Effects of Transcranial Electrical Stimulation on Cognition

Clinical EEG and Neuroscience 43(3) 192-199 © EEG and Clinical Neuroscience Society (ECNS) 2012 Reprints and permission: sagepub.com/journalsPermissions.nav DOI: 10.1177/1550059412444975 http://eeg.sagepub.com



Min-Fang Kuo¹ and Michael A. Nitsche¹

Abstract

Alterations of cortical excitability, oscillatory as well as non-oscillatory, are physiological derivates of cognitive processes, such as perception, working memory, learning, and long-term memory formation. Since noninvasive electrical brain stimulation is capable of inducing alterations in the human brain, these stimulation approaches might be attractive tools to modulate cognition. Transcranial direct current stimulation (tDCS) alters spontaneous cortical activity, while transcranial alternating current stimulation (tACS) and transcranial random noise stimulation (tRNS) are presumed to induce or interfere with oscillations of cortical networks. Via these mechanisms, the respective stimulation techniques have indeed been shown to modulate cognitive processes in a multitude of studies conducted during the last years. In this review, we will gather knowledge about the potential of noninvasive electrical brain stimulation to study and modify cognitive processes in healthy humans and discuss directions of future research.

Keywords

brain stimulation, neuroplasticity, learning, memory, perception, tDCS, tACS, tRNS

Introduction

Cognitive processes take place by physiological alterations of cerebral activity and excitability. Functional imaging, as well as newly developed electroencephalographic (EEG) analysis, have greatly enhanced our knowledge of specific cerebral alterations contributing to cognition. They have helped to identify the areas involved in specific tasks and mechanisms of communication between these areas. At the regional level, functional imaging, via magnetic resonance tomography (fMRI) or positron emission tomography (PET), can help to identify areas activated during cognitive processing, and network analysis, via imaging or EEG, is suited to identify taskrelated interregional communication, that is, functional connectivity. In recent years, noninvasive electrical brain stimulation techniques have been developed that are thought to mimic these physiological processes, at least to a certain extent. Transcranial direct current stimulation (tDCS) induces stimulation polarity-dependent cortical activity and excitability enhancements or reductions, which emerge during stimulation, but can remain for longer than 1 hour after stimulation,¹⁻⁴ and resemble neuroplastic alterations of cortical function, which are thought to be the basis of learning and memory formation.⁵ Since the primary mechanism is thought to be a modulation of resting membrane potential, tDCS affects spontaneous cortical activity. In contrast, transcranial alternating current stimulation (tACS) and transcranial random noise stimulation $(tRNS)^{6,7}$ are presumed to modulate specifically oscillatory cortical activity, dependent on the frequency of stimulation. Because of the

proposed similarity of the effects of brain stimulation and cognitive processes on cerebral physiology, it makes sense to use these techniques to alter cognition. Indeed, it has been demonstrated in numerous studies that all of the above-mentioned techniques are able to modify diverse cognitive processes. Brain stimulation techniques have been introduced for 2 main purposes. They can help to identify areas, and interactions between them, causally involved in cognitive functions, and the specific physiological mechanisms involved. They might be capable of improving cognition under certain preconditions. In this review, we will gather evidence for the impact of electrical brain stimulation techniques on cognitive processes in healthy humans and will suggest future research directions.

Effects of tDCS on Cognition

Stimulation with weak direct currents to modulate cortical activity and excitability was first described in animal models about 50 years ago, when it was shown that subthreshold stimulation, which does not elicit action potentials, modulates resting membrane potentials, and via this mechanism alters

Corresponding Author:

¹ Department of Clinical Neurophysiology, Georg-August University, Goettingen, Germany

Michael A. Nitsche, Department of Clinical Neurophysiology, Georg-August University, Robert-Koch-Str.40, 37099 Goettingen, Germany Email: mnitsch1@gwdg.de

spontaneous cortical activity stimulation polarity dependently.^{8,9} Anodal tDCS enhanced cortical activity and excitability, while cathodal stimulation had the opposite effect. Interestingly, stimulation for some minutes induced aftereffects, which lasted for at least some hours after the stimulation.⁸ Similar effects can be obtained by noninvasive stimulation with direct currents in humans.^{1-3,10,11} The after-effects of stimulation share some things in common with neuroplastic phenomena known from animal experimentation, such as dependency on the glutamatergic system and calcium channels.¹²⁻¹⁴ Since alterations of cortical activity are a common phenomenon observed in cognitive processes, and neuroplastic modifications of neuronal connections are thought to underlie learning and memory formation,^{5,15} it seems plausible that performance in cognitive tasks can be modified by tDCS. Numerous cognitive studies have been performed to probe the efficacy of tDCS to alter performance, ranging from relatively elementary perceptual tasks to more complex processes such as social cognition.

