

# The role of transcranial direct current stimulation (tDCS) in rehabilitation of stroke patients with aphasia

PANAGIOTIS D. KARAGOUNIS\*

**Key words:** TDCS, neurorehabilitation, stroke, aphasia

Transcranial direct current stimulation (tDCS) is a form of neurostimulation that uses constant, low direct current delivered via electrodes on the head.

It was originally developed to help patients with brain injuries or psychiatric conditions like major depressive disorders. tDCS appears to have some potential for treating depression. However, there is no good evidence that it is useful for cognitive enhancement in healthy people, memory deficits in Parkinson's disease and Alzheimer's disease, non-neuropathic pain, and non-improving upper limb function after stroke.

tDCS appears to be somewhat effective for depression. There is also evidence that tDCS is useful in treating neuropathic pain after spinal cord injury and improving activities of daily living assessment after stroke.

The adverse effects associated with tDCS appear to be mostly limited to headaches and itchiness and redness at the site of stimulation. When applied following established safety protocols, transcranial direct current stimulation is widely regarded as a safe method of brain stimulation. Safety protocols limit the current, duration, and frequency of stimulation, thereby limiting the effects and risk.

There has been much work done in the last 10 years to develop a safety protocol for administering transcranial direct current stimulation. Many studies have been conducted to determine the optimal time of stimulation and current used as well as steps to take in order to reduce or eliminate the side effects felt by the person receiving the stimulation. Present safety guidelines on the research and medical fields treat daily stimulation up to 60 min and up to 4 mA as safe. However, the tolerability of every day application for more than 10 sessions per two weeks remains unclear.

There is no strict limitation on the duration of stimulation set at this point but a stimulation time of 20 minutes is considered the ideal time. The longer the stimula-

tion duration, the longer the observed effects of the stimulation persist once the stimulation has ended. A stimulation length of 10 minutes results in observed effects lasting for up to an hour. It is generally encouraged to wait at least 48 hours to a week before repeating the stimulation. Also, it is advised to warn the person receiving the stimulation of the possible after effects of the tDCS stimulation.

There are a few minor side effects including skin irritation, a phosphene at the start of stimulation, nausea, headache, dizziness, and itching under the electrode. Nausea most commonly occurs when the electrodes are placed above the mastoid for stimulation of the vestibular system. There are several ways to reduce the skin irritation felt during stimulation. Electrodes may be prepared with saline solution and the skin prepared with electrode cream. Also, ramping up (slowly increasing) the current can reduce the irritation. It is not advised to administer this stimulation to people susceptible to seizures, such as people with epilepsy. However, seizures do not seem to be a risk for healthy individuals. One of the aspects of tDCS is its ability to achieve cortical changes even after the stimulation is ended. The duration of this change depends on the length of stimulation as well as the intensity of stimulation. The effects of stimulation increase as the duration of stimulation increases or the strength of the current increases.

The way that the stimulation changes brain function is either by causing the neuron's resting membrane potential to depolarize or hyperpolarize. When positive stimulation (anodal tDCS) is delivered, the current causes a depolarization of the resting membrane potential, which increases neuronal excitability and allows for more spontaneous cell firing. When negative stimulation (cathodal tDCS) is delivered, the current causes a hyperpolarization of the resting membrane potential. This decreases neuron excitability due to the decreased spontaneous cell firing.

Transcranial direct current stimulation works by sending constant, low direct current through the electrodes. When these electrodes are placed in the region of interest, the current induces intracerebral current flow. This current flow then either increases or decreases the

\*Physician of Physical Medicine and Rehabilitation  
Recovery and Rehabilitation Center FILOKTITIS  
MD, MSc, PhD UoA

neuronal excitability in the specific area being stimulated based on which type of stimulation is being used. This change of neuronal excitability leads to alteration of brain function, which can be used in various therapies as well as to provide more information about the functioning of the human brain.

