

### **HHS Public Access**

Author manuscript Ann Neurol. Author manuscript; available in PMC 2018 July 18.

Published in final edited form as:

Ann Neurol. 2016 July ; 80(1): 1-4. doi:10.1002/ana.24689.

### An Open Letter Concerning Do-It-Yourself Users of Transcranial Direct Current Stimulation

Rachel Wurzman, PhD<sup>1</sup>, Roy H. Hamilton, MD, MS<sup>2</sup>, Alvaro Pascual-Leone, MD, PhD<sup>3</sup>, and Michael D. Fox, MD, PhD<sup>3,4,5</sup>

<sup>1</sup>Department of Neurology, University of Pennsylvania, Philadelphia, PA

<sup>2</sup>Department of Neurology and Physical Medicine & Rehabilitation, University of Pennsylvania, Philadelphia, PA

<sup>3</sup>Department of Neurology, Beth Israel Deaconess Medical Center, Boston, MA

<sup>4</sup>Department of Neurology, Massachusetts General Hospital, Boston, MA

<sup>5</sup>Athinoula A. Martinos Center for Biomedical Imaging, Charlestown, MA

As clinicians and scientists who study noninvasive brain stimulation, we share a common interest with do-it-yourself (DIY) users, namely administering transcranial direct current stimulation (tDCS) to improve brain function. Evidence suggests that DIY users reference the scientific literature to guide their use of tDCS,<sup>1</sup> including published ethical and safety standards.<sup>2–4</sup> However, as discussed at a recent Institute of Medicine Workshop,<sup>5</sup> there is much about noninvasive brain stimulation in general, and tDCS in particular, that remains unknown. Whereas some risks, such as burns to the skin and complications resulting from electrical equipment failures, are well recognized,<sup>6–8</sup> other problematic issues may not be immediately apparent.<sup>9</sup> We perceive an ethical obligation to draw the attention of both professionals and DIY users to some of these issues.<sup>10</sup>

#### Stimulation affects more of the brain than a user may think

Electrodes are often placed in specific scalp locations to target specific brain regions. However, stimulation extends well beyond the regions beneath the electrodes. Current flows between electrodes in complex ways based on different tissues in the head, and can affect the function of various structures along its path.<sup>11–15</sup> Furthermore, the effects of tDCS can extend beyond brain regions directly affected by the stimulation to connected brain regions and networks.<sup>16–20</sup> These indirect effects of stimulation on connected brain networks may alter brain functions that are unintended. In other words, brain connectivity has an effect on —and can be affected by—brain stimulation.<sup>21–23</sup>

Address correspondence to Dr. Fox at foxmdphd@gmail.com.

**Potential Conflicts of Interest** 

M.D.F. and A.P.-L. share intellectual property with Neuroelectrics, a tDCS device manufacturer. A.P.-L. serves on the scientific advisory board of Neuroelectrics.

## Stimulation interacts with ongoing brain activity, so what a user does during tDCS changes tDCS effects

Brain stimulation with tDCS has a different effect on neurons that are active during the time of stimulation compared to neurons that are not.<sup>24,25</sup> Because of this feature, the cognitive or behavioral activity occurring while tDCS is applied will modify the effects.<sup>26–29</sup> Stimulation while reading a book, meditating, visually fixating on a point, watching TV, doing arithmetic, sleeping, or playing video games could all cause different changes in the brain. Even activity occurring before tDCS or the time of day tDCS is administered may change the effects of stimulation. Which activity or time of day is best to achieve a certain change in brain function is not yet known.

#### Enhancement of some cognitive abilities may come at the cost of others

Cognition involves functional networks, with different components (or combinations thereof) responsible for different functions. In addition, brain networks interact with each other, such that modifying activity in one network can change the activity in other networks. Therefore, stimulating one brain area may improve the ability to perform one task but hurt the ability to perform another. For example, tDCS can enhance the rate of learning new material, but at the cost of processing learned material, and vice versa, depending on the stimulation site.<sup>30</sup> Such tradeoffs are likely under-recognized, as most tDCS studies focus on only one or two tasks. Furthermore, such cognitive tradeoffs could develop over time and only become recognizable long after the stimulation.