Perception and Attention

Studies exploring the impact of tDCS on perception were performed for visual, somatosensory, auditory and multisensory perception. A study explored the impact of relatively short-lasting (7 min, 1 mA, electrode size 35 cm²) tDCS of the primary visual cortex on perception of static and dynamic contrasts. Excitability-diminishing cathodal tDCS reduced contrast perception, while anodal tDCS was without effect.¹⁶ In another study, somewhat stronger and longer stimulation (15 minutes, 1 mA, electrode size 35 cm²) of the same area showed enhanced contrast sensitivity of central visual regions via anodal tDCS.¹⁷ Different results between the studies might be caused by the variations in the stimulation protocols as well as by the more detailed analysis of contrast perception in the second study.

Stimulation of the motion-sensitive area V5 had discernable effects on motion perception, depending on the task. In a moving dot paradigm without distractors, anodal stimulation improved performance, while cathodal stimulation impaired it. With distractors, however, the effects of tDCS were reversed.¹⁰ These effects were explained by a noise-reducing effect of excitability-diminishing cathodal stimulation in the condition with distractors, whereas excitability-enhancing anodal stimulation was presumed to enhance performance via the increased activation of task-relevant neurons in the condition without distractors. Stimulation of the same area in a motion after-effect task resulted in a reduction of after-effects under both, anodal and cathodal stimulations,¹⁰ which was speculated to be caused by a reduction in activation of movementrepresenting neurons via cathodal stimulation and increased activation of interfering visual stimuli-representing neurons after the end of presentation of the moving stimuli via anodal tDCS. Transcranial DCS has also been shown to modify perception of more complex visual stimuli. Varga and colleagues¹⁸ describe a reduced effect of figural after-effects

induced by prolonged presentation of a face via cathodal tDCS of right lateral parietotemporal areas known to be involved in face perception.

For somatosensory perception, Rogalewski and colleagues¹⁹ explored the effect of tDCS applied to C4, thus covering sensorimotor areas of the human cortex, on the ability of healthy humans to discriminate between vibratory stimuli of different frequencies applied to the left ring finger. They describe reduced performance during and after cathodal tDCS, while anodal tDCS had no effect. However, anodal tDCS applied to S1 resulted in improved spatial acuity of the contralateral index finger in another study.²⁰ For perception of painful stimuli, Antal and colleagues describe a diminishing effect of cathodal tDCS over the somatosensory cortex.²¹ This result was not replicated in another study, where different pain induction procedures were used.²² In this study, however, temperature thresholds were increased by cathodal stimulation. Interestingly, in a companion study, which used the same somatosensory testing procedures, cathodal stimulation of the primary motor cortex increased cold and mechanical detection thresholds as well as mechanical pain thresholds.²³ Taken together, the studies conducted in the field of somatosensory perception show a somewhat heterogeneous outcome, and the effects of tDCS might critically depend on the kind of task under investigation.

With regard to the effects of tDCS on auditory perception, only 2 studies have been conducted. Loui and coworkers describe reduced auditory pitch matching ability, when cathodal tDCS was applied over areas involved in this perceptual task, namely inferior frontal and superior temporal areas.²⁴ In a subsequent study, anodal tDCS over the auditory cortex improved temporal processing in the auditory domain of healthy humans, while cathodal stimulation resulted in reversed effects.²⁵

Finally, tDCS of occipital and temporal areas altered multisensory perception in a "sound-induced flash illusion task." The perceptual "fission" of a single flash due to multiple beeps was enhanced by anodal tDCS of the temporal cortex and reduced by anodal tDCS of the occipital cortex. Cathodal tDCS of the same areas resulted in reversed effects.²⁶

For modulation of attention, Bolognini and coworkers explored the effects of anodal tDCS applied to the posterior parietal cortex on multisensory field exploration.²⁷ Stimulation of the right parietal cortex improved visual exploration and orienting, as compared to sham stimulation, underscoring the causal involvement of this area in visual attentional processes.

Taken together, tDCS has been demonstrated to alter perceptual performance bidirectionally in diverse sensory domains. Hereby, the effects are determined by stimulation polarity, area of stimulation, and most probably type of task. However, the number of currently available studies is limited, and efforts should be made to enhance our understanding of the reasons for the occasionally heterogeneous effects. The exploration of attentional processes via tDCS is currently at its very beginning.

Working Memory

The effect of tDCS on working memory performance has been probed in numerous studies. Since the prefrontal cortex, and specifically its dorsolateral area, is one of the most well-known areas involved in working memory, most of the available studies conducted prefrontal stimulation to modulate performance.

Fregni and colleagues explored the effects of anodal, sham, or cathodal stimulation of the left dorsolateral prefrontal cortex on performance in a 3-back letter task.²⁸ They describe increased accuracy in task performance selectively under anodal tDCS. In a related working memory task, it was shown that the beneficial effects of anodal tDCS on performance accuracy developed during performance were stable for up to 30 minutes after the end of stimulation.²⁹ Zaehle and coworkers describe similar positive effects of anodal tDCS on response accuracy in a 2-back working memory task, while cathodal tDCS disturbed the performance.³⁰ Interestingly, anodal tDCS enhanced alpha and theta activity, while cathodal tDCS had reversed effects, thus offering a plausible physiological substrate for the effects of tDCS on performance.

