Ethical Aspects of tDCS Use in Neuropsychiatry and the Risk of Misuse

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Abstract

There is growing enthusiasm about the potential of tDCS to be of value to clinical treatment and cognitive enhancement in neuropsychiatry. Yet despite its promise, the use of tDCS in clinical and nonclinical contexts faces several scientific and ethical challenges, which must be considered to protect against unanticipated or even adverse effects on individuals and groups in society. Scientific challenges include the lack of precise understanding of tDCS mechanisms, the present unreliability of predictions for the magnitude and nature of an individual's response to stimulation, the need for tDCS research to better capture dynamic effects in highly heterogeneous populations in whom comorbid diagnoses and the concurrent use of (multiple) medications may interact independently and interactively to affect tDCS response. Ethical challenges include issues of safety, character, justice, and autonomy. These considerations prompt a need to anticipate the trajectories of current and potential future use of tDCS both within and outside of clinical contexts, as there are likely to be evolving social and cultural consequences of tDCS use within neuropsychiatry. Likewise, neuroethical consequences from nonclinically oriented tDCS use are likely to have an impact on the way tDCS is used—and sought out—in clinical contexts. The accessibility of tDCS and its likelihood for broad use outside of medical contexts make it especially important to consider the promises, potential perils, and likely trajectories of tDCS use in multiple contexts from the outset. In this chapter, we reflect upon the way that the present degree of scientific understanding of tDCS motivates, justifies, and sometimes cautions against tDCS use.

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Introduction: Is tDCS Hope or Hype?

There is growing enthusiasm about the potential of transcranial direct current stimulation (tDCS) to be of value for clinical and cognitive enhancement purposes. With headlines like "Got a problem—put your electric thinking cap on" or "Trying a 9-volt shortcut to expertise," hundreds of enthusiastic print media articles have been published in the last few years [1–3]. The majority of media attention to tDCS has been optimistic and has praised the putative benefits of the technology [2]. However, while the tone of such coverage speaks in part to the considerable therapeutic potential of tDCS for disorders of cognition and mood, it also highlights the need to distinguish hope from hype. More than that, the science of tDCS and its potential applications present practical and ethical obstacles that warrant serious contemplation.

In many ways, practical and ethical considerations for tDCS mirror those of other forms of brain stimulation or neural interventions more broadly, but there are a few key features about tDCS that set it apart. Compared with other forms of noninvasive brain stimulation such as transcranial magnetic stimulation (TMS), tDCS is cheap, accessible, and portable. These factors multiply the contexts and applications for tDCS, some of which could present ethical, legal, and social problems if tDCS use were to become more widespread. At the same time, its very high level of accessibility also limits the range of potential actions that can be taken to prevent potentially problematic developments. Its low cost and relative technological simplicity make tDCS applicable to a broader set of contexts than other forms of invasive or even noninvasive brain stimulation, as it doesn't require surgery and can be easily self-administered. Consequently, tDCS is highly amenable to direct-to-consumer product development and marketing, as well as to increased use in so-called para-clinical contexts for enhancing cognitive and behavioral abilities, such as in the workplace, on the battlefield, or as a cosmetic enhancement in daily life. This potential for broad use both inside and outside of medical contexts calls for special consideration of the promises, potential perils, and implications for tDCS in the field of neuropsychiatry—both in how it is practiced as well as how it is perceived.

This chapter starts by exploring the promise of tDCS, first as a tool in cognitive neuroscience research, then as a clinical intervention, and finally as a technology to enhance normal cognition. Next, the scientific and ethical perils of tDCS are discussed in terms of the current state of the science, and how that informs the ways we think about the ethical challenges that tDCS poses with respect to safety, justice, character, and autonomy. For example, how can and should (or should not) knowledge learned in controlled research contexts be translated for potential safe and effective tDCS administration to complex real-world patients with multiple diagnoses, often on multiple medications? If cognitive self-enhancement becomes a social norm, what effects will that have on social structures, personal development, perhaps even clinical norms for what is considered normal versus pathological? Finally, we consider the ways in which tDCS presents specific advantages as well as challenges to neuropsychiatry and its role in society.

The field and scope of tDCS use (and other noninvasive brain stimulation and cognitive enhancement interventions) may already be developing at a rate that exceeds the pace of our scientific understanding [4]. One needs only to look at the recent and upcoming products released by the companies Thync (*Thync*, *Los Gatos*, *CA*) and Halo neuroscience (*Halo Neuroscience*, *San Fransisco*, *CA*)—not to mention their marketing

approaches—to glimpse the future role that tDCS could come to play in daily life. We may not be able to predict the rate at which the potential pitfalls may develop, but we can be sure that if tDCS continues to develop along its present trajectory, ethical, legal, and social issues will eventually arise. It is therefore important to consider these issues now, so that we can take proactive steps to mitigate against potentially unintended and undesirable consequences.

The Promise of tDCS

tDCS as a Cognitive Neuroscience Tool

Noninvasive brain stimulation (NIBS) methods are highly useful to cognitive neuroscience, in that they are used to modulate activity in brain regions or networks with varying degrees of anatomical selectivity and functional specificity. In general, NIBS add significant inferential strength to the ability of cognitive neuroscience to decipher causal brain region-function and network-function relationships. Following stimulation, subsequent changes in cortical activity, measured directly or indirectly by probing sensorimotor or cognitive behavioral functions, afford improved understanding of how brain activity in one region contributes to cognition and behavior. In recent years, tDCS has seen increasing use in the cognitive neuroscience community, with the number of publications published per year increasing over fivefold since 2010 [2]. TDCS has been applied to a variety of cognitive domains, including but not limited to skill learning, memory, executive functions, creativity, language, spatial processing, and social cognition [5]. This section provides a brief partial review of studies in which tDCS has been shown to manipulate cognition in informative ways, some of which have possible clinical applications.

