CHAPTER

3

The Perils of Using Electrical Stimulation to Change Human Brains

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THE UNIQUE TOOL

The modern visage of transcranial direct current stimulation (tDCS), born anew in the scientific community, has electrified the cognitive enhancement scene. At this nascent stage, this simple yet elegant technique has been shown to be relatively safe in the laboratory, rather effective in certain domains, and reasonably inexpensive to obtain and operate. Though the exact mechanisms are formally unknown, tDCS is thought to modify the excitability of neuronal membranes (depending on the polarity and montage of the electrodes), thereby facilitating or reducing plasticity in response to endogenous neural activity. The technique is often described as non-invasive, as the devices work by sending modest currents (~1–2 mA) from the outside of the head to the brain through saline-soaked pads. Today, tDCS generates excitement as: (1) a unique investigative tool in clinical and cognitive neuroscience, (2) a budding treatment for various neurologic and psychiatric conditions, and (3) a would-be cognitive enhancer for "normal," healthy adults and children.

It is natural to be excited about the possible applications for tDCS, in particular as the technique holds great promise for advancing our understanding of the normal function of the human brain as well as opening the door to novel treatments for disease (Nitsche et al., 2008; Stagg & Nitsche, 2011). If tDCS does indeed prove to be as effective as those treatments available via pharmacology, it may well change the modern practices of neurology and psychiatry, especially if it is safer and less expensive than the current standard of care. tDCS might even bridge new ethical terrain: a potential cognitive enhancer that by virtue of its simplicity and modest cost *promotes* fair distribution in society (Cohen Kadosh, Levy, O'Shea, Shea, & Savulescu, 2012). This is quite novel considering that distributive justice, the fair allocation of benefits (and burdens), is often among the most salient concerns in the debate over the propriety of cognitive enhancement, particularly in the face of growing achievement, economic, and social disparity (Murray, 2012; Stiglitz, 2012). Not only are tDCS devices inexpensive, but they are also relatively simple to operate[1], which marks them as a useful tool in areas that lack the requisite financial and technical resources for more advanced treatment (Pascal-Leone, Fregni, Steven-Wheeler, & Forrow, 2011).

Given its potential, investigators have explored tDCS for: motor learning (Boros, Poreisz, Münchau, Paulus, & Nitsche, 2008; Nitsche, Fricke, et al., 2003; Nitsche et al., 2007; Reis et al., 2008), numerical ability (Cohen Kadosh, Soskic, Iuculano, Kanai, & Walsh, 2010), episodic memory (Penolazzi et al., 2010), working memory (Fregni et al., 2005; Ohn et al., 2008), motor memory (Galea & Celnik, 2009), sleep-dependent consolidation of declarative memory (Marshall, 2004), learning and memory writ large (Brasil-Neto, 2012), attention (Coffman, Trumbo, & Clark, 2012), decision-making and risk (Coricelli & Rusconi, 2011; Fecteau et al., 2007), planning ability (Dockery, Hueckel-Weng, Birbaumer, & Plewnia, 2009), complex and creative problem-solving (Cerruti & Schlaug, 2009; Chi & Snyder 2012; Snyder, 2009), grammar (de Vries et al., 2010; Floel, Rösser, Michka, Knecht, & Breitenstein, 2008), object naming (Fertonani, Rosini, Cotelli, Rossini, & Miniussi, 2010; Sparing, Dafotakis, & Meister 2008), word retrieval (Fiori et al., 2011), verbal fluency (Iyer et al., 2005), reading efficiency (Turkeltaub et al., 2011), lying (Mameli et al., 2010; Priori et al., 2007), and the likelihood of utilitarian judgments (Fumagalli et al., 2010), to name but the most prominent applications of this exciting technique.

DIY ENHANCEMENT WITH tDCS

The very same qualities that constitute the egalitarian promise of tDCS – its efficacy and access – simultaneously give rise to its peril: the potential for long-lasting, and potentially irreversible, changes in the DIY home experimenter community. We encourage the thoughtful use of tDCS by professionals in the laboratory and clinic, and regulatory preparation for the potentially significant usage by *the public* at large. The scientific and popular interest in tDCS has kindled a fire: the rapidly increasing presence of tDCS in both the peer-reviewed literature and the popular press is contributing to the increase of DIY tDCS.

The emerging epistemic setting of tDCS might best be understood by considering the inception of functional magnetic resonance imaging (fMRI) in the latter half of the 20th century. While the introduction of magnetic resonance imaging itself had already substantially changed the medical diagnostic landscape, it was not until the 1990s that fMRI emerged as a powerful tool for brain mapping in living humans (Illes & Sahakian, 2011). Today, fMRI wields much explanatory power for public(s) of all stripes (Racine, Bar-Ilan, & Illes, 2005), and the scientific community has left very few experimental stones unturned in classical fMRI investigations. In much the same way as fMRI is a technique for observing the neural activity in behaving humans, tDCS is a technique for manipulating the neural activity of living people. Given the versatility of tDCS, it is reasonable to predict that it will similarly be used as an "uncover everything" investigational tool. The deep fascination with fMRI stems not only from its versatility but also from the putative ability to directly *see* the human mind, further bolstered by the visually arresting pseudocolor images (Dumit, 2004). While tDCS lacks the seductive allure of imaging, the seemingly endless potential to manipulate the human mind represents the opposite side of the fMRI coin.