In contrast, 20-minute anodal tDCS of the same area, when working memory (3-back letter and Sternberg task) was explored after the end of 20-minute tDCS, did not improve accuracy, but reduced the reaction times in the 3-back letter task in a complex time-dependent manner.³¹ In a related study, again the speed of performance was the only parameter that improved for a 2-back but not for a 1-back letter task, when anodal tDCS was conducted before performance.³² The reasons for these heterogeneous results are unclear. Possible explanations might be ceiling effects in the latter studies, since accuracy of performance was higher than 90% at baseline in the last one, stimulation protocol differences (tDCS started 10 minutes before performance or was stopped before performance in the latter studies), or other factors.

With regard to other cortical areas, Berryhill and colleagues explored the effects of tDCS over right inferior parietal regions on an object recognition and recall working memory task.³³ Anodal, cathodal, or sham tDCS were performed before task performance. Cathodal tDCS impaired task performance, in accordance with a role of the right parietal cortex in visual working memory. Ferrucci and coworkers probed the involvement of the cerebellum on performance of the Sternberg task and described disturbed performance induced by both, anodal and cathodal tDCS.³⁴

Taken together, tDCS seems to be an efficient tool to alter working memory performance in healthy humans. The effects have been most extensively tested for prefrontal cortex stimulation. However, results are not completely consistent, and studies systematically probing stimulation parameters might be needed to explore the reasons for these inconsistencies.

Learning and Long-Term Memory

Neuroplastic alterations of cerebral connectivity are the major physiological basis of learning and memory

formation.^{5,15} Therefore, modulation of plasticity via brain stimulation is a potentially attractive way to alter learning and memory formation. Indeed, numerous studies have demonstrated the effects of tDCS on these cognitive processes.

For motor learning, it is thought that within the motorrelated cortical networks, which include the primary motor cortex, premotor, and parietal association areas, the primary motor cortex is involved in early learning phases.³⁵ It was shown that for a motor sequence learning task, as well as for visuomotor coordination, excitability-enhancing anodal tDCS of the primary motor cortex performed during or immediately after task performance improved learning and early consolidation,³⁶⁻³⁹ as well as intrinsic generalization of joint movements.⁴⁰ Interestingly, anodal stimulation of the premotor cortex, which is involved in late sleepdependent consolidation of motor sequence learning,⁴¹ was not effective during task learning, but was during rapid eye movement sleep-dependent consolidation.⁴² This phase specificity of effective stimulation of cortical areas seems to be dependent on task characteristics. In a visuomotor adaption task, in which the primary motor cortex and the cerebellum are involved, cerebellar anodal stimulation improved learning, whereas anodal tDCS of the motor cortex improved consolidation of the learned movements. Moreover, it seems that stimulation *during* learningrelated cortical activation is crucial for obtaining the respective effects, since anodal stimulation before task performance in most studies did not, or only to a minor extent, alter performance level, and in some studies even worsened it.⁴³ Beyond these basic studies exploring the effects of tDCS on motor learning, recent studies refined stimulation protocols. Reis and coworkers showed that repetitive tDCS over 5 consecutive days combined with a motor learning protocol resulted in increasing effects on performance, lasting for at least 3 months after training.⁴⁴ For right-handed individuals, anodal stimulation of the left primary motor cortex seems to be most effective, regardless of the performing hand.45

The effect of tDCS on learning and retention of verbal material was explored in a couple of studies. Flöel and colleagues explored the effect of tDCS on associative verbal learning and showed that selectively anodal tDCS over the left perisylvian area applied during learning improved performance.⁴⁶ In contrast, learning of verbal material was impaired by cathodal tDCS of the left dorsolateral prefrontal cortex.47,48 Moreover, cathodal tDCS of the primary motor cortex reduced learning of action-related words, being in favor of an involvement of this area in learning this kind of material.⁴⁹ For the effect of tDCS on grammar learning, de Vries and colleagues applied anodal tDCS to the Broca area during artificial grammar learning.⁵⁰ Anodal stimulation resulted in improved performance, as compared to a sham-stimulated group. For consolidation and retrieval of declarative verbal material, Marshall and colleagues describe a positive effect of prefrontal sinusoidal anodal tDCS applied during slow wave

sleep.^{51,52} For naturally available material, Fiori and colleagues describe a positive effect of anodal tDCS over Wernicke's area on picture naming.⁵³ In principal accordance, anodal tDCS improved proper name retrieval for the pictures of famous individuals, when the anterior temporal lobes were stimulated.⁵⁴