Transcranial direct current stimulation is a relatively simple technique requiring only a few parts. These include two electrodes and a battery-powered device that delivers constant current. Control software can also be used in experiments that require multiple sessions with differing stimulation types so that neither the person receiving the stimulation nor the experimenter knows which type is being administered. Each device has an anodal, positively charged electrode and a cathodal, negative electrode. Current is conventionally described as flowing from the positive anode, through the intervening conducting tissue, to the cathode, creating a circuit. To set up the tDCS device, the electrodes and the skin need to be prepared. This ensures a low resistance connection between the skin and the electrode. The careful placement of the electrodes is crucial to successful tDCS technique. The electrode pads come in various sizes with benefits to each size. A smaller sized electrode achieves a more focused stimulation of a site while a larger electrode ensures that the entirety of the region of interest is being stimulated. If the electrode is placed incorrectly, a different site or more sites than intended may be stimulated resulting in faulty results. One of the electrodes is placed over the region of interest and the other electrode, the reference electrode, is placed in another location in order to complete the circuit. This reference electrode is usually placed on the neck or shoulder of the opposite side of the body than the region of interest. Since the region of interest may be small, it is often useful to locate this region before placing the electrode by using a brain imaging technique. After the stimulation has been started, the current will continue for the amount of time set on the device and then will automatically be shut off. Recently a new approach has been introduced where instead of using two large pads, multiple (more than two) smaller sized gel electrodes are used to target specific cortical structures. This new approach is called High Definition tDCS (HD-tDCS).

There are three different types of stimulation: anodal, cathodal, and sham. The anodal stimulation is positive (V+) stimulation that increases the neuronal excitability of the area being stimulated. Cathodal (V-) stimulation decreases the neuronal excitability of the area being stimulated. Cathodal stimulation can treat psychological disorders that are caused by the hyper-activity of an area of the brain. Sham stimulation is used as a control in experiments. Sham stimulation emits a brief current

but then remains off for the remainder of the stimulation time. With sham stimulation, the person receiving the tDCS does not know that they are not receiving prolonged stimulation. By comparing the results in subjects exposed to sham stimulation with the results of subjects exposed to anodal or cathodal stimulation, researchers can see how much of an effect is caused by the current stimulation, rather than by the placebo effect.

Transcranial direct current stimulation in the current period is beginning to be used more frequently as a brain stimulation technique because it is considered as a safe method for human use.