With respect to learning and memory, acquisition and retention of new procedural skills has been experimentally enhanced using tDCS. One study found that, compared to sham stimulation, increased motor cortex excitability and enhanced learning of motor movements resulted when simple repetitive practice was paired with anodal tDCS [6]. Similarly, tDCS delivered over 5 days paired with training on a complex motor task resulted in increased improvement between daily stimulation sessions and persistent superior skill retention 3 months after stimulation [7]. The implications of this are that repeated administration of tDCS may have "off-line" effects that consolidate skill acquisition, effectively enhancing the long-term effects of rehearsal on performance. Declarative verbal memory has also been investigated using tDCS. For example, stimulation applied to the left dorsolateral prefrontal cortex had the effect of increasing the rate of verbal learning [8]. Consistent with this, another study found that tDCS delivered to the same site but with the opposite polarity had an inhibitory effect on verbal learning [9].

Various executive functions such as cognitive and behavioral impulse control and working memory have also been investigated with tDCS. One study found that orbitofrontal cortex stimulation with tDCS enhanced decision making and improved cognitive impulse control, without any concurrent effects on attention, mood, or motor impulse control [10]. In another study, tDCS improved response inhibition, which refers to the ability to inhibit an action once initiated [11]. For working memory (WM) and related functions, tDCS-induced improvements of performance on some tasks appear to depend in part on the level of cognitive demand of the tasks. For example, one group found that stimulation over the right cerebellum or left DLPFC increased accuracy and decreased response times for an arithmetic task that was more difficult and attentionally demanding, but not for an easier arithmetic task [12, 13]. Similarly, Gill and colleagues (2015) found that stimulation effects were readily observed when a more cognitively demanding working memory task was used during stimulation, but not when the task was less challenging [14]. Importantly, these effects also required that domain-specific cognitive behaviors be engaged during stimulation; stimulation-induced improvements were absent when tDCS was not paired with a relevant behavioral task [14, 15]. In other work, cathodal tDCS was used to enhance aspects of cognitive flexibility, presumably by inhibiting certain frontal lobe functions. This research,

which found that subjects could come up with more uncommon uses for everyday objects with inhibitory stimulation of the left, but not right, prefrontal cortex, suggests that creativity could be enhanced by stimulation that increases the influence of unfiltered bottom-up information [16].

It may be possible to significantly enhance the ability to learn new languages using tDCS. For example, anodal tDCS over language regions of cortex enhanced new vocabulary learning in healthy young adults [17]. Even without a reference object to associate with a novel "nonword," tDCS facilitated the acquisition of the phonological form of the nonwords into long-term memory, beyond the stimulation session [18]. Reading skills may also be enhanced using tDCS. Compared with sham stimulation, subjects receiving real tDCS subjects exhibited significantly better nonword reading efficiency. Curiously, this seemed only to apply consistently to below-average readers in the cohort; subjects who were more efficient readers to begin with saw much more variable changes in reading performance during real tDCS [19].

TDCS has been used to manipulate and enhance aspects of visuospatial processing. For example, we showed [20] that anodal tDCS over the right posterior parietal cortex could be used to selectively enhance detection of left-sided allocentric targets, which is to say that stimulated subjects were better able to detect the left side of visual targets independent of where the targets were in the subjects' visual fields. Interestingly, tDCS has also been used to manipulate how spatial and temporal processing contribute to higher order mental representations, such as the perception of cause and effect. In a study by Woods and colleagues [21], subjects were asked to make judgments about the causal relationship between two virtual objects (i.e., did one object cause the other to move by striking it), while the spatial and temporal features of the objects' motions were manipulated. Consistent with the role of the parietal cortex in spatial processing, the authors found that parietal tDCS selectively influenced how sensitive subjects were to spatial manipulation as it related to their perception of causality. On the other hand, frontal cortex stimulation influenced both spatial and temporal judgments with respect to causality, consistent with the overarching role of the frontal cortex in cause-and-effect reasoning [22].

Brain stimulation has also been used to alter social cognition and behaviors, including those that affect moral decision making that balances self-interest with social values. For example, individuals will often reject an offer that they perceive as highly unfair, although accepting the offer would still be to their benefit, as reciprocal punishment for the perceived unfairness (a concept know as "altruistic punishment"). Noninvasive inhibitory stimulation of the right DLPFC makes people less likely to reject marginally beneficial but unfair offers, even when consciously recognized as highly unfair, suggesting that direct current stimulation might also be used to calibrate the impact of economic self-interest on people's enforcement of social norms [23, 24]. In research on lie detection, tDCS has been demonstrated to alter individuals' deception skills in fairly specific ways, such as influencing someone's deceptive abilities when trying to conceal one's guilt or in situations such as card games. Early studies found that the act of lying increases cortical excitability on both sides of the brain [25]. People became better liars in a simulated interrogation task when cathodal tDCS was used to inhibit the anterior prefrontal cortex. Not only did stimulation make people better at concealing guilty knowledge, decreasing the kinds of signals that a polygraph detects when someone is lying, it also decreased their feelings of guilt over deceiving the experimenter [26]. On the other hand, anodal excitation of the dorsolateral prefrontal cortex made people worse at pretending not to have knowledge about something true, like whether a particular card is in their hand; interestingly, this effect did not extend to subject's behavior when bluffing or telling the truth [27].