For visual memory performance, Chi and coworkers conducted a study which involved bilateral stimulation of the anterior temporal lobes during encoding and retrieval of a visual memory task.⁵⁵ They describe improved visual memory via right anodal/left cathodal stimulation but not under reversed stimulation polarities or sham stimulation. Penolazzi and colleagues explored the impact of bilateral frontotemporal stimulation on encoding of emotionally valenced pictures.⁵⁶ In this study, right anodal/left cathodal tDCS resulted in improved memory for emotionally pleasant, while left anodal/right cathodal stimulation increased the recall of emotionally unpleasant pictures. For the memorization of the localization of objects in a natural surrounding, Flöel and coworkers showed that anodal tDCS over the right temporoparietal cortex, which is involved in this type of task, improved memory consolidation, when performance was tested 1 week after learning.⁵⁷ Clark and colleagues explored the impact of tDCS on the identification of concealed objects via stimulation of the right inferior frontal and right parietal areas, which were shown to be involved in this type of task. Anodal tDCS resulted in improved performance.⁵⁸ Importantly, this effect was dosage dependent, and its size was larger for novices as compared to experienced participants, as shown in a consecutive study of this group.⁵⁹

Few studies were performed for other kinds of learning and memory formation. Numerical learning was enhanced by anodal tDCS of the parietal cortex, and this effect was stable for at least 6 months after training.⁶⁰ For probabilistic guessing and classification, it is known that the left prefrontal cortex is involved. In accordance, anodal tDCS of this region improved performance of respective tasks in 2 studies.^{61,62} With regard to the impact of false memories on task performance, the left anterior temporal cortex is thought to be involved. In accordance, anodal tDCS of this area reduced encoding and retrieval of false memories.⁶³

Taken together, an increasing number of studies have been conducted in which the impact of tDCS on learning and memory formation was explored. The results of these studies show that tDCS is a suitable method to evaluate the contribution of specific areas to task performance, including their time course, and that tDCS can have a beneficial effect on performance. Since the effects of stimulation still show some heterogeneity, it will be important for future studies to explore the determinants of the effects of stimulation to a larger degree.

Other Cognitive Processes

A limited set of studies explored the effects of tDCS on other cognitive processes, such as problem solving/creative thinking and social cognition.

Cerruti and Schlaug probed the ability of tDCS to alter complex associative thought.⁶⁴ They report a specific beneficial effect of anodal tDCS applied to the left dorsolateral prefrontal cortex on the remote associates test, in which the volunteers had to identify a word that forms a compound noun with 3 other words presented. Chi and Snyder describe performance enhancement with regard to solving an insight problem, when anodal tDCS of the right was combined with cathodal stimulation of the left anterior temporal lobe.⁶⁵ Dockery and colleagues describe a phase-specific effect of tDCS over the left dorsolateral prefrontal cortex on performance in the Tower of London task, which involves strategic planning.⁶⁶ Cathodal tDCS improved performance during the early acquisition phase of task performance, probably due to its reducing effect on distractive cortical noise, whereas anodal stimulation improved performance in the later stages of task performance, presumably via its activity-enhancing effect on task-related neuronal activity.

With regard to behavior in risk-taking tasks, it was reported that anodal tDCS of the right or left dorsolateral prefrontal cortex, which are involved in risky decision making, resulted in more cautious behavior, when combined with cathodal stimulation of the contralateral prefrontal cortex, thus altering hemispheric balance.⁶⁷ In another study of the same group, however, only anodal stimulation of the right combined with cathodal tDCS of the left dorsolateral prefrontal cortex reduced risky behavior.⁶⁸

In a task involving social cognition, Knoch and coworkers explored the importance of the right prefrontal cortex for performance in the ultimatum game.⁶⁹ In this game, a fixed monetary reward was to be split between 2 participants. One of the participants offers a specific percentage of the whole amount to the other, who can accept or reject the offer. If he accepts, the money is paid to the participants; if not, it is lost. The conflicting aspects involved in decision making are the perception of unfairness of a specific offer and economic selfinterest. In line with their hypothesis, cathodal stimulation of the right prefrontal cortex, which is involved in the generation of negative emotions, increased the acceptance rate of unfair offers.

Taken together, these studies show that tDCS affected performance in complex cognitive processes, including decision making and social cognition. However, the number of studies in these fields is relatively low.

Effects of tACS and tRNS on Cognition

Both tACS and tRNS are newly developed stimulation techniques that modulate cortical excitability and activity noninvasively. While tDCS induces neuroplasticity via constant polarization of neuronal membrane potentials with application of tonic subthreshold direct currents, tACS and tRNS are thought to affect neuronal membrane potentials by oscillatory electrical stimulation with specific or random frequencies. In addition to the modulation of corticospinal excitability, as demonstrated for the motor system,^{6,7,70} tACS and tRNS are thought to interact with ongoing rhythmic cortical activities during cognitive processes and hence could be useful tools to investigate the underlying mechanisms of human cognition.

tACS and Cognitive Processes

For visual perception, tACS of the primary visual cortex affects phosphene perception in a frequency-dependent manner, which is influenced by the brightness of the surrounding, and the predominant frequency range of spontaneous EEG oscillations. Phosphene perception was more effective when tACS was applied in the beta frequency range in an illuminated condition, whereas tACS at alpha frequencies improved phosphene perception in a dark surrounding.⁷¹ Since beta frequencies are predominant in illuminated surroundings, whereas alpha frequencies dominate under light deprivation, this study suggests that tACS can modulate visual perception via its impact on naturally occurring cortical oscillations. In a later study, tACS in the high gamma frequency range (60 Hz) applied over the primary visual cortex (V1) enhanced contrast perception, whereas no influence on spatial attention was observed,⁷² underscoring a specific effect of the stimulation on functions in which the stimulated area is involved. For the somatosensory modality, tactile sensations could be induced when S1 was stimulated by tACS, most effectively by stimulation within the alpha range frequency, followed by high gamma and beta stimulation.⁷³ The results of this study suggest that tACS might be suited not only to modulate but also to induce perceptions.

