology*, 55, 897–906. <http://dx.doi.org/10.1037/h0043190>
- Girelli, L., Lucangeli, D., & Butterworth, B. (2000). The development of automaticity in accessing number magnitude. *Journal of Experimental Child Psychology*, 76, 104–122. <http://dx.doi.org/10.1006/jecp.2000.2564>
- Gordon, P. (2004). Numerical cognition without words: Evidence from Amazonia. *Science*, 306, 496–499. <http://dx.doi.org/10.1126/science.1094492>
- Green, C. S., & Bavelier, D. (2003). Action video game modifies visual selective attention. *Nature*, 423, 534–537. <http://dx.doi.org/10.1038/nature01647>
- Halberda, J., Mazocco, M. M., & Feigenson, L. (2008). Individual differences in non-verbal number acuity correlate with maths achievement. *Nature*, 455, 665–668. <http://dx.doi.org/10.1038/nature07246>
- Hauser, T. U., Rotzer, S., Grabner, R. H., Méritat, S., & Jäncke, L. (2013). Enhancing performance in numerical magnitude processing and mental arithmetic using transcranial Direct Current Stimulation (tDCS). [Advance online publication]. *Frontiers in Human Neuroscience*, 7, 244. <http://dx.doi.org/10.3389/fnhum.2013.00244>
- Henik, A., & Tzelgov, J. (1982). Is three greater than five: The relation between physical and semantic size in comparison tasks. *Memory & Cognition*, 10, 389–395.
- Holland, R., Leff, A. P., Josephs, O., Galea, J. M., Desikan, M., Price, C. J., . . . Crinion, J. (2011). Speech facilitation by left inferior frontal

- cortex stimulation. *Current Biology*, 21, 1403–1407. <http://dx.doi.org/10.1016/j.cub.2011.07.021>
- Hubbard, E. M., Piazza, M., Pinel, P., & Dehaene, S. (2005). Interactions between number and space in parietal cortex. *Nature Reviews Neuroscience*, 6, 435–448. <http://dx.doi.org/10.1038/nrn1684>
- Iuculano, T., & Cohen Kadosh, R. (2013). The mental cost of cognitive enhancement. *The Journal of Neuroscience*, 33, 4482–4486. <http://dx.doi.org/10.1523/JNEUROSCI.4927-12.2013>
- Iuculano, T., & Cohen Kadosh, R. (2014). Preliminary evidence for performance enhancement following parietal lobe stimulation in Developmental Dyscalculia. [Advance online publication]. *Frontiers in Human Neuroscience*, 8, 38. <http://dx.doi.org/10.3389/fnhum.2014.00038>
- Izard, V., Sann, C., Spelke, E. S., & Streri, A. (2009). Newborn infants perceive abstract numbers. *Proceedings of the National Academy of Sciences of the United States of America*, 106, 10382–10385. <http://dx.doi.org/10.1073/pnas.0812142106>
- Jacobson, L., Koslowsky, M., & Lavidor, M. (2012). tDCS polarity effects in motor and cognitive domains: A meta-analytical review. *Experimental Brain Research*, 216, 1–10. <http://dx.doi.org/10.1007/s00221-011-2891-9>
- Jaeggi, S. M., Buschkuhl, M., Jonides, J., & Perrig, W. J. (2008). Improving fluid intelligence with training on working memory. *Proceedings of the National Academy of Sciences of the United States of America*, 105, 6829–6833. <http://dx.doi.org/10.1073/pnas.0801268105>
- Kasahara, K., Tanaka, S., Hanakawa, T., Senoo, A., & Honda, M. (2013). Lateralization of activity in the parietal cortex predicts the effectiveness of bilateral transcranial direct current stimulation on performance of a mental calculation task. *Neuroscience Letters*, 545, 86–90. <http://dx.doi.org/10.1016/j.neulet.2013.04.022>