One of the advantages of NIBS compared to classical methods in cognitive neuroscience and cognitive neurology like lesion studies is that these technologies can be used both to interfere with and enhance cognitive functions, at least temporarily. For example, the aforementioned studies on executive function and creativity illustrate how inverting the polarity of stimulation over brain regions responsible for cognitive control can either result

in favoring of cognitive abilities that require heavy filtering of extraneous information, such as sustained attention and working memory, or in favoring cognitive abilities that benefit from unfiltered intrusion of extraneous information, such as divergent thinking and creativity [10–16]. While enhancing aspects of cognition using such manipulation is a powerful tool for making inferences about brain function, it also opens the door to considering whether technologies like tDCS could be used to facilitate cognitive processes in patients with neurologic or psychiatric disorders of cognition, as well as in cognitively healthy individuals. For example, the ability of tDCS to manipulate perception of cause and effect could have implications for understanding and treatment of psychiatric disorders such as schizophrenia and obsessive compulsive disorder (OCD), where abnormal causal perceptions can contribute to symptoms [28, 29]. Moreover, the enhancement of allocentric spatial processing found by Medina and colleagues (2013) could have important implications for the treatment of spatial neglect in stroke patients [22], and studies related to executive function could lead to applications in a wide range of neurologic and psychiatric disorders [10–15]. Further research will be required so that group-level results from cognitive neuroscience studies, which are principally designed to reveal brain function, can be translated to clinical applications in which the goal is to alter specific functions in single individuals.

tDCS as a Clinical Intervention

With respect to clinical contexts, a growing body of literature suggests that tDCS is a potentially effective therapy for a wide variety of neuropsychiatric syndromes and symptoms, as well as other neurologic conditions affecting cognition [30, 31]. Depression and chronic pain in particular are two areas in which a substantial number of clinical trials support the utility of tDCS to alleviate symptoms [32, 33]. For depression, tDCS to the prefrontal cortex has shown promise as a treatment and medication adjunct to improve therapeutic outcomes [34–41]. With respect to tDCS as a treatment for pain, clinical trials for tDCS have been performed for chronic lower back pain [42, 43], chronic pain in the elderly [44], chronic temporomandibular disorders [45, 46], chronic pain in irritable bowel syndrome [47], neuropathic pain [48] such as in fibromyalgia [49, 50], or multiple sclerosis [51], and chronic pain associated with CNS damage from spinal cord injury [52] or stroke [53]. Although the results of clinical trials have in some cases been mixed [54], the potential utility of tDCS for clinical pain applications has been demonstrated in studies that show tDCS can affect aspects of nociception, pain thresholds, and affective (i.e., emotional) components of pain processing in healthy individuals [55–59]. Other neuropsychiatric conditions in which tDCS has been investigated include attention deficit hyperactivity disorder (ADHD) [60], schizophrenia [61–65], Alzheimer's disease [66] and mild cognitive impairment (MCI) [67], tinnitus [68], obsessive-compulsive disorder (OCD) [69], and generalized anxiety disorder [70]. TDCS is also being considered for PTSD, based on observed effects in fear extinction [71] and attentional bias for threat in anxiety [72, 73].

Other clinical applications for tDCS include disorders characterized by problematic behaviors related to abnormal executive function, including addictions and risk-taking behaviors [74, 75]. Studies have shown that tDCS may be useful for decreasing cigarette cravings and smoking behavior [76–80]. Interestingly, study of risk-taking behavior in smokers versus non-smokers found that tDCS was associated with personality-dependent effects [75], which emphasizes that existing cognitive patterns influence the specific nature of tDCS effects. Cravings and substance abuse in alcoholism [81–84] and drug addiction to methamphetamine [85] and crack cocaine [86–88] were also responsive to tDCS. Preliminary clinical studies of tDCS applied to DLPFC to intervene in obesity and disordered eating behavior have seen positive results. These have mostly examined acute tDCS effects on subjective reports of food craving, and attentional bias for food as probed with eye tracking following a single session of stimulation [89–93]. One 8-day, randomized, sham-controlled, crossover study found that anodal DLPFC stimulation decreased specific and nonspecific subjective

appetite and was associated with a decrease in calorie consumption at a standardized multi-choice test buffet by 14%, with a specific reductions in consumed carbohydrates [94].

Substantial promise has been found for tDCS in post-stroke neurorehabilitation. Following stroke, tDCS has been shown to assist in upper motor limb recovery from paresis [95, 96]. Similarly, anodal tDCS to the posterior parietal cortex mitigated unilateral visuospatial neglect [97] in one study, and in another study the response to prism-adaptation therapy was improved when therapy was paired with tDCS [98]. Anodal tDCS to the right premotor cortex also mitigated one patient's anosognosia for hemiplegia during stimulation [99], and in another case study, cognitive neglect therapy paired with biparietal tDCS, but not sham stimulation, enhanced the patient's response to therapeutic cognitive training [100]. Additionally, multiple studies have shown that when tDCS is paired with speech and language therapy, naming ability can be improved in stroke patients with aphasia [101–110]. Another neurorehabilitation application may be to post-stroke attentional decline, as anodal tDCS to the left DLPFC also improved attention in stroke patients, resulting in increased accuracy on a cognitive task of executive function [111]. Finally, tDCS is also being explored as enhancement to learning and memory in normal aging and in states of cognitive impairment [112–115].