Apart from the effects of tACS on perception, this stimulation protocol has a stimulation-frequency-dependent effect on motor learning. tACS over M1 facilitated motor sequence learning only when applied at alpha frequency, while high ripple frequency (140 Hz) stimulation had no effect on the same learning protocol.^{6,74} Alpha oscillations are associated with the inhibition of irrelevant stimuli during cognitive tasks,⁷⁵ and this may explain the facilitatory effect of alpha modulation on motor learning, while the relevance of fast ripple oscillations, better studied in the hippocampal region, remains unclear especially for the cognitive function of motor cortex. These results reveal that tACS could indeed influence cognitive functions, particularly when applied within certain task-related frequency ranges, possibly via interference or entrainment of cognition-related oscillations. This might make tACS an interesting tool not only for altering cognitive functions but also for exploring the causal relevance of cortical oscillations for cognitive processes.

Transcranial RNS and Cognitive Processes

Unlike the fixed frequency used in tACS protocols, tRNS is applied within a broad frequency spectrum (0.1-640 Hz) with random noise distribution.⁷ The frequency range covers specific physiological human brain oscillations, by which tRNS possibly induces LTP-like cortical plasticity via augmenting the activity of neuronal sodium channels.

For the effect of tRNS on working memory performance, only 1 study is available, which showed a null effect of stimulation of the dorsolateral prefronatal cortex on performance.³² However, tRNS of the primary motor cortex improved motor sequence learning⁷. Fertonani and colleagues also report a facilitation of perceptual learning with tRNS applied over the primary visual cortex. In the latter study, the accuracy of an orientation discrimination task was significantly increased by tRNS in the high-frequency range (100-640 Hz).⁷⁶ In contrast, application of tRNS on right dorsal lateral prefrontal cortex impaired categorical learning in a prototype distortion task.⁷⁷ The reasons for these heterogeneous effects are unclear at present, task specifics might contribute.

Due to the small number of both physiological and cognitive experiments conducted so far, the underlying mechanisms of tACS and tRNS are yet not sufficiently clear. Future studies should provide more information to improve our understanding of the neurophysiological basis of these stimulation tools and their application to investigate and modify human cognition.

General Remarks

This review has shown prominent effects of electrical brain stimulation on cognitive processes, both elementary and complex. Transcranial DCS has been used most frequently to study the neurophysiological basis of cognition and resulted in clear and specific effects in most studies. Newly emerged techniques, tACS and tRNS, might gain attractiveness in the future. In contrast to tDCS, they might be able to specifically alter task-related oscillatory activity, and thus tackle—beyond cortical activity alterations—another important physiological determinant of cognitive processes.

Beyond the principle ability of these stimulation techniques to modify cognitive performance, some studies have shown that the efficacy and direction of the effects depend on the timing of stimulation, electrode arrangement, and task characteristics, among others. Clearly, more studies are needed not only to learn more about the physiological basis of cognition, but also to optimize the efficacy of stimulation. Beyond basic cognitive neuroscience, these efforts will be relevant for the application of the techniques to neuropsychiatric diseases accompanied by cognitive disturbances. Here pilot studies, beyond the scope of the present review, have been shown to result in potentially meaningful effects.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

References

 Nitsche M, Nitsche M, Klein C, Tergau F, Rothwell J, Paulus W. Level of action of cathodal DC polarisation induced inhibition of the human motor cortex. *Clin Neurophysiol*. 2003;114(4): 600-604.