## Changes in brain activity (intended or not) may last longer than a user may think

Brain plasticity is an ongoing process that is in part driven by neural activity itself, so changes initiated during stimulation can be long lasting and even self-perpetuating. Cognitive enhancements (as well as concurrent tradeoffs) have been reported 6 months after stimulation, and may linger beyond then.<sup>30–32</sup> Ongoing regular application of tDCS may be especially effective for sustaining these benefits, but may also increase risks. We have never formally studied tDCS at the frequencies many DIY users experiment with—for example, stimulating daily for months or longer. Because we know that stimulation from just a few sessions can be quite lasting,<sup>31</sup> we infer that changes induced by these protocols may be even more so. We do not know yet whether such changes are reversible, and the possible risks of a cumulative dose over years or a lifetime have not been studied.

#### Small differences in tDCS parameters can have a big effect

Mild changes in tDCS settings including current amplitude, stimulation duration, and electrode placement can have big and unexpected effects. For example, increasing the stimulation amplitude from 1 to 2mA or increasing the duration from 10 to 20 minutes might be expected to double the effect, but can actually reverse the effect and cause the opposite change in brain function.<sup>33</sup> More stimulation is not necessarily better; more is simply

different. Similarly, slight differences in electrode placement can produce dramatic shifts in the shape of the current path, and thus the neurophysiological effects.<sup>34–36</sup>

#### tDCS effects are highly variable across different people

Results reported in the scientific literature are almost always averaged across groups of subjects because the effect of tDCS on any one individual is variable and unpredictable.<sup>37,38</sup> Even across groups of subjects, tDCS effects can be highly variable. Up to 30% of experimental subjects respond with changes in cortical excitability in the opposite direction from other subjects using identical tDCS settings. Even with consistent changes in cortical excitability, these changes can have different effects on individuals' ability to perform a task, <sup>37</sup> including potentially undesirable effects.<sup>39</sup> Furthermore, this variability occurs despite controlled experimental conditions designed to reduce it. Factors such as age,<sup>40,41</sup> gender,<sup>42</sup> hormones,<sup>43</sup> handedness,<sup>44,45</sup> cognitive ability,<sup>46,47</sup> neurological or psychiatric disorders, medications,<sup>48,49</sup> recreational drugs,<sup>50</sup> neurotransmitter levels,<sup>49</sup> prior exposure to brain stimulation,<sup>51</sup> and differences in head anatomy<sup>12,36,52,53</sup> are likely to impact and could potentially even reverse a given tDCS effect.

# The risk/benefit ratio is different for treating diseases versus enhancing function

Despite all the above uncertainty, risks, tradeoffs, and potential detrimental effects of tDCS, there are numerous studies that administer repeated sessions of tDCS with the intent of causing lasting changes in brain function. However, nearly all such studies are performed in patients with brain disease, with the goal of alleviating symptoms. Such studies provide detailed disclosure of risks, according to regulations for informed consent of human research subjects, and risks are evaluated for the patient population to be studied. Consider that the level of acceptable risk is different for healthy subjects, who in general are functioning quite well and thus have less to gain, and more to lose. Application of tDCS in children warrants special consideration given the particularities of the developing nervous system, the scarcity of studies in this population, and that minors are not fully able to assess the risks of tDCS for themselves.

In sum, it is important to know that: (1) the tissue stimulated and effects induced are less deterministic than a user may think, (2) significant tradeoffs may be part of the bargain for functional gains, and (3) whatever brain changes occur may be long-lasting—for better or worse. We encourage consideration of these issues and involvement of health care providers in making decisions regarding DIY brain stimulation.

#### Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

#### Acknowledgments

We thank the many tDCS experts with whom we discussed these matters. The names and affiliations of 39 colleagues who have endorsed the content of this letter are included in the Supplementary Table.

Ann Neurol. Author manuscript; available in PMC 2018 July 18.