## References

- 1 Chomsky N. *Language and mind*. New York: Harcourt, Brace & World, 1968.
- 2 Saur D, Hartwigsen G. Neurobiology of language recovery after stroke: lessons from neuroimaging studies. *Arch Phys Med Rehabil* (2012) 93:S15–25.
- 3 Penfield W. Conditioning the uncommitted cortex for language learning. *Brain* (1965) 88:787–798.
- 4 Ojemann GA. Brain organization for language from the perspective of electrical stimulation mapping. *Behav Brain Sci* (1983) 6:189–230.
- 5 Ojemann GA. Functional mapping of cortical language areas in adults. Intraoperative approaches. *Adv Neurol* (1993) 63:155–163.
- 6 Rapport RL, Tan CT, Whitaker HA. Language function and dysfunction among Chinese- and English-speaking polyglots: cortical stimulation, Wada testing, and clinical studies. *Brain Lang* (1983) 18:342–366.
- 7 Hamilton RH, Chrysikou EG, Coslett B. Mechanisms of aphasia recovery after stroke and the role of noninvasive brain stimulation. *Brain Lang* (2011) 118:40–50.
- 8 Reis J, Robertson EM, Krakauer JW, et al. Consensus: can transcranial direct current stimulation and transcranial magnetic stimulation enhance motor learning and memory formation? *Brain Stimul* (2008) 1:363–369.
- 9 Vallar G, Bolognini N. Behavioural facilitation following brain stimulation: implications for neurorehabilitation. *Neuropsychol Rehabil* (2011) 21:618–649.
- 10 Webster BR, Celnik PA, Cohen LG. Noninvasive brain stimulation in stroke rehabilitation. *NeuroRx* (2006) 3:474–481.
- 11 Hallett M. Transcranial magnetic stimulation: a primer. *Neuron* (2007) 55:187–199.
- 12 Lefaucheur JP. Stroke recovery can be enhanced by using repetitive transcranial magnetic stimulation (rTMS). *Neurophysiol Clin* (2006) 36:105–115.
- 13 Nitsche MA, Cohen LG, Wassermann EM, et al. Transcranial direct current stimulation: state of the art *Brain Stimul* (2008) 1:206–223.
- 14 Schlaug G, Renga V, Nair D. Transcranial direct current stimulation in stroke recovery. *Arch Neurol* (2008) 65:1571–1576.
- 15 Cherney LR. Cortical stimulation and aphasia: the state of the science. *Perspect Neurophysiol Neurogenic Speech Lang Disord* (2008) 18:33–39.
- 16 Martin PI, Naeser MA, Ho M, et al. Research with transcranial magnetic stimulation in the treatment of aphasia. *Curr Neurol Neurosci Rep* (2009) 9:451–458.
- 17 Brunoni AR, Moffa AH, Fregni F, Palm U, Padberg F, Blumberger DM, et al. Transcranial direct current stimulation for acute major depressive episodes: meta-analysis of individual patient data. *The British Journal of Psychiatry* (2016) 208: 522–531.
- 18 Horvath JF, Carter J Quantitative Review Finds No Evidence of Cognitive Effects in Healthy Populations From Single-session Transcranial Direct Current Stimulation (tDCS). *Brain Stimulation* (2015) 8: 535–550.
- 19 Bennabi D. Transcranial direct current stimulation for memory enhancement: from clinical research to animal models. *Front Syst Neurosci* (2014) 8: 159.
- 20 Agarwal SM. Transcranial direct current stimulation in schizophrenia. *Clin Psychopharmacol Neurosci* (2013) 11 (3): 118–125.
- 21 Luedtke K. Transcranial direct current stimulation for the reduction of clinical and experimentally induced pain: a systematic review and meta-analysis. *Clin J Pain* (2012) 28 (5): 452–61.
- 22 Feng WW. Review of transcranial direct current stimulation in poststroke recovery. *Top Stroke Rehabil* (2013) 20 (1): 68–77.
- 23 Nitsche MA et al. Safety criteria for transcranial direct current stimulation (tDCS) in humans". *Clinical Neurophysiology* (2003) 114(11):2220–2222.
- 24 Liebetanz, DK et al. Safety limits of cathodal transcranial direct current stimulation in rats. *Clinical Neurophysiology* (2009) 120(6): 1161–1167.
- 25 Bikson M, Datta A., Elwassif M. "Establishing safety limits for transcranial direct current stimulation. *Clinical Neurophysiology* (2009) 120(6): 1033–1034.
- 26 Nitsche MA et al. Transcranial direct current stimulation: State of the art 2008. *Brain Stimulation* (2008) 1(3): 206–223.
- 27 Poreisz CB et al. Safety aspects of transcranial direct current stimulation concerning healthy subjects and patients. *Brain Research Bulletin* (2007) 72 (4–6): 208–214.
- 28 Viganò A et al. "Transcranial Direct Current Stimulation (tDCS) of the visual cortex: A proof-of-concept study based on interictal electrophysiological abnormalities in migraine. *The Journal of Headache and Pain* (2013) 14(1): 23.
- 29 Utz KS, Dimova V, Oppenländer K, Kerkhoff G. Electrified minds: Transcranial direct current stimulation (tDCS) and Galvanic Vestibular Stimulation (GVS) as methods of non-invasive brain stimulation in neuropsychology—A review of current data and future implications. *Neuropsychologia* (2010) 48(10): 2789–2810.
- 30 Nitsche, MA, Paulus, W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *The Journal of Physiology* (2000) 527 (3): 633–639.
- 31 Monai H et al. Calcium imaging reveals glial involvement in transcranial direct current stimulation-induced plasticity in mouse brain. *Nature Communications* (2016) 7: 11100.
- 32 Sparing R and Mottaghy F. Noninvasive brain stimulation with transcranial magnetic or direct current stimulation (TMS/tDCS)—From insights into human memory to therapy of its dysfunction". *Methods* (2008) 44(4): 329–337.
- 33 Datta A et al. Gyriprecise head model of transcranial direct current stimulation: Improved spatial focality using a ring electrode versus conventional rectangular pad. *Brain Stimulation* (2009) 2(4): 201–207.
- 34 Borckardt JJ et al. A Pilot Study of the Tolerability and Effects of High-Definition Transcranial Direct Current Stimulation (HD-tDCS) on Pain Perception. *The Journal of Pain* (2012) 13 (2): 112–120.
- 35 Kuo H et al. Comparing Cortical Plasticity Induced by Conventional and High-Definition 4 × 1 Ring tDCS: A Neurophysiological Study". *Brain Stimulation* (2013) 6 (4): 644–8.

