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## The neuroethics of non-invasive brain stimulation

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### Abstract

Transcranial direct current stimulation (TDCS) is a brain stimulation tool that is portable, painless, inexpensive, apparently safe, and with potential long-term efficacy. Recent results obtained from TDCS experiments offer exciting possibilities for the enhancement and treatment of normal or impaired abilities, respectively. We discuss new neuroethical problems that have emerged from the usage of TDCS, and also focus on one of the most likely future applications of TDCS: enhancing learning and cognition in children with typical and atypical development.

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There is perennial interest in the neuroscience community in using its expanding understanding of the brain to devise ways of enhancing brain functions and, consequently, human abilities [1]. The main aim is usually to improve the abilities — and therefore the lives — of people with cognitive and other psychological disabilities. Most existing efforts to improve these abilities have focused on pharmacological interventions. In recent years, however, we have seen a new wave of research exploring whether non-invasive brain stimulation (NIBS) might be beneficial. NIBS methods, such as transcranial electrical stimulation (TES) and transcranial magnetic stimulation (TMS), especially in combination with behavioural training, offer promising alternatives or adjuvant strategies for conditions in which pharmacological intervention has not been successful [2]. In this Essay, we focus on transcranial direct current stimulation (TDCS), the most frequently used mode of TES. This recently emerging and easily applied technique raises the main neuroethical dilemmas of NIBS techniques and makes some issues particularly pressing.

In TDCS, weak electrical currents, for example 1 mA, are applied for a short duration (~20 minutes) to the head via electrodes that are placed on the scalp. The currents pass through the skull and alter spontaneous neural activity. Studies in animals and humans have found that anodal stimulation pushes neural resting membrane potentials closer to the activation threshold and therefore increases tissue excitability, while cathodal stimulation inhibits cell firing and decreases excitability [3].

The long-lasting effects of TDCS, which can last up to 12 months [4], are protein synthesis-dependent and are accompanied by modifications of intracellular cAMP and calcium levels [5], and therefore share some features with long-term potentiation and long-term depression [6]. Experiments in humans have found that following TDCS there are changes in the local concentration of neurotransmitters GABA and glutamate, important in synaptic mechanisms implementing learning and memory [6].

These characteristics of TDCS make it an attractive tool for manipulating neurobehavioural plasticity and underlie its potential as an adjuvant intervention for cognitive rehabilitation.

Compared to other NIBS techniques, TDCS is portable, painless, inexpensive, apparently safe, and therefore feasible for home use. Most importantly, growing evidence indicates that TDCS has the key distinct advantage of enhancing psychological functions with potential long-term efficacy [5,7].

TDCS studies have shown that it is possible to enhance fundamental human capacities, such as motor and sensorimotor skills, vision, decision making and problem solving, mathematical cognition, language, memory, and attention – improvements that seem to persist without apparent cognitive side effects [2]. We shall refer to all these different skills, from basic sensory abilities to higher cognitive functions, as ‘psychological’ functions.

#### New ethical issues

TDCS has the potential not only to treat congenital or acquired neural disease or dysfunction but also to enhance the psychological skills of subjects already performing within the normal range [5,7]. The issue of cognitive enhancement using TDCS raises special ethical issues that differ in important ways from those raised by pharmacological interventions [8]. First, once a TDCS machine has been purchased, it can be used at any time, even many years later, for any function, by anyone. Although Food and Drug Administration (FDA) approval is required for marketing purposes, the FDA cannot prevent its wider use.

Second, the relative cheapness and portability of TDCS means its use is not restricted to laboratories or clinics. Indeed, some companies already offer the device for personal use at home by adults.

Third, unlike pharmaceuticals, TDCS is not ingested into the body. People may intuit a moral difference between external enhancements, such as education or computing, and internal enhancements, such as, drugs. While external enhancements, such as education, can be dangerous, for example when they are used to breed hate, and internal enhancements such as nutrition can be used for better health and cognition, there seems to be a widespread perception that external enhancements are less problematic than internal ones. The intuition that TDCS is an external intervention may create the misplaced perception that its use is less problematic than more obviously internal enhancements, and thus lower the threshold for premature use [9].

Last, TDCS can be applied to any cortical brain area, including areas beyond that for which its use may be indicated. Moreover, it can have enduring effects [5,7].

These unique features of TDCS technology raise important ethical issues for scientists, ethicists, policy makers and the general public. Other ethical issues are similar to those pertaining to other medical interventions [10]. It is the potential application of TDCS for improving psychological functioning in children (Figure 1) that causes most concern, as we will discuss in the next section.

## Stimulating the developing brain

### Premature use of TDCS

The fact that the technology is so simple and easy to apply raises distinctive issues. The apparatus is relatively inexpensive (some forms of TES machines can be purchased for less than £500), can be built using off-the-shelf components (for example <http://www.electronicpoint.com/9-volt-batterysteped-down-1-2-milliamps-t10189.html>) and, when used within suggested guidelines, the acute safety risks (of seizures, for example) seem very low (in contrast to TMS, there are no reports of seizures) [11]. As a result there is a danger that it can be tried out ad hoc on adults and children — especially on vulnerable patient groups seeking help with serious and currently intractable developmental disorders (such as autism, epilepsy, dyscalculia, dyslexia or schizophrenia) — before enough is known about potential psychological side effects, the appropriate method of stimulating (for example, the optimal duration and location of stimulation) and about how psychological training protocols can be designed that are selective for the desired effects.