#### References

- 1. Wexler A. The practices of do-it-yourself brain stimulation: implications for ethical considerations and regulatory proposals. J Med Ethics. 2016; 42:211–215. [PubMed: 26324456]
- 2. Davis NJ, van Koningsbruggen MG. "Non-invasive" brain stimulation is not non-invasive. Front Syst Neurosci. 2013; 7:76. [PubMed: 24391554]
- Nitsche MA, Liebetanz D, Lang N, et al. Safety criteria for transcranial direct current stimulation (tDCS) in humans. Clin Neurophysiol. 2003; 114:2220–2222. author reply 2222–2223. [PubMed: 14580622]
- Cabrera LY, Evans EL, Hamilton RH. Ethics of the electrified mind: defining issues and perspectives on the principled use of brain stimulation in medical research and clinical care. Brain Topogr. 2014; 27:33–45. [PubMed: 23733209]
- Bain L, Posey Norris S, , Stroud C, editorsInstitute of MedicineNon-invasive neuromodulation of the central nervous system: opportunities and challenges: workshop summary Washington, DC: National Academies Press; 2015
- Frank E, Wilfurth S, Landgrebe M, et al. Anodal skin lesions after treatment with transcranial direct current stimulation. Brain Stimul. 2010; 3:58–59. [PubMed: 20633432]
- Loo CK, Martin DM, Alonzo A, et al. Avoiding skin burns with transcranial direct current stimulation: preliminary considerations. Int J Neuropsychopharmacol. 2011; 14:425–426. [PubMed: 20923600]
- Shiozawa P, da Silva ME, Raza R, et al. Safety of repeated transcranial direct current stimulation in impaired skin: a case report. J ECT. 2013; 29:147–148. [PubMed: 23303424]
- International Federation of Neurophysiology. [Accessed March 14, 2016] Transcranial electric stimulation in do-it-yourself applications 2015 Available at: http://www.ifcn.info/uploadfiles/ documents/2015/Using\_tES\_devices\_as\_DIY\_FINAL\_13Dec15.pdf
- Fitz NS, Reiner PB. The challenge of crafting policy for do-it-yourself brain stimulation. J Med Ethics. 2015; 41:410–412. [PubMed: 23733050]
- Datta A, Bansal V, Diaz J, et al. Gyri-precise head model of transcranial direct current stimulation: improved spatial focality using a ring electrode versus conventional rectangular pad. Brain Stimul. 2009; 2(4):201–207. 207.e1. [PubMed: 20648973]
- Datta A, Truong D, Minhas P, et al. Inter-individual variation during transcranial direct current stimulation and normalization of dose using MRI-derived computational models. Front Psychiatry. 2012; 3:91. [PubMed: 23097644]
- Ruffini G, Fox MD, Ripolles O, et al. Optimization of multifocal transcranial current stimulation for weighted cortical pattern targeting from realistic modeling of electric fields. Neuroimage. 2014; 89:216–225. [PubMed: 24345389]
- 14. Wagner T, Fregni F, Fecteau S, et al. Transcranial direct current stimulation: a computer-based human model study. Neuroimage. 2007; 35:1113–1124. [PubMed: 17337213]
- Ruffini G, Wendling F, Merlet I, et al. Transcranial current brain stimulation (tCS): models and technologies. IEEE Trans Neural Syst Rehabil Eng. 2013; 21:333–345. [PubMed: 22949089]
- Ardolino G, Bossi B, Barbieri S, Priori A. Non-synaptic mechanisms underlie the after-effects of cathodal transcutaneous direct current stimulation of the human brain. J Physiol. 2005; 568(pt 2): 653–663. [PubMed: 16037080]
- 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. [PubMed: 22037126]
- Frohlich F, McCormick DA. Endogenous electric fields may guide neocortical network activity. Neuron. 2010; 67:129–143. [PubMed: 20624597]
- Parra LC, Bikson M. Model of the effect of extracellular fields on spike time coherence. Conf Proc IEEE Eng Med Biol Soc. 2004; 6:4584–4587. [PubMed: 17271327]
- Reato D, Rahman A, Bikson M, Parra LC. Low-intensity electrical stimulation affects network dynamics by modulating population rate and spike timing. J Neurosci. 2010; 30:15067–15079. [PubMed: 21068312]

Ann Neurol. Author manuscript; available in PMC 2018 July 18.