- Kaufmann, L., Wood, G., Rubinsten, O., & Henik, A. (2011). Meta-analyses of developmental fMRI studies investigating typical and atypical trajectories of number processing and calculation. *Developmental Neuropsychology*, 36, 763–787. <http://dx.doi.org/10.1080/87565641.2010.549884>
- Keiser, D., Meindl, T., Bor, J., Palm, U., Pogarell, O., Mulert, C., . . . Padberg, F. (2011). Prefrontal transcranial direct current stimulation changes connectivity of resting-state networks during fMRI. *The Journal of Neuroscience*, 31, 15284–15293. <http://dx.doi.org/10.1523/JNEUROSCI.0542-11.2011>
- Klein, E., Mann, A., Huber, S., Bloechle, J., Willmes, K., Karim, A. A., . . . Moeller, K. (2013). Bilateral bi-cephalic tDCS with two active electrodes of the same polarity modulates bilateral cognitive processes differentially [corrected]. *PLoS ONE*, 8, e71607. <http://dx.doi.org/10.1371/journal.pone.0071607>
- Klingberg, T. (2010). Training and plasticity of working memory. *Trends in Cognitive Sciences*, 14, 317–324. <http://dx.doi.org/10.1016/j.tics.2010.05.002>
- Krause, B., & Cohen Kadosh, R. (2013). Can transcranial electrical stimulation improve learning difficulties in atypical brain development? A future possibility for cognitive training. *Developmental Cognitive Neuroscience*, 6, 176–194. <http://dx.doi.org/10.1016/j.dcn.2013.04.001>
- Krause, B., & Cohen Kadosh, R. (2014). Not all brains are created equal: The relevance of individual differences in responsiveness to transcranial electrical stimulation. [Advance online publication]. *Frontiers in Systems Neuroscience*, 8, 25. <http://dx.doi.org/10.3389/fnsys.2014.00025>
- Krause, B., Márquez-Ruiz, J., & Cohen Kadosh, R. (2013). The effect of transcranial direct current stimulation: A role for cortical excitation/inhibition balance? [Advance online publication]. *Frontiers in Human Neuroscience*, 7, 602. <http://dx.doi.org/10.3389/fnhum.2013.00602>
- Kuo, M. F., & Nitsche, M. A. (2012). Effects of transcranial electrical stimulation on cognition. *Clinical EEG and Neuroscience*, 43, 192–199. <http://dx.doi.org/10.1177/1550059412444975>
- Libertus, M. E., Feigenson, L., & Halberda, J. (2011). Preschool acuity of the approximate number system correlates with school math ability. *Developmental Science*, 14, 1292–1300. <http://dx.doi.org/10.1111/j.1467-7687.2011.01080.x>
- Libertus, M. E., Odic, D., & Halberda, J. (2012). Intuitive sense of number correlates with math scores on college-entrance examination. *Acta Psychologica*, 141, 373–379. <http://dx.doi.org/10.1016/j.actpsy.2012.09.009>
- Link, T., Moeller, K., Huber, S., Fischer, U., & Nuerk, H. C. (2013). Walk the number line—An embodied training of numerical concepts. *Trends in Neuroscience and Education*, 2, 74–84. <http://dx.doi.org/10.1016/j.tine.2013.06.005>
- Looi, C. Y., Duta, M., Brem, A.-K., Huber, S., Nuerk, H.-C., & Cohen Kadosh, R. (2015). Combining brain stimulation and video gaming to promote long-term transfer and cognitive enhancement. Manuscript submitted for publication.