The excitement bespeaks responsibility: without proper regulatory review, it will prove difficult to balance both the enthusiasms and safety of the public.

As a part of the broader conversation on human enhancement, tDCS raises many of the same concerns – for example, safety, peer pressure, distributive justice, authenticity, medicalization, and more (Bostrom & Sandberg, 2009; Chatterjee, 2004; Conrad, 2007; Degrazia, 2005; Farah et al., 2004; Forlini & Racine, 2009; Greely et al., 2008; Hyman, 2011; Reiner, 2010; Turner & Sahakian, 2006) – seen in the debate over pharmacological cognitive enhancement (PCE). However, the ethical implications of tDCS differ from those of PCE in important ways (Cohen Kadosh et al., 2012; Hamilton, Messing, & Chatterjee, 2011), and, in our view, among the most important of these is DIY enhancement with tDCS. Notably, interest in cognitive enhancement has not engendered any substantial DIY ethos toward PCEs. While there has been concern surrounding the sale of PCEs from those with prescriptions to those without prescriptions (DeSantis, Webb, & Noar, 2008; McCabe, Knight, Teter, & Wechsler, 2005; Vidourek, King, & Knopf, 2010), there has never been a real worry about "home brewing" PCEs. Moreover, and contrary to popular thought, existing PCEs are only modestly successful at enhancing cognitive skills (Greely, 2010; Ilieva, Boland, & Farah, 2012; Smith & Farah, 2011). Already, brain stimulation technologies might be more effective (Cohen Kadosh et al., 2010; Floel et al., 2008; Marshall, 2004; Ukueberuwa & Wassermann, 2010) – and less value-laden or stigmatized (Forlini & Racine, 2011; Franke, Lieb, & Hildt, 2012; Heinrichs, 2012; Outram, 2012; Pillow, Naylor, & Malone, 2012) – than PCEs we might develop in the near future. To be sure, self-medication of individuals using drugs such as methylphenidate intended for the treatment of ADHD without the requisite prescription is, in some ways, akin to DIY tDCS: both scenarios feature an untutored individual making a decision about changing his or her brain using technology without the supervision of a medical professional. The key difference lies in the scope of individual power to manipulate the technology itself. In the case of PCE, prospective users have only the most basic morphological freedom: to take, or not take, the pill. While tDCS might be safer *prima facie*, the mounting concern stems from the unchecked morphological freedom of an uninformed public to modulate polarity, current intensity, stimulation duration and frequency, and electrode size and placement, as well as alterations in endogenous neural activity or employing the technique upon a background of neuroactive pharmaceuticals. In this analysis, we assess the unique, unprecedented, and potentially widespread rise of the DIY world.

FROM BENCH TO HOME: THE GOOD, THE BAD, AND THE UGLY

The first waves of results with respect to therapy and enhancement using tDCS are quite encouraging. The potential of a minimally invasive, non-pharmacological approach is rather exciting, and more research is in the pipeline. In terms of explicit physical side effects in the short term, tDCS appears to be remarkably safe: adverse effects, if reported at all (Brunoni et al., 2011), tend to include mild headache and irritation of the skin under the electrodes (Arul-Anandam, Loo, & Sachdev, 2009; Tadini et al., 2011). Nitsche et al. originally developed what has become the standard of safety criteria for the field, eruditely summarizing safety thresholds for relevant parameters (Nitsche, Liebetanz, et al., 2003). Given their careful awareness of inducing long-term effects, admittedly necessary for possible clinical application, they conclude with a call for more research on safety (Nitsche, Liebetanz, et al., 2003).

Bikson et al. update the safety limits for tDCS, opining that "it is neither accurate nor prudent to determine quantitative safety standards for tDCS from these [existing] reports," and conclude with a call for further research (Bikson, Datta, & Elwassif, 2009). In the same edition of *Clinical Neurophysiology*, an oft-cited experiment appeared that explored the level of current density necessary for inducing overt damage to brain tissue: 142.9 A/m^2 for durations greater than 10 minutes (Liebetanz et al., 2009). Given that researchers employ significantly less current density – usually between 0.029 and 0.08 mA/m^2 (Nitsche et al., 2008) – this study is suitable for ameliorating tissue damage concerns in the laboratory, and sets a useful parameter for future research. However, there may yet be concern in the DIY world about the likelihood of inducing brain damage as users will undoubtedly modify much of the protocol, in particular by manipulating current density, total charge, stimulation duration, electrode location, drug–device interaction, handedness (including some lateralized function), and more. In ensuring the safety of *the public*, we focus on *plausible* scenarios detailing the neurobiological sequelae of using tDCS. Though it is still early days in the development of guidelines for tDCS, we do not currently possess strong data that might inform situations such as these that are likely to arise if and when the public embraces this technology. Today, almost a decade after Nitsche et al.'s safety criteria, most of the literature continues to include a quick caveat on the lack of longitudinal work and/or the possibility of unsuspected side effects (Cohen Kadosh et al., 2012; Hamilton et al., 2011; Utz, Dimova, Oppenländer, & Kerkhoff, 2010). As we detail below, there is an urgent need to investigate these questions now.