- Boros K, Poreisz C, Munchau A, et al. Premotor transcranial direct current stimulation (tDCS) affects primary motor excitability in humans. Eur J Neurosci. 2008; 27:1292–1300. [PubMed: 18312584]
- Keeser D, Meindl T, Bor J, et al. Prefrontal transcranial direct current stimulation changes connectivity of resting-state networks during fMRI. J Neurosci. 2011; 31:15284–15293. [PubMed: 22031874]
- Lang N, Siebner HR, Ward NS, et al. How does transcranial DC stimulation of the primary motor cortex alter regional neuronal activity in the human brain? Eur J Neurosci. 2005; 22:495–504. [PubMed: 16045502]
- Stagg CJ, Nitsche MA. Physiological basis of transcranial direct current stimulation. Neuroscientist. 2011; 17:37–53. [PubMed: 21343407]
- 25. Bikson M, Rahman A. Origins of specificity during tDCS: anatomical, activity-selective, and input-bias mechanisms. Front Hum Neurosci. 2013; 7:688. [PubMed: 24155708]
- Andrews SC, Hoy KE, Enticott PG, et al. Improving working memory: the effect of combining cognitive activity and anodal transcranial direct current stimulation to the left dorsolateral prefrontal cortex. Brain Stimul. 2011; 4:84–89. [PubMed: 21511208]
- Bortoletto M, Pellicciari MC, Rodella C, Miniussi C. The interaction with task-induced activity is more important than polarization: a tDCS study. Brain Stimul. 2015; 8:269–276. [PubMed: 25464828]
- Gill J, Shah-Basak PP, Hamilton R. It's the thought that counts: examining the task-dependent effects of transcranial direct current stimulation on executive function. Brain Stimul. 2015; 8:253– 259. [PubMed: 25465291]
- Learmonth G, Thut G, Benwell CSY, Harvey M. The implications of state-dependent tDCS effects in aging: behavioural response is determined by baseline performance. Neuropsychologia. 2015; 74:108–119. [PubMed: 25637226]
- Iuculano T, Cohen Kadosh R. The mental cost of cognitive enhancement. J Neurosci. 2013; 33:4482–4486. [PubMed: 23467363]
- Cohen Kadosh R, Soskic S, Iuculano T, et al. Modulating neuronal activity produces specific and long-lasting changes in numerical competence. Curr Biol. 2010; 20:2016–2020. [PubMed: 21055945]
- 32. Snowball A, Tachtsidis I, Popescu T, et al. Long-term enhancement of brain function and cognition using cognitive training and brain stimulation. Curr Biol. 2013; 23:987–992. [PubMed: 23684971]
- Batsikadze G, Moliadze V, Paulus W, et al. Partially non-linear stimulation intensity-dependent effects of direct current stimulation on motor cortex excitability in humans. J Physiol. 2013; 591(pt 7):1987–2000. [PubMed: 23339180]
- Moliadze V, Antal A, Paulus W. Electrode-distance dependent after-effects of transcranial direct and random noise stimulation with extracephalic reference electrodes. Clin Neurophysiol. 2010; 121:2165–2171. [PubMed: 20554472]
- Nitsche MA, Doemkes S, Karakose T, et al. Shaping the effects of transcranial direct current stimulation of the human motor cortex. J Neurophysiol. 2007; 97:3109–3117. [PubMed: 17251360]
- 36. Opitz A, Paulus W, Will S, et al. Determinants of the electric field during transcranial direct current stimulation. Neuroimage. 2015; 109:140–150. [PubMed: 25613437]
- Krause B, Cohen Kadosh R. Not all brains are created equal: the relevance of individual differences in responsiveness to transcranial electrical stimulation. Front Syst Neurosci. 2014; 8:25. [PubMed: 24605090]
- López-Alonso V, Cheeran B, Río-Rodríguez D, Fernández-DelOlmo M. Inter-individual variability in response to non-invasive brain stimulation paradigms. Brain Stimul. 2014; 7:372–380. [PubMed: 24630849]
- 39. Steenbergen L, Sellaro R, Hommel B, et al. "Unfocus" on foc.us: commercial tDCS headset impairs working memory. Exp Brain Res. 2016; 234:637–643. [PubMed: 26280313]
- 40. Fujiyama H, Hyde J, Hinder MR, et al. Delayed plastic responses to anodal tDCS in older adults. Front Aging Neurosci. 2014; 6:115. [PubMed: 24936185]