- Luber, B., & Lisanby, S. H. (2014). Enhancement of human cognitive performance using transcranial magnetic stimulation (TMS). *NeuroImage*, 85, 961–970. <http://dx.doi.org/10.1016/j.neuroimage.2013.06.007>
- MacLeod, C. M. (1991). Half a century of research on the Stroop effect: An integrative review. *Psychological Bulletin*, 109, 163–203. <http://dx.doi.org/10.1037/0033-2909.109.2.163>
- Márquez-Ruiz, J., Leal-Campanario, R., Sánchez-Campusano, R., Molaei-Ardekani, B., Wendling, F., Miranda, P. C., . . . Delgado-García, J. M. (2012). Transcranial direct-current stimulation modulates synaptic mechanisms involved in associative learning in behaving rabbits. *Proceedings of the National Academy of Sciences of the United States of America*, 109, 6710–6715. <http://dx.doi.org/10.1073/pnas.1121147109>
- Meck, W. H., & Church, R. M. (1983). A mode control model of counting and timing processes. *Journal of Experimental Psychology: Animal Behavior Processes*, 9, 320–334. <http://dx.doi.org/10.1037/0097-7403.9.3.320>
- Meinzer, M., Antonenko, D., Lindenberg, R., Hetzer, S., Ulm, L., Avirame, K., . . . Flöel, A. (2012). Electrical brain stimulation improves cognitive performance by modulating functional connectivity and task-specific activation. *The Journal of Neuroscience*, 32, 1859–1866. <http://dx.doi.org/10.1523/JNEUROSCI.4812-11.2012>
- Meinzer, M., Jähnigen, S., Copland, D. A., Darkow, R., Grittner, U., Avirame, K., . . . Flöel, A. (2014). Transcranial direct current stimulation over multiple days improves learning and maintenance of a novel vocabulary. *Cortex*, 50, 137–147. <http://dx.doi.org/10.1016/j.cortex.2013.07.013>
- Meinzer, M., Lindenberg, R., Antonenko, D., Flaisch, T., & Flöel, A. (2013). Anodal transcranial direct current stimulation temporarily reverses age-associated cognitive decline and functional brain activity changes. *The Journal of Neuroscience*, 33, 12470–12478. <http://dx.doi.org/10.1523/JNEUROSCI.5743-12.2013>
- Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience*, 24, 167–202. <http://dx.doi.org/10.1146/annurev.neuro.24.1.167>
- Nieder, A., & Miller, E. K. (2003). Coding of cognitive magnitude: Compressed scaling of numerical information in the primate prefrontal cortex. *Neuron*, 37, 149–157. [http://dx.doi.org/10.1016/S0896-6273\(02\)01144-3](http://dx.doi.org/10.1016/S0896-6273(02)01144-3)
- Nieratschker, V., Kiefer, C., Giel, K., Krüger, R., & Plewnia, C. (2015). The COMT val/met polymorphism modulates effects of tDCS on response inhibition. *Brain Stimulation*, 8, 283–288.
- Nitsche, M. A., Cohen, L. G., Wassermann, E. M., Priori, A., Lang, N., Antal, A., . . . Pascual-Leone, A. (2008). Transcranial direct current stimulation: State of the art 2008. *Brain Stimulation*, 1, 206–223. <http://dx.doi.org/10.1016/j.brs.2008.06.004>
- Nitsche, M. A., & Paulus, W. (2000). Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *The Journal of Physiology*, 527, 633–639. <http://dx.doi.org/10.1111/j.1469-7793.2000.t01-1-00633.x>

- Owen, A. M., Hampshire, A., Grahn, J. A., Stenton, R., Dajani, S., Burns, A. S., . . . Ballard, C. G. (2010). Putting brain training to the test. *Nature*, 465, 775–778. <http://dx.doi.org/10.1038/nature09042>
- Parsons, S., & Bynner, J. (2005). *Does numeracy matter more?* London: National Research and Development Centre for Adult Literacy and Numeracy.