To be quite clear, the current discourse on safety is openly intended for the experimental or clinical setting, and is not meant to assess potential safety concerns for the growing demographic of individuals in the DIY sphere. While tDCS seems safe *prima facie* (Nitsche, Liebetanz, et al., 2003), certain aspects of the technology raise legitimate concerns that would be relevant for the DIY demographic: the current data (and prevailing ethos) regarding the safety of tDCS are gleaned from a nascent body of literature that (1) was conducted in the laboratory, not in the field, (2) offers no longitudinal perspective as of yet, (3) contains issues in properly blinding experiments (O'Connell et al., 2012), and (4) appears to show rather malleable effects (from polarity, electrode montage, or stimulation duration). The vast majority of researchers in the field are aware of these concerns as they move forward in their exciting tDCS investigations, but the lay public remains in the dark.

THE POTENTIAL ROOTS OF UNINTENDED CHANGE

Of primary concern is the potential abuse of the technology beyond the purview of the experimental world – a possibility all the more likely without proper supervision and education in best practices. Many have quickly embraced tDCS technology as perfectly safe, quite effective, operationally flexible, and capable of instantiating long-lasting changes in the brain (Cohen Kadosh et al., 2010). For most, the enthusiasm is purely evidence-based, while the eagerness of others arises from biopolitical or financial interest. Indeed, its potential is certainly exciting; we simply advocate thoughtful reflection in light of some important concerns. Taken individually, the claims about tDCS – that it is safe, effective, and long lasting – are certainly data driven. Yet ethical analysis is often tasked with parsing the aggregate effect(s) whilst navigating the slippery slope of incrementalist findings. Although proponents tout tDCS as extremely safe, even the most ardent advocates would not claim that it is unequivocally safe. Adopting an approach that includes humility – recognizing that we understand a great deal about the structure and function of the brain, but we still have even more to learn – will prove indispensable in averting unexpected, unwanted, and perhaps even enduring changes in brains.

Reversing Polarity Can Impair Function

By simply reversing the polarity (from anodal to cathodal or *vice versa*) of tDCS stimulation, one may sometimes impair the targeted function, as the direction of neuronal excitability depends upon – among other factors – polarity (Nitsche, Liebetanz, et al., 2003). In one widely discussed paper on tDCS in enhancing cognitive ability, it was found that left cathodal stimulation caused better performance in numerical tasks while the opposite configuration "led to underperformance, comparable to that observed in young children" (Cohen Kadosh et al., 2010). In verbal testing, anodal tDCS led to better accuracy and speed while cathodal tDCS led to significantly worse performance on those measures (Javadi, Cheng, & Walsh, 2012), and authors have found that stimulation leads to "enhancement or impairment of verbal memorization depending on the polarity of the stimulation" (Javadi & Cheng, 2012; Javadi & Walsh, 2012). In some cases, reversing the polarity appears to affect only certain groups of individuals, e.g., women (Fumagalli et al., 2010), and in other cases, cathodal stimulation unexpectedly leads to better performance (Antal et al., 2004; Dockery et al., 2009).

Building on earlier literature suggesting that TMS over the DLPFC affects decision-making (Knoch, Gianotti, et al., 2006; Knoch, Schneider, Schunk, Hohmann, & Fehr, 2009; Knoch, Pascual-Leone, Meyer, Treyer, & Fehr, 2006; van 't Wout, Kahn, Sanfey, & Aleman, 2005), Fecteau et al. investigated the effects of tDCS over the DLFPC on decision-making in healthy participants (Fecteau et al., 2007). The results quite cleanly reveal the possibility of impairment due simply to the specific polarity configuration: in comparison to the sham group, those receiving anodal stimulation over the right DLPFC chose safe prospects more often, were faster to make that choice, and were not nearly as influenced by the magnitude of the reward. Participants receiving the opposite polarity configuration (anodal stimulation over left DLPFC; cathodal stimulation over right DLPFC) did not differ in their choice of risk, but were significantly slower to come to their decision. Research of this ilk elucidates the capability of tDCS to impair higher-order judgment. In a recent meta-analysis, this trend appears most commonly in motor functions and less commonly in cognitive functions (Jacobson, Koslowsky, & Lavidor, 2012). In an exhaustive review, by the authors, of the effects of tDCS stimulation parameters upon enhancement and impairment, we found numerous studies that either did not follow up with the impaired (or just non-enhanced) group or did not run an opposite-polarity configuration. To be clear, reversing polarity does not necessarily modify the effect (Antal, Terney, Poreisz, & Paulus, 2007; Boggio et al., 2007). In some instances it has shown to have no effect, or, at least, no effect on the *specific domain that was measured* – (see "The Underappreciated Peril," below).