- Nitsche M, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *J Physiol.* 2000;527(pt 3):633-639.
- Nitsche M, Paulus W. Sustained excitability elevations induced by transcranial DC motor cortex stimulation in humans. *Neurol*ogy. 2001;57(10):1899-1901.
- Nitsche MA, Cohen LG, Wassermann EM, et al. Transcranial direct current stimulation: state of the art 2008. *Brain Stimul*. 2008;1(3):206-223.
- Malenka R, Bear M. LTP and LTD: an embarrassment of riches. *Neuron.* 2004;44(1):5-21.
- Antal A, Boros K, Poreisz C, Chaieb L, Terney D, Paulus W. Comparatively weak after-effects of transcranial alternating current stimulation (tACS) on cortical excitability in humans. *Brain Stimul.* 2008;1(2):97-105.
- Terney D, Chaieb L, Moliadze V, Antal A, Paulus W. Increasing human brain excitability by transcranial high-frequency random noise stimulation. *J Neurosci*. 2008;28(52):14147-14155.
- Bindman L, Lippold O, Redfearn JWT. 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. *J Physiol (Lond)*. 1964;172:369-382.
- Purpura DP, McMurtry JG. Intracellular activities and evoked potential changes during polarization of motor cortex. *J Neurophysiol.* 1965;28:166-185.
- Antal A, Nitsche M, Kruse W, Kincses T, Hoffmann K, Paulus W. Direct current stimulation over V5 enhances visuomotor coordination by improving motion perception in humans. *J Cogn Neurosci.* 2004;16(4):521-527.
- Matsunaga K, Nitsche M, Tsuji S, Rothwell J. Effect of transcranial DC sensorimotor cortex stimulation on somatosensory evoked potentials in humans. *Clin Neurophysiol.* 2004;115(2):456-460.
- Nitsche M, Fricke K, Henschke U, et al. Pharmacological modulation of cortical excitability shifts induced by transcranial direct current stimulation in humans. *J Physiol*. 2003;553(pt 1): 293-301.
- Nitsche M, Jaussi W, Liebetanz D, Lang N, Tergau F, Paulus W. Consolidation of human motor cortical neuroplasticity by D-cycloserine. *Neuropsychopharmacology*. 2004;29(8):1573-1578.
- Liebetanz D, Nitsche M, Tergau F, Paulus W. Pharmacological approach to the mechanisms of transcranial DC-stimulationinduced after-effects of human motor cortex excitability. *Brain*. 2002;125(pt 10):2238-2247.
- Rioult-Pedotti M, Friedman D, Donoghue J. Learning-induced LTP in neocortex. *Science*. 2000;290(5491):533-536.
- Antal A, Nitsche M, Paulus W. External modulation of visual perception in humans. *Neuroreport*. 2001;12(16):3553-3555.
- Kraft A, Kehrer S, Hagendorf H, Brandt SA. Hemifield effects of spatial attention in early human visual cortex. *Eur J Neurosci* 2011;33(12):2349-2358.
- Varga ET, Elif K, Antal A, et al. Cathodal transcranial direct current stimulation over the parietal cortex modifies facial gender adaptation. *Ideggyogy Sz.* 2007;60(11-12):474-479.
- Rogalewski A, Breitenstein C, Nitsche M, Paulus W, Knecht S. Transcranial direct current stimulation disrupts tactile perception. *Eur J Neurosci.* 2004;20(1):313-316.

- Ragert P, Vandermeeren Y, Camus M, Cohen LG. Improvement of spatial tactile acuity by transcranial direct current stimulation. *Clin Neurophysiol*. 2008;119(4):805-811.
- Antal A, Brepohl N, Poreisz C, Boros K, Csifcsak G, Paulus W. Transcranial direct current stimulation over somatosensory cortex decreases experimentally induced acute pain perception. *Clin J Pain*. 2008;24(1):56-63.
- Grundmann L, Rolke R, Nitsche MA, et al. Effects of transcranial direct current stimulation of the primary sensory cortex on somatosensory perception. *Brain Stimul.* 2011;4(4):253-260.
- Bachmann CG, Muschinsky S, Nitsche MA, et al. Transcranial direct current stimulation of the motor cortex induces distinct changes in thermal and mechanical sensory percepts. *Clin Neurophysiol.* 2010;121(12):2083-2089.
- Loui P, Hohmann A, Schlaug G. Inducing disorders in pitch perception and production: a reverse-engineering approach. *Proc Meet Acoust.* 2010;9(1):50002.
- Ladeira A, Fregni F, Campanha C, et al. Polarity-dependent transcranial direct current stimulation effects on central auditory processing. *PLoS One*. 2011;6(9):e25399.
- Bolognini N, Rossetti A, Casati C, Mancini F, Vallar G. Neuromodulation of multisensory perception: a tDCS study of the soundinduced flash illusion. *Neuropsychologia*. 2011;49(2):231-237.
- Bolognini N, Fregni F, Casati C, Olgiati E, Vallar G. Brain polarization of parietal cortex augments training-induced improvement of visual exploratory and attentional skills. *Brain Res.* 2010;1349: 76-89.
- Fregni F, Boggio P, Nitsche M, et al. Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. *Exp Brain Res.* 2005;166(1):23-30.
- Ohn SH, Park CI, Yoo WK, et al. Time-dependent effect of transcranial direct current stimulation on the enhancement of working memory. *Neuroreport*. 2008;19(1):43-47.
- Zaehle T, Sandmann P, Thorne JD, Jancke L, Herrmann CS. Transcranial direct current stimulation of the prefrontal cortex modulates working memory performance: combined behavioural and electrophysiological evidence. *BMC Neurosci*. 2011;12:2.
- Teo F, Hoy KE, Daskalakis ZJ, Fitzgerald PB. Investigating the role of current strength in tDCS modulation of working memory performance in healthy controls. *Front Psychiatry*. 2011;2:45.
- Mulquiney PG, Hoy KE, Daskalakis ZJ, Fitzgerald PB. Improving working memory: exploring the effect of transcranial random noise stimulation and transcranial direct current stimulation on the dorsolateral prefrontal cortex. *Clin Neurophysiol*. 2011; 122(12):2384-2389.
- Berryhill ME, Wencil EB, Branch Coslett H, Olson IR. A selective working memory impairment after transcranial direct current stimulation to the right parietal lobe. *Neurosci Lett.* 2010;479(3): 312-316.
- Ferrucci R, Marceglia S, Vergari M, et al. Cerebellar transcranial direct current stimulation impairs the practice-dependent proficiency increase in working memory. *J Cogn Neurosci*. 2008; 20(9):1687-1697.
- Honda M, Deiber M, Ibanez V, Pascual-Leone A, Zhuang P, Hallett M. Dynamic cortical involvement in implicit and explicit