- Pascual-Leone, A., Horvath, J. C., & Robertson, E. M. (2012). Enhancement of normal cognitive abilities through noninvasive brain stimulation. In R. Chen & J. C. Rothwell (Eds.), *Cortical connectivity* (pp. 207–249). Berlin: Springer-Verlag. http://dx.doi.org/10.1007/978-3-662-45797-9_11
- Peretti, C. S., Danion, J. M., Gierski, F., & Grangé, D. (2002). Cognitive skill learning and aging: A component process analysis. *Archives of Clinical Neuropsychology*, 17, 445–459. <http://dx.doi.org/10.1093/arclin/17.5.445>
- Piazza, M., & Izard, V. (2009). How humans count: Numerosity and the parietal cortex. *The Neuroscientist*, 15, 261–273. <http://dx.doi.org/10.1177/1073858409333073>
- Piazza, M., Izard, V., Pinel, P., Le Bihan, D., & Dehaene, S. (2004). Tuning curves for approximate numerosity in the human intraparietal sulcus. *Neuron*, 44, 547–555. <http://dx.doi.org/10.1016/j.neuron.2004.10.014>
- Piazza, M., Pinel, P., Le Bihan, D., & Dehaene, S. (2007). A magnitude code common to numerosities and number symbols in human intraparietal cortex. *Neuron*, 53, 293–305. <http://dx.doi.org/10.1016/j.neuron.2006.11.022>
- Pica, P., Lemer, C., Izard, V., & Dehaene, S. (2004). Exact and approximate arithmetic in an Amazonian indigene group. *Science*, 306, 499–503. <http://dx.doi.org/10.1126/science.1102085>
- Plewnia, C., Zwissler, B., Längst, I., Maurer, B., Giel, K., & Krüger, R. (2013). Effects of transcranial direct current stimulation (tDCS) on executive functions: Influence of COMT Val/Met polymorphism. *Cortex*, 49, 1801–1807.
- Price, G. R., Palmer, D., Battista, C., & Ansari, D. (2012). Nonsymbolic numerical magnitude comparison: Reliability and validity of different task variants and outcome measures, and their relationship to arithmetic achievement in adults. *Acta Psychologica*, 140, 50–57.
- Priori, A., Hallett, M., & Rothwell, J. C. (2009). Repetitive transcranial magnetic stimulation or transcranial direct current stimulation? *Brain Stimulation*, 2, 241–245. <http://dx.doi.org/10.1016/j.brs.2009.02.004>
- Reigosa-Crespo, V., Valdés-Sosa, M., Butterworth, B., Estévez, N., Rodríguez, M., Santos, E., . . . Lage, A. (2012). Basic numerical capacities and prevalence of developmental dyscalculia: The Havana Survey. *Developmental Psychology*, 48, 123–135. <http://dx.doi.org/10.1037/a0025356>
- Reis, J., Schambra, H. M., Cohen, L. G., Buch, E. R., Fritsch, B., Zarahn, E., . . . Krakauer, J. W. (2009). Noninvasive cortical stimulation enhances motor skill acquisition over multiple days through an effect on consolidation. *Proceedings of the National Academy of Sciences of the United States of America*, 106, 1590–1595. <http://dx.doi.org/10.1073/pnas.0805413106>
- Renzi, C., Vecchi, T., Silvanto, J., & Cattaneo, Z. (2011). Overlapping representations of numerical magnitude and motion direction in the posterior parietal cortex: A TMS-adaptation study. *Neuroscience Letters*, 490, 145–149.
- Richardson, F. C., & Suinn, R. M. (1972). The Mathematics Anxiety Rating Scale: Psychometric data. *Journal of Counseling Psychology*, 19, 551–554. <http://dx.doi.org/10.1037/h0033456>
- Richmond, L. L., Wolk, D., Chein, J., & Olson, I. R. (2014). Transcranial direct current stimulation enhances verbal working memory training performance over time and near transfer outcomes. *Journal of Cognitive Neuroscience*, 26, 2443–2454. http://dx.doi.org/10.1162/jocn_a.00657
- Ritchie, S. J., & Bates, T. C. (2013). Enduring links from childhood mathematics and reading achievement to adult socioeconomic status. *Psychological Science*, 24, 1301–1308. <http://dx.doi.org/10.1177/0956797612466268>
- Rivera, S. M., Reiss, A. L., Eckert, M. A., & Menon, V. (2005). Developmental changes in mental arithmetic: Evidence for increased functional specialization in the left inferior parietal cortex. *Cerebral Cortex*, 15, 1779–1790. <http://dx.doi.org/10.1093/cercor/bhi055>
- Rubinsten, O., & Henik, A. (2005). Automatic activation of internal magnitudes: A study of developmental dyscalculia. *Neuropsychology*, 19, 641–648. <http://dx.doi.org/10.1037/0894-4105.19.5.641>
- Rubinsten, O., & Henik, A. (2006). Double dissociation of functions in developmental dyslexia and dyscalculia. *Journal of Educational Psychology*, 98, 854–867. <http://dx.doi.org/10.1037/0022-0663.98.4.854>
- Rubinsten, O., Henik, A., Berger, A., & Shahar-Shalev, S. (2002). The development of internal representations of magnitude and their association with Arabic numerals. *Journal of Experimental Child Psychology*, 81, 74–92. <http://dx.doi.org/10.1006/jecp.2001.2645>
- Ruffini, G., Fox, M. D., Ripolles, O., Miranda, P. C., & Pascual-Leone, A. (2014). Optimization of multifocal transcranial current stimulation for weighted cortical pattern targeting from realistic modeling of electric fields. *NeuroImage*, 89, 216–225.