Wurzman et al.

- Moliadze V, Schmanke T, Andreas S, et al. Stimulation intensities of transcranial direct current stimulation have to be adjusted in children and adolescents. Clin Neurophysiol. 2015; 126:1392– 1399. [PubMed: 25468234]
- 42. Meiron O, Lavidor M. Unilateral prefrontal direct current stimulation effects are modulated by working memory load and gender. Brain Stimul. 2013; 6:440–447. [PubMed: 22743075]
- 43. Smith MJ, Keel JC, Greenberg BD, et al. Menstrual cycle effects on cortical excitability. Neurology. 1999; 53:2069–2072. [PubMed: 10599783]
- 44. Schade S, Moliadze V, Paulus W, Antal A. Modulating neuronal excitability in the motor cortex with tDCS shows moderate hemispheric asymmetry due to subjects' handedness: a pilot study. Restor Neurol Neurosci. 2012; 30:191–198. [PubMed: 22377833]
- Shiozawa P, da Silva ME, Cordeiro Q. Transcranial direct current stimulation for treating depression in a patient with right hemispheric dominance: a case study. J ECT. 2015; 31:201–202. [PubMed: 25203287]
- Furuya S, Klaus M, Nitsche MA, et al. Ceiling effects prevent further improvement of transcranial stimulation in skilled musicians. J Neurosci. 2014; 34:13834–13839. [PubMed: 25297109]
- 47. Sarkar A, Dowker A, Kadosh RC. Cognitive enhancement or cognitive cost: trait-specific outcomes of brain stimulation in the case of mathematics anxiety. J Neurosci. 2014; 34:16605–16610.
  [PubMed: 25505313]
- Brunoni AR, Ferrucci R, Bortolomasi M, et al. Interactions between transcranial direct current stimulation (tDCS) and pharmacological interventions in the major depressive episode: findings from a naturalistic study. Eur Psychiatry. 2013; 28:356–361. [PubMed: 23182847]
- 49. Nitsche MA, Kuo M-F, Karrasch R, et al. Serotonin affects transcranial direct current-induced neuroplasticity in humans. Biol Psychiatry. 2009; 66:503–508. [PubMed: 19427633]
- Boggio PS, Zaghi S, Villani AB, et al. Modulation of risk-taking in marijuana users by transcranial direct current stimulation (tDCS) of the dorsolateral prefrontal cortex (DLPFC). Drug Alcohol Depend. 2010; 112:220–225. [PubMed: 20729009]
- Alonzo A, Brassil J, Taylor JL, et al. Daily transcranial direct current stimulation (tDCS) leads to greater increases in cortical excitability than second daily transcranial direct current stimulation. Brain Stimul. 2012; 5:208–213. [PubMed: 22037139]
- Truong DQ, Magerowski G, Blackburn GL, et al. Computational modeling of transcranial direct current stimulation (tDCS) in obesity: impact of head fat and dose guidelines. Neuroimage Clin. 2013; 2:759–766. [PubMed: 24159560]
- Datta A, Bikson M, Fregni F. Transcranial direct current stimulation in patients with skull defects and skull plates: high-resolution computational FEM study of factors altering cortical current flow. Neuroimage. 2010; 52:1268–1278. [PubMed: 20435146]