## References

- 36 Nitsche MA et al. Level of action of cathodal DC polarisation induced inhibition of the human motor cortex. *Clinical Neurophysiology* (2003) 114(4): 600–604.
- 37 Nitsche MA, Liebetanz D, Antal A, et al. Modulation of cortical excitability by weak direct current stimulation—technical, safety and functional aspects. *Suppl Clin Neurophysiol* (2003) 56:255–276.
- 38 Poreisz C, Boros K, Antal A, et al. Safety aspects of transcranial direct current stimulation concerning healthy subjects and patients. *Brain Res Bull* (2007) 72:208–214.
- 39 Brunoni AR, Nitsche MA, Bolognini N, et al. Clinical research with transcranial direct current stimulation (tDCS): challenges and future directions. *Brain Stimul* (2012) 5:175–195
- 40 Stagg CJ, Nitsche MA. Physiological basis of transcranial direct current stimulation. *Neuroscientist* (2011) 17:37–53.
- 41 Ardolino G, Bossi B, Barbieri S, et al. Non-synaptic mechanisms underlie the after-effects of cathodal transcutaneous direct current stimulation of the human brain. *J Physiol* (2005) 568:653–63.
- 42 Bindman LJ, Lippold OC, Redfearn JW. Long-lasting changes in the level of the electrical activity of the cerebral cortex produced by polarizing currents. *Nature* (1962) 196:584–585.
- 43 Bindman LJ, Lippold OC, Redfearn JW. 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* (1964) 172:369–382.
- 44 Creutzfeldt OD, Fromm GH, Kapp H. Influence of transcortical d-c currents on cortical neuronal activity. *Exp Neurol* (1962) 5:436–452.
- 45 Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *J Physiol* (2000) 527:633–639.
- 46 Priori A. Brain polarization in humans: a reappraisal of an old tool for prolonged non-invasive modulation of brain excitability. *Clin Neurophysiol* (2003) 114: 589–595.
- 47 Priori A, Berardelli A, Rona S, et al. Polarization of the human motor cortex through the scalp. *Neuroreport* (1998) 9:2257–2260.
- 48 Purpura DP, McMurtry JG. Intracellular activities and evoked potential changes during polarization of motor cortex. *J Neurophysiol* (1965) 28:166–185.
- 49 Liebetanz D, Nitsche MA, Tergau F, et al. Pharmacological approach to the mechanisms of transcranial DC-stimulation-induced after-effects of human motor cortex excitability. *Brain* (2002) 125:2238–2247.
- 50 Nitsche MA, Fricke K, Henschke U, et al. Pharmacological modulation of cortical excitability shifts induced by transcranial direct current stimulation in humans. *J Physiol* (2003) 553:293–301.
- 51 Gartside IB. Mechanisms of sustained increases of firing rate of neurons in the rat cerebral cortex after polarization: reverberating circuits or modification of synaptic conductance? *Nature* (1968) 220:382–383.
- 52 Islam N, Aftabuddin M, Moriwaki A, et al. Increase in the calcium level following anodal polarization in the rat brain. *Brain Res* (1995) 684:206–208.
- 53 Trollinger DR, Isseroff RR, Nuccitelli R. Calcium channel blockers inhibit galvanotaxis in human keratinocytes. *J Cell Physiol* (2002) 193:1–9.
- 54 Titushkin I, Cho M. Regulation of cell cytoskeleton and membrane mechanics by electric field: role of linker proteins. *Biophys J* (2009) 96:717–728.
- 55 Merzagora AC, Foffani G, Panyavin I, et al. Prefrontal hemodynamic changes produced by anodal direct current stimulation. *Neuroimage* (2010) 49: 2304–2310.
- 56 Suzuki K, Fujiwara T, Tanaka N, et al. Comparison of the after-effects of transcranial direct current stimulation over the motor cortex in patients with stroke and healthy volunteers. *Int J Neurosci* (2012) 122:675–681.
- 57 Ambrus GG, Al-Moyed H, Chaieb L, et al. The fade-in—short stimulation—fade out approach to sham tDCS—reliable at 1 mA for naive and experienced subjects, but not investigators. *Brain Stimul* (2012) 10:134–138
- 58 Priori A, Hallett M, Rothwell JC. Repetitive transcranial magnetic stimulation or transcranial direct current stimulation? *Brain Stimul* (2009) 2:241–245.
- 59 Iyer MB, Mattu U, Grafman J, et al. Safety and cognitive effect of frontal DC brain polarization in healthy individuals. *Neurology* (2005) 64:872–875.
- 60 Bastani A, Jaberzadeh S. Does anodal transcranial direct current stimulation enhance excitability of the motor cortex and motor function in healthy individuals and subjects with stroke: a systematic review and meta-analysis. *Clin Neurophysiol* (2011) 123:644–657.
- 61 Fertonani A, Rosini S, Cotelli M, et al. Naming facilitation induced by transcranial direct current stimulation. *Behav Brain Res* (2010) 208:311–318.
- 62 de Vries MH, Barth AC, Maiworm S, et al. Electrical stimulation of Broca's area enhances implicit learning of an artificial grammar. *J Cogn Neurosci* (2010) 22:2427–2436.
- 63 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: 1745–1751.
- 64 Cattaneo Z, Pisoni A, Papagno C. Transcranial direct current stimulation over Broca's region improves phonemic and semantic fluency in healthy individuals. *Neuroscience* (2011) 183:64–70.
- 65 Holland R, Leff AP, Josephs O, et al. Speech facilitation by left inferior frontal cortex stimulation. *Curr Biol* (2011) 21:1403–1407.
- 66 Wirth M, Rahman RA, Kuenecke J, et al. Effects of transcranial direct current stimulation (tDCS) on behaviour and electrophysiology of language production. *Neuropsychologia* (2011) 49:3989–3998.
- 67 Sparing R, Dafotakis M, Meister IG, et al. Enhancing language performance with non-invasive brain stimulation—a transcranial direct current stimulation study in healthy humans. *Neuropsychologia* (2008) 46:261–268.
- 68 Floel A, Rosser N, Michka O, et al. Noninvasive brain stimulation improves language learning. *J Cogn Neurosci* (2008) 20:1415–1422.