Electrode Placement is Important

The specific placement of electrodes affects different brain regions in different ways – positioning is "of crucial significance for the spatial distribution and direction of the flow of current which together determine the effectiveness of the stimulation" (Utz et al., 2010; see also Chapter 4). This simple notion is essential in considering the use of tDCS by an uninformed lay public. The two early flag-carrying investigations of tDCS in modern investigations reveal the malleable nature of its effects. Priori et al. used a weak direct current (less than 0.5 mA for 7 s) to explore changes in motor evoked potentials (MEP) from TMS, and found that anodal stimulation significantly *depressed* the excitability of the motor cortex (Priori, Berardelli, Rona, Accornero, & Manfredi, 1998). Nitsche and Paulus found that anodal stimulation *enhanced* excitability of the motor cortex whereas cathodal stimulation diminished excitability (again, measured by MEP during TMS) (Nitsche & Paulus, 2000). Traditionally considered irrelevant, the only salient difference between the two experiments, aside from the current level, was the placement of the *reference* electrode (under the chin in the former, and over the contralateral supraorbital in the latter). At the very least, this exemplar illuminates the unknown function of underlying neurophysiological mechanisms active in tDCS.

Most tDCS studies so far show positive effects of anodal stimulation on the left DLPFC for working memory (Brasil-Neto, 2012). This effect may not occur, or may even be reversed, with different electrode montages, such as bilateral anodal prefrontal stimulation (Marshall, Mölle, Siebner, & Born, 2005) or use of a non-cephalic cathode (Ferrucci et al., 2008). We do know that the location of electrodes affects how – and through which neural networks – current travels in the brain, but "little is known about the practical consequences of this for therapy" (Rothwell, 2012).

For an example of import of electrode placement in practice, consider handedness. Most study participant pools select for right-handedness, given that left-handed participants may have lateralized brain function. Of course, not everyone in the world is right handed, and tDCS may differentially activate neural networks in those that have partially lateralized function. Underscoring this point, experimenters have demonstrated that the modulating effects of tDCS on excitability differ moderately in the left- and mixed-handed population compared to right-handed subjects, and that this needs to be taken into account in future work (Schade, Moliadze, Paulus, & Antal, 2012). How this will affect those left-handed experimenters in the DIY world who are stimulating using protocols created for right-handed laboratory participants and not mapping their brains to account for any lateralization is unknown.

Brain Stimulation Interacts with Pharmacology

When changing the brain with tDCS, there is a very real potential for interaction effects with neuroactive pharmaceuticals. It is already established that certain medications modulate the effects of tDCS, "such as neuroleptic and antiepileptic drugs, antidepressants, benzodiazepines and L-Dopa" (Utz et al., 2010), and other studies have shown that in the presence of several different psychoactive drugs the specific polarity montage results in unexpected (and often opposite) function than that observed in healthy subjects (Kuo, Paulus, & Nitsche, 2008; Kuo, Datta, Bikson, Paulus, & Kuo 2013; Liebetanz, Nitsche, Tergau, & Paulus, 2002; Nardone et al., 2012; Nitsche, Schauenburg, et al., 2003; Nitsche et al., 2006). These observations are instructive, but the extent of such interactions with the wide array of prescription medications that modify brain function is unknown. At a minimum, the existing data suggest that the underlying pharmacological status of the brain may have an impact on the specific effects of tDCS.

Not only are there concerns with respect to prescription medications; there is also the possibility that the effects of tDCS interact with non-prescription drugs that are in wide use in the population. For example, nicotine usage can modulate excitability caused by tDCS (Grundey et al., 2012). In a study of the effects of tDCS in chronic users of marijuana (the most widely used illicit substance in the world, with 125–203 million users [Degenhardt & Hall, 2012]) investigators found that: (1) chronic marijuana users demonstrated more conservative decision-making than the normal population (comparing the sham stimulation groups), (2) while right anodal stimulation of the DLPFC enhanced conservative decision-making in healthy volunteers, both right anodal and left anodal DLPFC stimulation *increased* the propensity for risk-taking in marijuana users, and (3) right anodal/left cathodal tDCS of DLPFC is significantly associated with a diminished craving for marijuana (Boggio et al., 2010). While many research laboratories exclude individuals who have used recreational drugs in the past 24 hours (Roi Cohen Kadosh, personal communication), much more research on these interactions is needed. In particular, given the likelihood that the DIY crowd includes individuals who use psychoactive agents, it seems important to communicate these findings to the public.