motor sequence learning. A PET study. *Brain*. 1998;121 (pt 11): 2159-2173.

- Antal A, Nitsche M, Kincses T, Kruse W, Hoffmann K, Paulus W. Facilitation of visuo-motor learning by transcranial direct current stimulation of the motor and extrastriate visual areas in humans. *Eur J Neurosci*. 2004;19(10):2888-2892.
- Nitsche M, Schauenburg A, Lang N, et al. Facilitation of implicit motor learning by weak transcranial direct current stimulation of the primary motor cortex in the human. *J Cogn Neurosci.* 2003; 15(4):619-626.
- Hunter T, Sacco P, Nitsche MA, Turner DL. Modulation of internal model formation during force field-induced motor learning by anodal transcranial direct current stimulation of primary motor cortex. *J Physiol.* 2009;587(pt 12):2949-2961.
- Tecchio F, Zappasodi F, Assenza G, et al. Anodal transcranial direct current stimulation enhances procedural consolidation. *J Neurophysiol*. 2010;104(2):1134-1140.
- Orban de Xivry J-J, Marko MK, Pekny SE, et al. Stimulation of the human motor cortex alters generalization patterns of motor learning. *J Neurosci.* 2011;31(19):7102-7110.
- Maquet P, Laureys S, Peigneux P, et al. Experience-dependent changes in cerebral activation during human REM sleep. *Nat Neurosci.* 2000;3(8):831-836.
- Nitsche MA, Jakoubkova M, Thirugnanasambandam N, et al. Contribution of the premotor cortex to consolidation of motor sequence learning in humans during sleep. *J Neurophysiol*. 2010;104(5):2603-2614.
- Antal A, Begemeier S, Nitsche MA, Paulus W. Prior state of cortical activity influences subsequent practicing of a visuomotor coordination task. *Neuropsychologia*. 2008;46(13): 3157-3161.
- Reis J, Schambra HM, Cohen LG, et al. Noninvasive cortical stimulation enhances motor skill acquisition over multiple days through an effect on consolidation. *Proc Natl Acad Sci U S A*. 2009;106(5):1590-1595.
- Schambra HM, Abe M, Luckenbaugh DA, Reis J, Krakauer JW, Cohen LG. Probing for hemispheric specialization for motor skill learning: a transcranial direct current stimulation study. *J Neurophysiol.* 2011;106(2):652-661.
- Flöel A, Rosser N, Michka O, Knecht S, Breitenstein C. Noninvasive brain stimulation improves language learning. *J Cogn Neurosci*. 2008;20(8):1415-1422.
- Elmer S, Burkard M, Renz B, Meyer M, Jancke L. Direct current induced short-term modulation of the left dorsolateral prefrontal cortex while learning auditory presented nouns. *Behav Brain Funct*. 2009;5:29.
- Hammer A, Mohammadi B, Schmicker M, Saliger S, Munte TF. Errorless and errorful learning modulated by transcranial direct current stimulation. *BMC Neurosci*. 2011;12:72.
- Liuzzi G, Freundlieb N, Ridder V, et al. The involvement of the left motor cortex in learning of a novel action word lexicon. *Curr Biol.* 2010;20(19):1745-1751.
- de Vries MH, Barth AC, Maiworm S, Knecht S, Zwitserlood P, Floel A. Electrical stimulation of Broca's area enhances implicit learning of an artificial grammar. *J Cogn Neurosci*. 2010;22(11): 2427-2436.