Not coincidentally, tDCS has been explored clinically in many areas where the underlying impaired cognitive constructs have been shown in cognitive neuroscience research to be manipulable using stimulation. For example, cognitive neuroscience studies showing effective tDCS modulation on decision-making, including risk-taking, reward-seeking, impulsivity, and fairness consideration are considered as promising for addictive disorders, in which the hallmarks of clinical symptomatology are compromises in such decision-making capacities [116].

There are many practical reasons to favor tDCS in clinical settings. In addition to being small and portable, tDCS is inexpensive compared to other neuromodulation technologies like TMS. As currently used tDCS protocols are also safe, tDCS is an ideal form of neuromodulation to pair with existing therapies, and could potentially be self-administered by patients who may benefit from repeated stimulation on a regular basis.

tDCS to Enhance Normal Cognition

In addition to clinical applications and cognitive neuroscience studies designed to elucidate brain function (described above), there has been growing interest in explicitly enhancing normal cognition. In particular, tDCS joins a variety of neuroscience tools applied to so-called neuroergonomic purposes, referring to applications intended to aid human operators in the performance of their work duties [20]. Academic investigations for this purpose include—and in many cases expand upon—cognitive neuroscience studies of effects on isolated cognitive abilities, by examining tDCS effects on the performance of more complex tasks. Frequently, these experiments involve more naturalistic paradigms with clear applications to specific occupational functions, and assess improvements in the cognitive functions of implicit memory (e.g., procedural and motor learning; probabilistic learning), explicit learning and memory (e.g., declarative memory encoding with retrieval), working memory, attention, and perception [117]. For example, tasks in which tDCS has shown accelerated learning, enhanced performance, and/or prolonged training effects include threat detection in virtual-reality simulated urban warfare scenes [118–120], simulated air traffic controller games [121], a complex multi-task game "Space Fortress" [122], and an image analysis task in which target objects must be identified from synthetic aperture radar images of terrain with buildings and vehicles [123]. Not surprisingly, much of this research has been funded by the US Department of Defense [124].

On the other end of the spectrum from defense and security organizations, a community of individual "do-it-yourself" (DIY) tDCS users are also actively pursuing cognitive self-improvement [125]. The practices of this community were recently described in detail by Wexler [126]. The DIY community refers collectively to tDCS use outside of professional or academic settings, and can be subdivided

into those who seek to enhance their cognition and those who intend to alleviate clinical symptoms of neuropsychiatric disorders [126].

A burgeoning wearables market is also emerging, producing tDCS products controlled by companion apps for cognition and athletic performance enhancement, in both healthy individuals and clinical populations. Two of these companies supply direct-to-consumer devices for recreational and lifestyle indications (Thync and Foc.us), and another has a stimulator intended for healthy and "impaired" populations in a well-funded development pipeline (Halo Neuroscience; http://halo-neuro.com/#science) [124]. These companies are at the forefront of trends that could potentially to lead to widespread, if not ubiquitous, use of neuromodulatory technologies in daily life.

However, at present the effects of tDCS are far from established. Despite growing excitement about the possibility of using tDCS for enhancement of otherwise normal cognition, caution is warranted before extrapolating observations and lessons learned in cognitive neuroscience and clinical contexts to cognitive enhancement in healthy individuals due to fundamental differences in the theoretical, practical, and ethical issues related to each (as will be discussed in the next section).

The Perils of tDCS

Despite its promise, the use of tDCS in cognitive neuroscience, clinical research, and para-clinical applications faces several scientific and ethical challenges, which must be considered to protect against unanticipated or even adverse effects on the bio-psycho-social health of individuals and communities. It is especially important to accurately assess the state of the science, and reflect upon the way that the present degree of scientific understanding of tDCS motivates, justifies, and sometimes cautions against tDCS use.

Scientific Challenges

Scientific challenges stem from the fact that there is much that we do not yet understand about the underlying neural mechanisms of tDCS. Our incomplete understanding of tDCS mechanisms is underscored by data that indicates that the effects of stimulation on brain function are neither monotonic nor invariant. The initial dogma based on studies in motor cortex, which attributed enhancement or diminishment of cortical excitability to anodal or cathodal stimulation, respectively, often conflicts with experimental results. On the contrary, dose-response relationships are still poorly understood. For example, one study found that 1 mA cathodal stimulation diminished motor cortex excitability, but 2 mA cathodal stimulation enhanced it [127]. Similarly, doubling the time of stimulation can reverse the behavioral and cortical excitability effects [128, 129]. Moreover, the "anodal-facilitation versus cathodal-disruption" schema is a clear oversimplification; particularly beyond motor cortex, anodal and cathodal stimulation does not have equal and opposite effects on behavior. In cognitive studies, anodal and cathodal stimulation is sometimes found to have the same net facilitative effect on behavior, or only one stimulation polarity over the target will be found to influence a given behavior [11].