Long-Lasting Changes

One of the key unknowns in the use of tDCS is the duration of the evoked changes. In their safety guidelines for the field, Nitsche, Liebetanz, et al., (2003) warn against stimulation durations that would result in excitability changes of more than an hour as excitability changes lasting for that long "could be dysfunctional." Indeed, studies have shown that the timing and duration of a tDCS session can lead to effects lasting up to several months (Cohen Kadosh et al., 2010; Dockery et al., 2009; John, 2012; Monte-Silva, Kuo, Liebetanz, Paulus, & Nitsche, 2010; Nitsche, Liebetanz, et al., 2003; Reis et al., 2009). For many, more is better[2]. People experimenting with tDCS might intuitively posit that more current will result in larger effects (John, 2012), but we have no data on more powerful currents[3]. The brain is quite plastic, and though tDCS is quite safe under certain conditions, we are in need of more data overall. As Reis et al., (2009) eloquently opine: "*if there is an evolutionary reason why maximal potential levels of learning are not reached in the absence of stimulation, then there could be a hidden cost to learning enhancement that we do not currently appreciate*" (p. 1593).

In principle, the kinds of effects that have been seen – improvements in cognitive function – are based upon facilitating plasticity in the brain. Since it is well established that short-term changes in plasticity can morph into long-term changes (McGaugh, 2000), there is no neurobiological reason why tDCS will not result in long-lasting changes in the brain. Such changes may be too subtle to measure with extant cognitive tests, but the possibility of the sequelae of unwise use of tDCS – as might occur in the DIY community – makes this issue much more than an academic concern. In order to mitigate the potential for damage in the growing DIY population, we will need sound regulatory policy that creates an environment of safe use.

THE UNDERAPPRECIATED PERIL: IF tDCS CAN CHANGE ONE FUNCTION, IT CAN CHANGE ANOTHER

The nature of tDCS is that it causes modest changes in membrane potential of many neurons (probably millions) (Creutzfeldt, Fromm, & Kapp, 1962; Purpura & McMurtry, 1965) that lie within the effective penumbra of the electrodes. Some but not all of those neuronal membranes may be involved in the functions being targeted, while an unknown number of them may be involved in other functions. From these observations derives an underappreciated peril in the use of tDCS: it may alter neuronal function in unintended ways. While experimenters have generally been meticulous in documenting the effects of tDCS upon specific cognitive functions, it is impossible for them to comment upon effects that the stimulation protocol had upon cognitive functions that were not measured. Even more insidious, tDCS may produce occult effects that do not manifest in overt changes in cognitive function, yet may still be of significance to individuals[4].

The movie *The Fly* depicts a scientist who has perfected a teleportation machine, but when he uses the machine himself, a fly is inadvertently included in the final product. The film is hyperbolic, but it illustrates a quandary that bedevils both the community of professionals employing tDCS, and even more so for DIY tDCS: the prospect of enhancing (or reinforcing) unwanted neural activity.

To test the hypothesis that this might already be at play, we carried out a meta-analysis of the extant literature on tDCS and observed several instances in which it seemed likely that such unintended changes were occurring. We parsed 112 well-cited papers in the literature experimenting with tDCS into brain region, stimulation polarity, and observed effects[5]. From this, we are able to compare, across the literature, the range of effects found from the stimulation of a specific cortical structure for many different domains of cognition. In the hypothetical: if an experimental group studies the effect of anodal stimulation of the DLPFC for craving, and then someone else studies the effect of anodal stimulation of the DLPFC for deception, we might observe (through this aggregate analysis) that a multitude of effects were occurring for each participant – and could occur for anyone employing stimulation of the DLPFC – and yet the unintended effects might not be measured.

A couple of examples illustrate the issue. Numerous experiments have investigated applying anodal stimulation to the left DLPFC and have found similar stimulation paradigms to result in reduction of risk-taking behavior (Fecteau et al., 2007), reduction in smoking craving (Fregni et al., 2008), facilitated recall of unpleasant images (Penolazzi et al., 2010), enhanced verbal fluency (Iyer et al., 2005), and decrease in sleep efficiency (Roizenblatt et al., 2007; see also Fig. 3.1). A similar situation holds when we examined cathodal stimulation to the left DLPFC; investigators have reported decreased verbal fluency, increase in safe choices (Fecteau et al., 2007), impaired declarative memory (Javadi & Walsh 2012), selectively facilitated pleasant image recall (Penolazzi et al., 2010), and impaired verbal memory (Javadi et al., 2012). Finally, Iuculano and Cohen Kadosh have recently demonstrated that a tDCS protocol, which enhanced numerical learning, impaired automaticity for the learned material, while a different protocol that enhanced automaticity impaired numerical learning (Iuculano & Cohen Kadosh, 2013). Such observations provide strong empirical evidence in support of our suggestion that unintended changes in cognitive function may ensue from tDCS.