- Marshall L, Kirov R, Brade J, Molle M, Born J. Transcranial electrical currents to probe EEG brain rhythms and memory consolidation during sleep in humans. *PLoS One.* 2011;6(2):e16905.
- Marshall L, Molle M, Hallschmid M, Born J. Transcranial direct current stimulation during sleep improves declarative memory. *J Neurosci*. 2004;24(44):9985-9992.
- Fiori V, Coccia M, Marinelli CV, et al. Transcranial direct current stimulation improves word retrieval in healthy and nonfluent aphasic subjects. *J Cogn Neurosci.* 2011;23(9):2309-2323.
- Ross LA, McCoy D, Wolk DA, Coslett HB, Olson IR. Improved proper name recall by electrical stimulation of the anterior temporal lobes. *Neuropsychologia*. 2010;48(12):3671-3674.
- 55. Chi RP, Fregni F, Snyder AW. Visual memory improved by non-invasive brain stimulation. *Brain Res.* 2010;1353:168-175.
- Penolazzi B, Di Domenico A, Marzoli D, et al. Effects of transcranial direct current stimulation on episodic memory related to emotional visual stimuli. *PLoS One*. 2010;5(5):e10623.
- Flöel A, Suttorp W, Kohl O, et al. Non-invasive brain stimulation improves object-location learning in the elderly. *Neurobiol Aging*. 2011 doi: http://dx.doi.org/10.1016/j.neurobiolaging.2011.05.007.
- Clark VP, Coffman BA, Mayer AR, et al. TDCS guided using fMRI significantly accelerates learning to identify concealed objects. *Neuroimage*. 2012;59(1):117-128.
- Bullard LM, Browning ES, Clark VP, et al. Transcranial direct current stimulation's effect on novice versus experienced learning. *Exp Brain Res.* 2011;213(1):9-14.
- Cohen Kadosh R, Soskic S, Iuculano T, Kanai R, Walsh V. Modulating neuronal activity produces specific and long-lasting changes in numerical competence. *Curr Biol.* 2010;20(22): 2016-2020.
- Hecht D, Walsh V, Lavidor M. Transcranial direct current stimulation facilitates decision making in a probabilistic guessing task. *J Neurosci.* 2010;30(12):4241-4245.
- Kincses T, Antal A, Nitsche M, Bartfai O, Paulus W. Facilitation of probabilistic classification learning by transcranial direct current stimulation of the prefrontal cortex in the human. *Neuropsychologia*. 2004;42(1):113-117.
- 63. Boggio PS, Fregni F, Valasek C, et al. Temporal lobe cortical electrical stimulation during the encoding and retrieval phase reduces false memories. *PLoS One*. 2009;4(3):e4959.
- 64. Cerruti C, Schlaug G. Anodal transcranial direct current stimulation of the prefrontal cortex enhances complex verbal associative thought. *J Cogn Neurosci*. 2009;21(10):1980-1987.
- 65. Chi RP, Snyder AW. Facilitate insight by non-invasive brain stimulation. *PLoS One*. 2011;6(2):e16655.
- Dockery CA, Hueckel-Weng R, Birbaumer N, Plewnia C. Enhancement of planning ability by transcranial direct current stimulation. *J Neurosci*. 2009;29(22):7271-7277.
- Fecteau S, Knoch D, Fregni F, Sultani N, Boggio P, Pascual-Leone A. Diminishing risk-taking behavior by modulating activity in the prefrontal cortex: a direct current stimulation study. *J Neurosci.* 2007;27(46):12500-12505.
- Fecteau S, Pascual-Leone A, Zald DH, et al. Activation of prefrontal cortex by transcranial direct current stimulation reduces appetite for risk during ambiguous decision making. *J Neurosci*. 2007;27(23):6212-6218.

- Knoch D, Nitsche MA, Fischbacher U, Eisenegger C, Pascual-Leone A, Fehr E. Studying the neurobiology of social interaction with transcranial direct current stimulation–the example of punishing unfairness. *Cereb Cortex*. 2008;18(9):1987-1990.
- Feurra M, Bianco G, Santarnecchi E, Del Testa M, Rossi A, Rossi S. Frequency-dependent tuning of the human motor system induced by transcranial oscillatory potentials. *J Neurosci*. 2011; 31(34):12165-12170.
- Kanai R, Chaieb L, Antal A, Walsh V, Paulus W. Frequencydependent electrical stimulation of the visual cortex. *Curr Biol.* 2008;18(23):1839-1843.
- Laczo B, Antal A, Niebergall R, Treue S, Paulus W. Transcranial alternating stimulation in a high gamma frequency range applied over V1 improves contrast perception but does not modulate spatial attention. *Brain Stimul.* 2011 doi:10.1016/j.brs.2011.08.008.

- Feurra M, Paulus W, Walsh V, Kanai R. Frequency specific modulation of human somatosensory cortex. *Front Psychol.* 2011;2:13.
- Moliadze V, Antal A, Paulus W. Boosting brain excitability by transcranial high frequency stimulation in the ripple range. *J Physiol*. 2010;588(pt 24):4891-4904.
- Jensen O, Mazaheri A. Shaping functional architecture by oscillatory alpha activity: gating by inhibition. *Front Hum Neurosci*. 2011;4:186.
- Fertonani A, Pirulli C, Miniussi C. Random noise stimulation improves neuroplasticity in perceptual learning. *J Neurosci.* 2011;31(43):15416-15423.
- Ambrus GG, Zimmer M, Kincses ZT, et al. The enhancement of cortical excitability over the DLPFC before and during training impairs categorization in the prototype distortion task. *Neuropsychologia*. 2011;49(7):1974-1980.

Reproduced with permission of the copyright owner. Further reproduction prohibited without permission.