More broadly, we know that stimulation parameters matter a lot, but we are limited in our knowledge of what difference they actually make. For example, finite element models of tDCS-induced electrical current flow tell us that the size and location of the "reference" electrode strongly influences the effects of stimulation [130, 131]. Small changes in electrode position and individual head shapes can also greatly modify current flow patterns [132, 133]. However, the results of these models vary considerably based on model assumptions [134]. In other words, the best tools we have for understanding what stimulation is doing are themselves quite limited.

Other unknown variables when considering the perils of broader applications of tDCS to enhance cognition are the interactions that brain stimulation may have with comorbid diagnoses and the concurrent use of medications. The interaction of brain stimulation with agents that act on different neurotransmitters is of special concern in neuropsychiatry, since many (or perhaps most) people who suffer from these problems are taking

one or more such medications. Some drugs have been found to have profound, complex and varied influences on tDCS-induced neuromodulation [135–137]. In one very large clinical study of tDCS and depression, an additional naturalistic study systematically evaluated how tDCS responses were affected by concurrent treatment with psychiatric medications, including benzodiazepines, serotonin-noradrenergic reuptake inhibitors (SNRIs), selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), first- and second-generation antipsychotics, and mood stabilizers, and found that medication-stimulation interactions are significant considerations [138]. Specifically, they confirmed that antidepressants generally increased tDCS effects, but found that taking benzodiazepines actually worsened outcomes. They also found that tDCS did not interact with non-benzodiazepine anticonvulsants and antipsychotics, which are frequently used as mood stabilizers in patients with depression. Considering that there have been reports of hypomanic switches after tDCS in depression patients [139, 140], including an episode of manic psychosis in a stimulated patient taking sertraline [36], these findings warrant further investigation in order to develop safety guidelines for treating mood disorders with tDCS [141].

In sum, we have an incomplete understanding of how stimulation parameters and other dose variables act on the brain or interact with medications. This lack of precise mechanistic understanding limits our ability to predict the effects of tDCS in individuals. It is essential that clinicians and self-applicators of tDCS temper their enthusiasm with an understanding of these limitations. There are ethical and pragmatic obligations to resolve these uncertainties and to seek a more detailed mechanistic understanding of tDCS.

Ethical Challenges

The potential for tDCS use to become widespread raises a number of social and existential risks that must be carefully weighed against its benefits. By their nature, the effects of tDCS on cognition and affect blur the distinctions between treatment and enhancement. Moreover, its accessibility makes its use especially difficult to confine within the bounds of clinical medicine. Thus, ethical issues raised by tDCS cannot be viewed solely through a clinical ethics lens. Like pharmacological treatments that also have the potential to be used for enhancement purposes, the use of tDCS has not and will not remain in the medical realm. However, there is much still unknown about cognitive enhancement [4], both in terms of the science and in terms of its broader effects in ethical, legal, and social spheres. As discussed below, the ethical issues surrounding tDCS can be broadly categorized into concerns regarding *safety*, *justice*, *character*, and *autonomy*. The latter three concerns deal with potential trajectories of tDCS technology development and use patterns that are, at present, still speculative. However, it is important to consider the ethical implications of possibilities so that the negative consequences can be anticipated, and if possible, avoided.

Safety

In most traditional ways of thinking about safety, tDCS is of low concern; all current evidence indicates that tDCS delivery by currently applied protocols is very safe. While there are some recognized minor risks associated with tDCS such as mild headache and a mild itching or burning sensation under the electrodes [142], the risk of obvious physical injury from tDCS is extremely low. The most severe recognized potential medical risks associated with tDCS are burns to the skin and complications resulting from electrical equipment failures [143–145], but these are very rare and more likely to result from DIY systems than commercially manufactured stimulators.

The main potential concern with safety is that tDCS may alter cognition in unintended ways [146, 147]. Evidence suggests that stimulation at different sites may benefit some cognitive abilities but impair others [148]. Additionally, inhibiting or exciting the same region of brain can elicit different types of benefits. For example, anodal stimulation to the

lateral prefrontal cortex not only improved working memory, but also related fronto-executive functions that require a high degree of cognitive control, such as selective attention and set-switching. However, some aspects of cognitive flexibility and divergent thinking could be more consistent with a loosening of cognitive control, resulting in less "top-down" regulatory filtering of low-level information. Accordingly, cathodal stimulation to lateral prefrontal cortex has been shown to enhance cognitive flexibility in tool use [16]. Viewed together, these studies raise theoretical concerns that stimulation delivered with the intent of enhancing attention or working memory could have detrimental tradeoffs for cognition associated with creativity.

These kinds of tDCS-induced mental tradeoffs have been demonstrated for other aspects of cognition [148]. For instance, Iulcano and Kadosh (2013) recently explored how tDCS affected two dissociable aspects of learning that were relevant to mastery of a novel mathematical task: skill acquisition rate, and skill automaticity whereby tasks are performed quickly, effortlessly, and without conscious intention. Using tDCS to brain regions associated with learning (posterior parietal cortex; PPC) or automaticity (DLPFC) the investigators demonstrated a double dissociation wherein tDCS to the PPC enhanced learning rate but impaired automaticity while tDCS of the DLPFC enhanced automaticity at the expense of learning rate [148].

The nature of stimulation benefits may be specific to certain traits or states. For example, tDCS improved arithmetic decision making efficiency in healthy subjects who had high levels of pre-existing math anxiety, but it slowed reaction times in healthy subjects who had low-math anxiety, whose arithmetic efficiency was already unimpaired [149]. In several studies, state-dependent tDCS effects were linked to one's starting level of ability, with factors that lead to better performance at baseline associated with less improvement, and potentially impairment [114, 150, 151]. In a related fashion, the effects of tDCS on learning and memory task may depend on the stage of training [152].