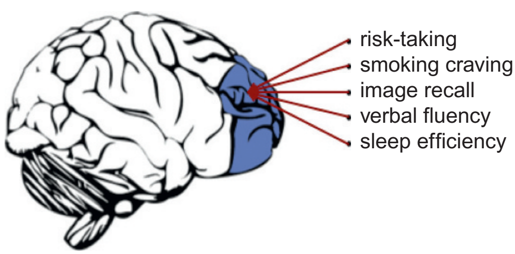

FIGURE 3.1 The shaded section marks the prefrontal cortex and the arrows point to the dorsolateral prefrontal cortex.

The current consensus is that tDCS proves most effective when coupled with some form of behavioral training (Cohen Kadosh et al., 2012). Indeed, mental activity has been shown to alter the efficacy of tDCS (Antal et al., 2007), and part of the elegance of the technique is that it is thought to affect mostly those circuits that are active while the stimulation is being applied. If tDCS is most effective when one is actively engaged in thought, the concern of intention arises: people may be enhancing unwanted extant neural activity. For example, one may be stimulating neural structures associated with memory or self-control, and an unanticipated environmental event might cause anxiety during the session. It is plausible that the presence of tDCS under such conditions may transform a transient event such as this into a long-lasting memory. In a similar fashion, tDCS might also modify the brain's response to uncontrolled internal thoughts. This is a modest problem in the case of the well-controlled laboratory experiment; it is a disaster waiting to happen in the case of DIY tDCS.

tDCS appears to be safe under certain conditions, but this is *provisional*. If, as an experimental community, we are inducing changes – whether transient or long lasting – that we are not aware of in our experimental paradigm, what might be the unintended effects? Fortunately, the institution of scientific inquiry is built in a way that will slowly shine the light over the entire walkway of effects. Unfortunately, there may be widespread use in the public – with effects both unanticipated and unwanted – well before experimenters develop this wider knowledge base. To say that it would be helpful to know what these effects might be would be an understatement.

DIY tDCS IS ONLINE RIGHT NOW

The world of DIY tDCS is quite alive: conversations online and experiments offline are taking place at this very moment. Many in this community are realistically informed, but, as is surely the case for any DIY community in its early stages, some are not (Schmidt 2008; Wohlsen, 2011). To contextualize the growing DIY tDCS within the larger do-it-yourself zeitgeist, consider the following[6]:

- The Maker Community, an extensive "directory of hackerspaces, chaptered geek orgs like Dorkbot, our 'own' independent Make: City groups, and other, similar DIY organizations," created "to support and foster the maker community world-wide" (http://makezine.com/groups/index.csp).
- DIY Bio, a thoughtful[7] organization "dedicated to making biology an accessible pursuit for citizen scientists, amateur biologists and biological engineers who value openness and safety" (http://diybio.org).

- DIY Genomics, a "non-profit research organization founded in March 2010 to realize personalized medicine through crowd sourced health studies and apps" (http://www.diygenomics.org/about.php).
- Genspace, the self-proclaimed "first-ever community biotechnology laboratory, a Biosafety Level One facility" which offers "hands-on courses to the public, provide extracurricular experiences for students, and encourage scientific entrepreneurship, particularly in the fields of molecular and synthetic biology" (http://genspace.org/page/About)[8], created in December 2010.
- DIY Drones (http://diydrones.com), a social networking community (based on the Ning platform) "focused on non-commercial ('recreational') projects by amateurs" (http://diydrones.com/profiles/blog/show?id=705844:BlogPost:17789), with the aim of creating new amateur Unmanned Aerial Vehicle platforms.
- The Hackerspace Prague brmlab, which, since 2010, has been "a place to meet and hack for all people interested in computers, electronics, science, digital art and inventing stuff in general" (https://brmlab.cz/start). Hackerspace Prague brmlab has a lengthy, open, and active wiki on tDCS (https://brmlab.cz/project/brain_hacking/tdcs).
- DIY tDCS, a blog with the purpose of "keeping tabs" on tDCS for the DIY audience (http://www.diytdcs.com).

If DIY tDCS does indeed go viral[9], how should we approach the deluge of people using tDCS devices at home? The answers range from the conservative and reactive (i.e., *laissez-faire* or watchful waiting attitudes) to the pre-emptively active (i.e., running around with our hair on fire because of concerns). We do not want the latter, but we certainly cannot sit back and allow the former. Unfortunately, the time for discussion has already passed – tDCS devices are already being sold to the public in the United States and Canada (www.foc.us). Given some real concerns, our ethos is one akin to managed technological optimism: a perspective which acknowledges both (1) the promise of great benefit from technology, and (2) the role of an active government in making that promise a reality (Sarewitz & Karas 2007)[10].