- Sack, A. T., Cohen Kadosh, R., Schuhmann, T., Moerel, M., Walsh, V., & Goebel, R. (2009). Optimizing functional accuracy of TMS in cognitive studies: A comparison of methods. *Journal of Cognitive Neuroscience*, 21, 207–221.
- Santarnecchi, E., Polizzotto, N. R., Godone, M., Giovannelli, F., Feurra, M., Matzen, L., . . . Rossi, S. (2013). Frequency-dependent enhancement of fluid intelligence induced by transcranial oscillatory potentials. *Current Biology*, 23, 1449–1453.
- Sarkar, A., Dowker, A., & Kadosh, R. C. (2014). Cognitive enhancement or cognitive cost: Trait-specific outcomes of brain stimulation in the case of mathematics anxiety. *The Journal of Neuroscience*, 34, 16605–16610.
- Schmiedek, F., Lövdén, M., & Lindenberger, U. (2010). Hundred days of cognitive training enhance broad cognitive abilities in adulthood: Findings from the COGITO study. [Advance online publication]. *Frontiers in Aging Neuroscience*, 2.
- Schwarz, W., & Ischebeck, A. (2003). On the relative speed account of number-size interference in comparative judgments of numerals. *Journal of Experimental Psychology: Human Perception and Performance*, 29, 507–522.
- Shalev, R. S. (2007). Prevalence of developmental dyscalculia. In D. B. Berch & M. M. M. Mazzocco (Eds.), *Why is math so hard for some children? The nature and origins of mathematical learning difficulties and disabilities* (pp. 49–60). Baltimore, MD: Brookes.
- Shallice, T. (1982). Specific impairments of planning. *Philosophical Transactions of the Royal Society of London Series B, Biological Sciences*, 298, 199–209. <http://dx.doi.org/10.1098/rstb.1982.0082>
- Siegler, R. S., & Booth, J. L. (2004). Development of numerical estimation in young children. *Child Development*, 75, 428–444.
- Siegler, R. S., & Opfer, J. E. (2003). The development of numerical estimation: Evidence for multiple representations of numerical quantity. *Psychological Science*, 14, 237–250. <http://dx.doi.org/10.1111/1467-9280.02438>
- Slagter, H. A., Lutz, A., Greischar, L. L., Francis, A. D., Nieuwenhuis, S., Davis, J. M., & Davidson, R. J. (2007). Mental training affects distribution of limited brain resources. *PLoS Biology*, 5, e138. <http://dx.doi.org/10.1371/journal.pbio.0050138>
- Snowball, A., Tachtsidis, I., Popescu, T., Thompson, J., Delazer, M., Zamarian, L., . . . Cohen Kadosh, R. (2013). Long-term enhancement of brain function and cognition using cognitive training and brain stimulation. *Current Biology*, 23, 987–992. <http://dx.doi.org/10.1016/j.cub.2013.04.045>
- Snyder, A., Bahramali, H., Hawker, T., & Mitchell, D. J. (2006). Savant-like numerosity skills revealed in normal people by magnetic pulses. *Perception*, 35, 837–845.

- Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology*, 18, 643–662. <http://dx.doi.org/10.1037/h0054651>
- Terhune, D. B., Tai, S., Cowey, A., Popescu, T., & Cohen Kadosh, R. (2011). Enhanced cortical excitability in grapheme-color synesthesia and its modulation. *Current Biology*, 21, 2006–2009. <http://dx.doi.org/10.1016/j.cub.2011.10.032>
- Terney, D., Chaieb, L., Moliadze, V., Antal, A., & Paulus, W. (2008). Increasing human brain excitability by transcranial high-frequency random noise stimulation. *The Journal of Neuroscience*, 28, 14147–14155. <http://dx.doi.org/10.1523/JNEUROSCI.4248-08.2008>
- Truong, D. Q., Magerowski, G., Blackburn, G. L., Bikson, M., & Alonso-Alonso, M. (2013). Computational modeling of transcranial direct current stimulation (tDCS) in obesity: Impact of head fat and dose guidelines. *NeuroImage*, 2, 759–766.
- Tseng, P., Hsu, T. Y., Chang, C. F., Tzeng, O. J., Hung, D. L., Muggleton, N. G., . . . Juan, C. H. (2012). Unleashing potential: Transcranial direct current stimulation over the right posterior parietal cortex improves change detection in low-performing individuals. *The Journal of Neuroscience*, 32, 10554–10561. <http://dx.doi.org/10.1523/JNEUROSCI.0362-12.2012>
- Tzelgov, J., Yehene, V., Kotler, L., & Alon, A. (2000). Automatic comparisons of artificial digits never compared: Learning linear ordering relations. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, 26, 103–120. <http://dx.doi.org/10.1037/0278-7393.26.1.103>
- Villringer, A., & Chance, B. (1997). Non-invasive optical spectroscopy and imaging of human brain function. *Trends in Neurosciences*, 20, 435–442. [http://dx.doi.org/10.1016/S0166-2236\(97\)01132-6](http://dx.doi.org/10.1016/S0166-2236(97)01132-6)
- Villringer, A., Planck, J., Hock, C., Schleinkofer, L., & Dirnagl, U. (1993). Near infrared spectroscopy (NIRS): A new tool to study hemodynamic changes during activation of brain function in human adults. *Neuroscience Letters*, 154, 101–104. [http://dx.doi.org/10.1016/0304-3940\(93\)90181-J](http://dx.doi.org/10.1016/0304-3940(93)90181-J)
- Wagner, T., Valero-Cabre, A., & Pascual-Leone, A. (2007). Noninvasive human brain stimulation. *Annual Review of Biomedical Engineering*, 9, 527–565. <http://dx.doi.org/10.1146/annurev.bioeng.9.061206.133100>
- Walsh, V. (2003). A theory of magnitude: Common cortical metrics of time, space and quantity. *Trends in Cognitive Sciences*, 7, 483–488. <http://dx.doi.org/10.1016/j.tics.2003.09.002>
- Waters-Metenier, S., Husain, M., Wiestler, T., & Diedrichsen, J. (2014). Bihemispheric transcranial direct current stimulation enhances effector-independent representations of motor synergy and sequence learning. *The Journal of Neuroscience*, 34, 1037–1050. <http://dx.doi.org/10.1523/JNEUROSCI.2282-13.2014>
- Weber, M. J., Messing, S. B., Rao, H., Detre, J. A., & Thompson-Schill, S. L. (2014). Prefrontal transcranial direct current stimulation alters activation and connectivity in cortical and subcortical reward systems: A tDCS-fMRI study. *Human Brain Mapping*, 35, 3673–3686. <http://dx.doi.org/10.1002/hbm.22429>
- Xu, F., & Spelke, E. S. (2000). Large number discrimination in 6-month-old infants. *Cognition*, 74, B1–B11. [http://dx.doi.org/10.1016/S0010-0277\(99\)00066-9](http://dx.doi.org/10.1016/S0010-0277(99)00066-9)
- Zamarian, L., Ischebeck, A., & Delazer, M. (2009). Neuroscience of learning arithmetic—Evidence from brain imaging studies. *Neuroscience and Biobehavioral Reviews*, 33, 909–925. <http://dx.doi.org/10.1016/j.neubiorev.2009.03.005>

Received January 11, 2015

Accepted June 29, 2015 ■