In some cases where tDCS is associated with worse outcomes, stimulation does not directly cause cognitive degradation, but rather may block typical improvement by factors such as practice. One group discovered this while looking at the effects of tDCS on repeated IQ testing, employed as a means to simultaneously assess multiple domains for cognition. The study found that practice-related improvements for subtests of fluid intelligence (e.g., perceptual reasoning) were specifically attenuated when right, left, *or* bilateral anodal tDCS was delivered before retesting [153]. While in retrospect these results are consistent with expected effects of frontal anodal tDCS on cognitive flexibility, the authors initially hypothesized that tDCS would improve IQ test performance because previous studies had found that other types of task performance were improved by such stimulation. Such evidence highlights that tDCS is not a panacea, and further suggests that perhaps we should consider a more nuanced notion than "cognitive enhancement" for framing tDCS applications.

One of the challenges in understanding the risks, benefits, and trade-offs of using tDCS to enhance cognition is that, while many in the DIY stimulation community and elsewhere look toward the cognitive neuroscience community to inform how stimulation for enhancement could be pursued, the fundamental approach taken by most cognitive neuroscience studies does not adequately address the "cognitive safety" of enhancement with tDCS in at least two ways. First, the scientific methodology used in most cognitive neuroscience studies of tDCS only test one or a very limited number of cognitive functions in order to test specific hypotheses about the relationships between the brain areas stimulated and those specific mental operations. They do not test to make sure there are no deleterious effects on every other intellectual function. Second, cognitive neuroscience studies generally do not test for the durations that one might consider relevant if one was trying to make long-term changes in cognition. We simply do not know what the effects of increased frequencies and durations of stimulation are for individuals with healthy cognition. While this is not terribly relevant for basic

cognitive neuroscience studies, it is extremely relevant for cognitive enhancement studies, due to the increased likelihood of repeated and potentially prolonged stimulation sessions in the latter. Similarly patient studies do not wholly inform what the likely effects of neural enhancement with brain stimulation are because the brains in which therapeutic stimulation is being applied have already been altered by disease. Thus, safety considerations for tDCS underscore that the science has yet to support the technical application of tDCS for unmitigated cognitive enhancement.

Justice

Distributive justice refers to the equitable distribution of benefits. The development of "cosmetic" tDCS as a boutique service for cognitive remediation or enhancement could exacerbate social disparities by introducing a new type of "cognitive" privilege for those who can afford to exogenously treat or augment their own intellect [154]. Moreover, if boutiqued cognitive enhancement becomes a norm that is taken for granted, expectations regarding a "normal" range of cognitive abilities could become distorted to the point where unaugmented cognition is perceived as pathological. This could result in (further) medicalization of systemic disadvantage, which may introduce further obstacles to the remediation of social inequality, since access to education, medical care, and nutrition are already inequitable. Thus, explicit "cognitive health" disparities might further entrench systems of privilege and socioeconomic inequality. In many ways, this problem is not new or unique to enhancement with NIBS, but is symptomatic of the already vast separation in privilege between the haves and the have-nots.

On the other hand, compared with other technologies (including pharmaceutical agents) with utility as treatments or enhancements, justice may arguably constitute less of an issue for tDCS than other neurotechnologies, because it is relatively inexpensive and easy to create and employ with only modest technical training [155]. Noninvasive brain stimulation in healthcare is currently inequitable; if tDCS could confer comparable benefits while requiring less medical or technological infrastructure, it could increase justice in medically oriented neurostimulation [156].

Character

Issues of character relate to our essential humanity and how we find meaning in life. Ethical issues of character with brain simulation are those that impact our experience of personhood [157]. With its potential to alter our experience of behavior and cognition, brain stimulation raises two key questions. The first question is about identity and the integral core constellation of mental and behavioral characteristics that define us. It asks, "To what extent *can* and *should* we have the ability to change the core of who and what we are?" In part, the answers depend on the degree to which the core traits that distinguish us are considered to be stable, consistent, and integrated, and whether tDCS can disintegrate or change this subjective "core." The second question is about Self and the potential long-term consequences of self-enhancement on character building, as well as other more general aspects of psychosocial development, both within individuals and as a society. What sort of experiences are necessary for wisdom and maturity and virtue, and what are the consequences of avoiding them? These questions have already been deeply explored for neural interventions, in particular invasive deep brain stimulation (DBS) [158–162]. However, the scope of access to tDCS adds an additional dimension to such ethical consideration, as the potential effects on character development or change shifts from being an issue that affects select patients and their loved ones to something that could extend more directly to everyone.

Aspects of life experience that are not necessarily subjectively positive are integral to shaping a person's bearing, demeanor, and personality. It is a widely accepted social norm that adversity breeds character. If cognitive and emotional challenges can all be eased by exogenously stimulating the brain, how does that affect the resilience

and moral quality of a society in which this life of convenience is available? On the other hand, how much suffering is enough, and who gets to decide? After all, we do not consider it a moral failing if a person treats pain associated with childbirth or medical procedures. At what point, if any, does relief from difficult experiences diminish us? The consequence of tDCS on individual development ultimately affects society and culture in ways that are evolving and reciprocal, because social dynamics among individuals and groups influence, and are influenced by, the ambient culture. Thus, the adoption of widespread self-enhancement will bring questions about whether there should be limits to alter our fundamental nature to the forefront in formulating social and policy responses to growing use of tDCS.