While the concern of safety in human enhancement is by no means unique to tDCS, its unique access and application (stemming from its low cost and its ease of use) might easily translate into widespread usage. Indeed, the plausibility of widespread availability and usage of tDCS in the short term raises pressing safety issues. In the egalitarian world of tDCS, we are not concerned with the safety of a small demographic (namely, those with sufficient socioeconomic resources to obtain current – and expensive – cognitive enhancement technologies), but rather with the entire populous. As mentioned, those same ingredients that ameliorated concerns about distributive justice ([relatively] safe, effective, inexpensive, and easy/portable) have already resulted in an easily accessible world of DIY tDCS enhancement. Essentially, one needs only a 9-V battery, simple electronic parts, and basic instruction (found online) to build and operate an individual tDCS device, as hobbyists are doing now (Fox, 2011). The rise of the DIY sphere presents a very real concern in the near term.

Already, there are a number of online sources providing information (or even materials) for the purposes of obtaining a tDCS device for home use[11]. The amateur community is quite varied in ideology[12], but the prevailing ethos is one of fast-paced trial-by-fire activity, and the community is growing rapidly. We have no interest in restricting individual autonomy. However, the time is ripe to create policy that safely governs tDCS for all involved in the field.

REGULATION OR LACK THEREOF

At this juncture – the intersection of public health, market forces, and knowledge dissemination – the time is right for the regulatory authorities to enter the picture. The key questions are: (1) how *is* tDCS regulated? (2) what is the likelihood that tDCS devices will be brought before the regulatory authorities? and (3) how *should* tDCS be regulated?

The answer to the first question is clear, at least in the US: at present there is no regulatory framework in place for tDCS devices for either therapeutic or enhancement uses (Marjenin, 2012). The FDA does regulate Cranial Electrotherapy Stimulator (CES) devices, but does not consider tDCS to be CES, given that tDCS utilizes direct current (CES uses an alternating signal), and the electrode placement of a tDCS device may be different from that of cleared CES devices (Marjenin, 2012). Here, two important questions arise: (1) will tDCS rise to the level of concern that the FDA has about devices that affect humans? and (2) would the FDA regulate an enhancement? The answer to (1) is certainly yes, but we do not yet know the answer to (2), given the FDA's mandated reactive focus on therapeutic devices. Indeed, given its wide jurisdiction over medical devices, it appears likely that the FDA will regulate tDCS devices when faced with device applications. Given that, as of February 2012, the FDA does not consider tDCS to be a CES device (Marjenin, 2012), those with an interest in bringing tDCS devices to market might need to apply for the more costly Premarket Approval process, costing $5–300 million depending on the complexity of the device and FDA regulatory approval path, in order to gain access to commercial markets.

While some have opined that, due to the device's low cost and simplicity, tDCS is not of interest to the medical industry (Heinrichs, 2012), we believe just the opposite: there is likely to be significant interest from private industry, given how quickly and easily tDCS might spread in the public domain.

It is always speculative to predict the future, but consider the ways in which the introduction of the iPhone has revolutionized markets ranging from desktop computers to advertising on a global basis. Given the value people put on cognitive ability (Brooks, 2008), the potential size of the market for cognitive enhancement (Stix, 2009), and the resources that the private sector has available to pursue tDCS as a new market, the potential for the emergence of a lucrative market for home tDCS is substantial.

The regulatory authorities face at least two new challenges with tDCS. The first of these is that the technology engages extant neural function by way of a device that places control in the hands of the user. On the one hand, this offers more individual autonomy – users have an unprecedented amount of discretion over their treatment. On the other, this opens a Pandora's Box of safety concerns. Consider the case of existing PCEs: the user either takes the pill or does not take the pill. The pill is "safe and effective" – that is, it does what the company claims that it does. This is a simple and workable model: one might break the pill down or modify it in some way, but there is really not much room for tampering – the pill is what it is, so to speak. This is quite different with tDCS: in the hands of a user, tDCS might be utilized for any number of purposes – some of which (but not all) are safe, and some of which (but not all) are effective. This is what is so hard about creating a prudent regulatory environment for tDCS: so much is left up to the nuanced details – and user control – of polarity, electrode placement, duration, and extant neural function.

The second challenge is even more daunting: tDCS may be the technology that forces the regulatory authorities to directly confront the full range of issues that have been swirling in the enhancement debate. While it seems unlikely that tDCS devices will be submitted specifically for the purposes of enhancement, the freedom to use the devices for such purposes cannot escape the notice of anyone who has been following the subject. As the regulatory authorities begin to grapple with this issue, they will be well advised to engage the neuroethics community to integrate ethical analysis in their regulatory deliberations.

RECOMMENDATIONS

We offer three recommendations for thoughtful reflection to help individuals communicating the excitement of tDCS better able to be deliberate about the messages they offer.