## References

- 69 Fiori V, Coccia M, Marinelli CV, et al. Transcranial direct current stimulation improves word retrieval in healthy and non-fluent aphasic subjects. *J Cogn Neurosci* (2011) 23:2309–2323.
- 70 Galdo Alvarez S, Lindin Novo M, Diaz Fernandez F. Naming faces: a multidisciplinary and integrated review. *Psicothema* (2009) 21:521–527.
- 71 Ross LA, McCoy D, Wolk DA, et al. Improved proper name recall by electrical stimulation of the anterior temporal lobes. *Neuropsychologia* (2010) 48:3671–3674.
- 72 Monti A, Cogiamanian F, Marceglia S, et al. Improved naming after transcranial direct current stimulation in aphasia. *J Neurol Neurosurg Psychiatry* (2008) 79:451–453.
- 73 Lang N, Nitsche MA, Paulus W, et al. Effects of transcranial direct current stimulation over the human motor cortex on corticospinal and transcallosal excitability. *Exp Brain Res* (2004) 156:439–443.
- 74 Hesse S, Werner C, Schonhardt EM, et al. Combined transcranial direct current stimulation and robot-assisted arm training in subacute stroke patients: a pilot study. *Restor Neurol Neurosci* (2007) 25:9–15.
- 75 Baker JM, Rorden C, Fridriksson J. Using transcranial direct-current stimulation to treat stroke patients with aphasia. *Stroke* (2010) 41:1229–1236.
- 76 Marangolo P, Marinelli CV, Bonifazi S, et al. Electrical stimulation over the left inferior frontal gyrus (IFG) determines long-term effects in the recovery of speech apraxia in three chronic aphasics. *Behav Brain Res* (2011) 225:498–504.
- 77 Kang EK, Kim YK, Sohn HM, et al. Improved picture naming in aphasia patients treated with cathodal tDCS to inhibit the right Broca's homologue area. *Restor Neurol Neurosci* (2011) 29:141–152.
- 78 Vines BW, Norton AC, Schlaug G. Non-invasive brain stimulation enhances the effects of melodic intonation therapy. *Front Psychol* (2011) 2:230.
- 79 Jung IY, Lim JY, Kang EK, et al. The factors associated with good responses to speech therapy combined with transcranial direct current stimulation in post-stroke aphasic patients. *Ann Rehabil Med* (2011) 35:460–469.
- 80 Fridriksson J, Richardson JD, Baker JM, et al. Transcranial direct current stimulation improves naming reaction time in fluent aphasia: a double-blind, sham-controlled study. *Stroke* (2011) 42:819–821.
- 81 You DS, Kim DY, Chun MH, et al. Cathodal transcranial direct current stimulation of the right Wernicke's area improves comprehension in subacute stroke patients. *Brain Lang* (2011) 119:1–5.
- 82 Floel A, Meinzer M, Kirstein R, et al. Short-term anomia training and electrical brain stimulation. *Stroke* (2011) 42:2065–2067.
- 83 Holland R, Crinion J. Can tDCS enhance treatment of aphasia after stroke? *Aphasiology* (2012) 26:1169–1191.
- 84 Coffman BA, Trumbo MC, Flores RA, et al. Impact of tDCS on performance and learning of target detection: interaction with stimulus characteristics and experimental design. *Neuropsychologia* (2012) 50:1594–1602.
- 85 Zaehle T, Sandmann P, Thorne JD, et al. Transcranial direct current stimulation of the prefrontal cortex modulates working memory performance: combined behavioural and electrophysiological evidence. *BMC Neurosci* (2011) 12:2.
- 86 Loo CK, Alonzo A, Martin D, et al. Transcranial direct current stimulation for depression: 3-week, randomised, sham-controlled trial. *Br J Psychiatry* (2012) 200:52–59.