Despite potential concerns, the effects of widespread tDCS use on character may not necessarily be negative. For instance, ongoing research is exploring the role of the brain in sports and fatigue (http://www.neuroelectrics.com/use-case/), and seeks to leverage this understanding to develop stimulation that could remove neural obstacles to maximum physical athletic performance. One could argue that removing obstacles to maximum performance *given maximum effort* is a categorically different type of enhancement than enhancement that makes something require *less* effort. In such a context, tDCS could be viewed as an *enabling* tool that could *enhance character*, rather than to act as a *substitute* for qualities that character would ordinarily supply to ensure success, such as commitment, patience, perseverance, and self-transcendence. This distinction is potentially relevant not only to athletics, but also to treatment in neuropsychiatry, wherein stimulation could potentially enable rather than rather than substitute for self-driven efforts to cultivate positive character traits. For example, enhancement of executive function in someone with ADHD to improve impulse control and the ability to sustain attention might *enable* such individuals to practice acts of high character, such as finishing what one has started or keeping commitments. The cardinal distinction applying to both situations is that high sustained effort is still required, and that absent the intervention, there are limits to the degree that such effort could affect performance. Assuming that the same amount of effort is exerted with or without tDCS, what is the true nature of the effect, if any, on the character of the athlete or individual with ADHD? These are all largely philosophical and psychological questions whose answers hinge on arguments about the relative influence afforded to *situational context* versus *personality* when assessing of character. Although this subject is beyond the scope this chapter, it is worth noting that a meaningful discussion of the impact of tDCS on character may require further consideration of a broader conceptual framework to address the daunting philosophical challenge of relating concepts such as identity and self to behavior and neurobiological functions.

Autonomy

Autonomy can be thought of as the right to one's own life, to make choices based on reasons and motivations that are not the product of manipulating or distorting external forces. In the context of tDCS, autonomy can be considered in terms of two types of freedom: (1) the freedom *not* to be stimulated, and (2) the freedom *to be* stimulated.

The freedom *from* stimulation can be threatened by hard or soft coercion. In hard coercion, the individual is forced into an activity for the perceived "good of society". Neuropsychological hard coercion is far from unheard of. Examples include psychopharmacologic agents given to soldiers to maintain battlefield performance and chemical castration to diminish the libido of imprisoned sex offenders [163, 164]. It is not all that hard to imagine cognitive enhancement with brain stimulation potentially following a similar course with similar vulnerable populations. With soft coercion, the individual feels societal pressure to keep up with norms and mores. As we know from many examples in professional sports, in high-stakes competitive environments, individuals turn readily to performance enhancers to give themselves a competitive edge. With respect to mental performance, we can see examples of

soft coercion currently in individuals who take pharmacologic cognitive agents in hopes of optimizing their performance at school or work. With respect to neuropsychology, the hazard of soft coercion again highlights that tDCS could potentially blur the distinctions between pathologically poor brain function and brain function that is normal but suboptimal for the tasks one desires to accomplish.

The freedom *to* be stimulated is unlikely to be overtly threatened given the accessibility of tDCS components. In this, lessons can be learned from other examples of cognitive self-enhancement, and cosmetic applications of medical technologies, including neuropharmacology. While it is important to remember that individuals are free to do as they see fit with respect to their own bodies and minds, inevitably, autonomy must necessarily be balanced with other ethical imperatives that arise from pragmatic or moral justifications, such as the need to consider the health of the community. Just as soft coercion can be used to encourage stimulation, social pressures can be exerted to influence the actions of those who would elect to use tDCS for medical or enhancement purposes. Given the complexity of the issues surrounding the use of tDCS for medical or enhancement, monolithic laws are unlikely to be helpful—or effective.

Ethical Considerations Pertaining to Neuropsychiatry

It may be taken for granted that the principle ethical considerations for tDCS with respect to the practice of neuropsychiatry boil down to whether tDCS is an acceptable way to treat patients. To this end, it is important to keep in mind that the distinction between normal and pathological is indiscrete and often culturally determined. Importantly, individuals whose thoughts and behaviors may objectively deviate from typical behavioral norms do not always do so in a way that leads to suffering; the moral imperative to medically treat dysfunction depends on the qualitative impact it has on an individual's life rather than the mere presence of abnormality [165]. Indeed, neurodiversity is increasingly being recognized as an intrinsic and valuable part of the spectrum of human experience that confers value and vigor to our overall ability to cognitively adapt to social and environmental changes [166]. Medicalizing neurodiversity pressures individuals and professionals (to some extent) into enforcing conformity to sociocultural norms of what is considered a "valuable" life. Neuropsychiatry as a field should consider tDCS alongside other dilemmas involving neurodiversity that drive the overall societal disposition towards psychiatry. These are not necessarily different issues than those pertaining to medicating neuropsychiatric disorders, but the fact that one doesn't necessarily need a prescription to self-administer tDCS (in some form) could shape perspectives on whether neuropsychiatric therapeutic applications of tDCS are perceived as legitimate, relative to other contexts in which tDCS could be used for enhancement or recreation.