1. *Balance Enthusiasm with Restraint*. The promise of tDCS has caught the eye of many in the popular press (Adee, 2012; Belluck, 2013; Fields, 2011; Lewis, 2012). Certainly, some unique implications of tDCS merit attention in the lab, the home, the clinic, and the medical industry.

Rarely, however, is there more than passing mention of concerns that might arise with use. For those using tDCS without professional supervision, these include the placement of electrodes, impairment from reversing polarity, interaction effects with other brain-changing agents, and potentially lasting effects. Those who speak about the promise of this new technology might take pains to balance their enthusiasm with discussion of the perils of tDCS, and authors, both in the scientific literature and in the popular press, might consider the impact of their diction. A particularly important example is the repeated use of the phrase "non-invasive." Deriving as it does from the surgical literature, the term distinguishes tDCS from technologies such as DBS that penetrate the brain. However, the innocuous nature of the term carries rhetorical power that affects everyone: journalists, home enthusiasts, policy-makers, practicing physicians, and more. To be clear, scholars were well intentioned in using the phrase (Chi & Snyder, 2011; Cohen Kadosh et al., 2012; Heinrichs, 2012; Priori, 2003; Sparing et al., 2008; Utz et al., 2010), but, given the surge in lay interest, it is time to switch to a more nuanced and appropriate term to encourage thoughtful use. As an insightful commentator on such matters has put it: "if thought corrupts language, language can also corrupt thought. A bad usage can spread by tradition and imitation even among people who should and do know better" (Orwell, 1946).

2. *Develop Robust Safety Standards*. The absence of overt physical side effects when using tDCS is quite promising for improving the current state of medical care. However, tDCS can enhance one function *at the expense of another unintended function* (Iuculano & Cohen Kadosh, 2013). From the standpoint of basic neurobiology, the worry is that non-targeted functions that happen to share neural elements which extend into the penumbra of the stimulated area are unintentionally affected in some way during stimulation. If the technique enjoys widespread use in the home, this worry becomes a real concern. We call on the scientific community to put a premium on carefully designed long-term studies.
3. *Engage and Regulate*. We advocate bringing tDCS under regulatory review to create an ethical climate of safe use (Fitz & Reiner, 2013; for a similar view see Maslen, Savulescu, Douglas, Levy, & Cohen Kadosh, 2013; Maslen, Douglas, Cohen Kadosh, Levy, & Savulescu, 2013). We eschew paternalistic control over individual freedom, but thoughtful and balanced regulation can generate best practices, which, at the very least, create guidelines that biohackers might incorporate into the DIY field. At its best, regulation should not constrain the promise of tDCS but rather propagate norms of safe use, offering tools to those interested in experimenting carefully. The approach that we advocate is one of safety, humility, and realism, bolstered by the excitement of scientific exploration – the key drivers of ingenuity and innovation.

ENDNOTES

1. The ease with which one can set up a tDCS device differentiates the technique from even transcranial magnetic stimulation (TMS). The ethical issues surrounding TMS are quite relevant (Horvath, Perez, Forrow, Fregni, & Pascual-Leone, 2011; Illes, Gallo, & Kirschen, 2006), but do not capture all that deserves reflection for tDCS.
2. Specifically, the humans living within the modern capitalistic market society.
3. However, adverse effects were reported more often in studies using higher current densities (Brunoni et al., 2011).
4. To illustrate this, Hamilton et al. have offered the example of adjusting the weights on a complicated mobile: "pushing on one piece may have inadvertent effects on the others" (Hamilton et al., 2011).
5. Inclusive of other relevant data: domain of cognition, duration, current density, side effects, and notes on patients and montage.
6. This list is meant to paint the picture of the growing DIY world writ large, and is not representative of *all* of the relevant DIY movements in existence today.
7. Indeed, they feature the statement that: "this project will require mechanisms for amateurs to increase their knowledge and skills, access to a community of experts, the development of a code of ethics, responsible oversight, and leadership on issues that are unique to doing biology outside of traditional professional settings" (http://diybio.org).
8. And "for a $100-per-month membership, anyone can use the space for whatever experiments they dream up" (http://www.wired.com/wiredscience/2010/12/genspace-diy-science-laboratory/).
9. Recall that it is inexpensive, online, and considered safe and effective under certain conditions.
10. And ideally, distributing the benefit(s) equally for the public.
11. (DaSilva, Volz, Bikson, & Fregni, 2011; "GoFlow: World's First tDCS Kit", 2012 [tdcsdevicekit.com]) (http://www.youtube.com/watch?v=hgFWEBwT6BE). Moreover, a video in the open-access *Journal of Visualized Experiments* is a comprehensive and insightful piece on tDCS operation (DaSilva et al., 2011), and functions as the most complete (albeit advanced) guide to constructing and using a tDCS device at home.
12. As well as in terminology, from libertarian "biohacker" to citizen scientist "home experimenter."

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