Neuropsychiatry as a field should also be aware of the ways that widespread and even non-medical use of tDCS could influence perceptions of normality versus pathology. It can, at times, be difficult to distinguish between true "diseases" of the mind and more mundane dissatisfaction with mental states. Psychological aspects of individuals that are considered to be symptoms can often be conceptualized as traits that vary along a continuous spectrum of expression, for example, from inattentiveness to an attention deficit, or from sadness or emotional exhaustion to depression. This slippery slope of spectrum is especially problematic considering the capacity of tDCS to alter intellectual performance or mood. While most neuroscientists would argue that we are still far from being able to reliably alter mental states on an individualized basis using tDCS, the marketing for products like Thync and subjective experiences reported by DIY users indicate that at least the *perception* that tDCS can be used to induce targeted changes to mood (for example) exists presently. Having the power to so easily remedy dissatisfaction with one's mental states using tDCS—or even just believing that one has that power—has the potential to further obscure boundaries between what is considered normal, sub-clinical, or pathological.

Clinical fields that purport to distinguish between normal and pathological mental functioning face special obstacles when clinical values conflict with sociocultural norms, such as individuality or self-reliance. This has implications for clinical uses of tDCS. It is already difficult to determine when it is ethical to use technology to intervene in one's mental functioning. Widespread use of neural enhancement technologies like tDCS could further pathologize aspects of cognitive performance that would otherwise be considered along a spectrum of normalcy. This distortion could have the effect of decreasing individual autonomy by exerting positive pressure on clinical professionals to treat patients using neurostimulation or on individuals to "treat" themselves. As with pharmacological self-enhancement, some individuals might seek neuropsychiatric treatment for the purpose of procuring access to such technology as opposed to alleviating the suffering caused by illness. Thus neuropsychiatrists run the theoretical risk of becoming dispensers of cognitive commodities in tDCS as well as neuropharmacology. On the other hand, if there is general cultural pushback to increasing use of NIBS for self-enhancement, the application of tDCS in neuropsychiatric contexts, even where therapeutically beneficial, could come to be seen as problematic. Consider, for example, the stigma that popular culture has placed on electroconvulsive therapy (ECT), a highly effective treatment for refractory and life-threatening cases of depression, and how that stigma has had a sustained negative influence on its acceptance and use as a therapy. If tDCS becomes similarly stigmatized, this could raise obstacles to the development effective treatments for a variety of neurologic and neuropsychiatric conditions.

Several points raised in this chapter also have ethical implications for clinician-patient encounters. Because tDCS is not yet approved for specific clinical indications, we will here consider concerns that apply primarily to users of DIY or direct-to-consumer products. As public use of these technologies becomes more widespread, patients may sometimes confide to their neurologists or psychiatrists that they are experimenting with tDCS for self-treatment. In this situation, it is important that patients understand the safety consequences tDCS, including possible unintentional alteration of cognition or emotions. It will also be important for patients to recognize the current limits of the scientific literature, which cannot reliably predict what effects tDCS will have in the context of polypharmacy or other concurrent treatments. Conversations about the state of tDCS science and what is and is not known about tDCS might help patients to make better-informed decisions for themselves. However, insofar as there is currently no compelling evidence of serious medical risk posed by tDCS, some patients may be inclined to disregard the advice of their clinician and continue to self-administer tDCS in ways that, at least theoretically, seem potentially deleterious. This raises ethical issues of how best to engage with the patients regarding the risk of tDCS misuse in the absence of clear evidence for or against long-term harms. The issue of clinical misuse or overuse is similarly likely to arise in the event that tDCS is approved for specific indications such as depression or pain. While there is no clear one-size-fits-all strategy for navigating this topic with patients, it is an issue that neurologists and psychiatrists should be aware and ask about in their patients, especially as awareness of the therapeutic potential of tDCS becomes much more widespread in the public sphere.

Conclusion

In sum, there are pragmatic considerations specific to the practice of neuropsychiatry that bear weight in assessing both the utility and risks of employing tDCS as therapy. As it is presently understood, the mechanism of tDCS effects may be of particular utility for disorders in which dysfunction coincident and overlapping neural circuits leads to a range of psychiatric and cognitive symptoms. Targeting those common neural substrates with tDCS may lead to a variety of salutary effects in patients with complex disorders of mood, affect, and cognition. However, stimulation of overlapping neural circuits may also give

rise to cognitive tradeoffs that should prompt caution, particularly when the intent is to use tDCS to enhance normal cognition as opposed to treat disease. It is important to consider what is known versus what is not known about tDCS when designing clinical and cognitive research studies, and even more so when developing public policy and communicating with potential tDCS users (both consumers and patients). Clinicians and neuroscientists alike have an ethical responsibility to ensure that the lay public can access accurate information about what is and is not known about the mechanisms, effects, and safety of tDCS. In some cases, this may mean tempering unbridled enthusiasm for tDCS expressed in media coverage. The benefits and risks of tDCS clearly vary according to the context of administration, both with respect to the research, clinical, and cosmetic purposes for stimulation, as well as the states and traits of individual recipients.

All these considerations prompt a need to anticipate the trajectories of current and potential future use of tDCS both within and outside of clinical contexts, as there are likely to be dynamic broader social and cultural consequences of tDCS use within neuropsychiatry. Likewise, neuroethical consequences from nonclinically oriented tDCS use are also likely to have an impact on the way tDCS is used and sought out by patients. Thus, the use of tDCS in neuropsychiatry may have profound impacts not only on the social-cultural milieu, but also on the perceptions and practices of neuropsychiatry as a field.

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