As little is yet known about the best ways to utilize TDCS, there is no training program or licensing regime for clinicians applying the technique. Inadequately trained clinicians might misidentify suitable sites for stimulation — an important issue as different cognitive abilities may be subserved by different brain areas at different stages across the life span [12]. They might also fail to ensure that stimulation parameters are within safety guidelines (indeed, such guidelines have not yet been devised for the developing brain). And they might combine NIBS with inappropriate behavioural training. At best, this situation could result in the exploitation of vulnerable patients or parents for financial gain; at worst, it may risk long-term damage to the brain and exacerbate disadvantage, potentially worsening other psychological functions.

For example, repeated stimulation of the parietal cortex in order to increase numerical competence during developmental stages when the prefrontal cortex [13] is more important might not only fail to give any improvement but it could even worsen performance and lead to atypical brain development. Like other types of atypical experience during sensitive periods [14], the stimulation of the wrong brain area might induce abnormal patterns of brain activity in this brain region and interconnected areas, and increase metabolic consumption in brain areas that are irrelevant to the specific psychological function. Hence, research into the safety and potential hazards of TDCS in children is urgently needed. This will enable parents and clinicians to be better informed of the risks involved in applying the technique and for the appropriate training of people who will administer TDCS for different conditions in different age groups.

### Should we stimulate the developing brain?

Some issues pertaining to the application of NIBS to children are relatively familiar from other contexts [15], such as the need to obtain valid consent either from a competent adolescent or from the primary caretaker, usually a parent. An issue that is more specific to the use of TDCS, as well as other NIBS techniques, in children concerns its possible effects on brain development and the degree to which enhancing some capacities may lead to a

deterioration of other capacities. To date, most research on cognitive enhancement using pharmacological agents or NIBS has focused on improving average or impaired abilities. However, such enhancement may come at a cost in some cases [16]. Highly-developed capacities in certain cognitive domains in some individuals are accompanied by reduced functioning in others [17].

It would be premature to allow children, or their parents, to make the choices that lead to higher functioning in one domain (such as language) at a cost to functioning in other valuable domains (such as face recognition), as they might lack understanding of the ways in which the development of cognitive abilities may depend on earlier cognitive functions, as well as on brain organisation [12]. We recognize that parents have a great deal of leeway over what they might do to their children; for example, we allow them to do things that cannot be expected to better their children (such as feed them largely on crisps). However, depending on how bad the negative effects of an enhancement are, it might be appropriate to block parents' access to the enhancement. We do already consider it grounds for intervention if parents do things that are too detrimental to their children, for example, if they refuse to educate them. In addition, there are things that parents may legitimately do to their children, but which medical or scientific authorities should not enable or facilitate. Therefore, those involved in the professional use of TDCS should not facilitate the choices of parents if the side effects are sufficiently bad, or sufficiently ill understood.

If TDCS does enhance some abilities at a cost to others, then assessing its ethical permissibility will involve weighing its costs and benefits. By contrast, if treatments like TDCS are shown to be clearly in a child's best interest, without detrimental effects on other psychological functions, parents should have no ethical (or legal, at least in Anglo-American jurisdictions) right to refuse them for their children. This could mean that TDCS might in the future become mandatory as a treatment for developmental disorders. Indeed, if TDCS was shown to significantly improve acquisition of core skills in normal children, it might become as mandatory as basic education.

It is not possible to assess the safety of TDCS for higher cognitive functions such as language, reading, or mathematics via standard pre-clinical experimental routes (for example, using animal models). As the mature brain and the developing brain differ in anatomy and function [↑ 2], data on the effect of TDCS on the mature brain may not reveal possible side effects of stimulating a developing brain. Further, the atypically developing brain may respond differently from the typically developing brain. Thus, it seems impossible to gather adequate data on efficacy and side effects without testing the specific target population directly. In addition, it is still unclear whether adverse effects might occur in younger subjects that do not seem to appear in adults (for example, seizures or cognitive impairments).

Some might argue that in light of this lack of understanding, scientists should not proceed to examine the potential use of TDCS in children. The issues that we raise in this section are indeed difficult to address. However, we believe that failing to address them would deprive a large population of children of potentially improved psychological abilities, which will have adverse individual and social implications [18]. For example, enhancing the

mathematical skills of children opens up wider employment opportunities for them and benefits society in general [18].

## **NIBS, behavioural training and cheating**

Much of neurorehabilitation and therapy requires patients to re-learn old or acquire new ways of implementing behaviours because the normal neural pathways have been compromised by injury. Evidence from healthy controls suggests that NIBS can boost psychological functions [5,7]. Combining NIBS with an appropriate training regime may boost the gain of the rehabilitation intervention, yielding larger and long-lasting functional improvements. With this approach, the behavioural training is the key driver of change, but NIBS may play an important role in ‘priming’ the neural environment, making the brain more receptive to the training effects.

An intriguing and open question that is of clear scientific, clinical and ethical interest is whether NIBS-induced changes would be specific to the trained tasks only, or whether the beneficial effects might generalize to other kinds of performance. Generalization of skill learning is usually desirable, but needs to be balanced against the concern that NIBS-enhanced performance on one cognitive measure may entail decrements on other measures [16].

The current consensus is that TDCS is likely to prove most effective when coupled with appropriate behavioural training. If this is true, it reduces a common objection to cognitive enhancements: the objection that artificially induced capacities do not belong authentically to the person. We think that the widespread view that individuals can make aspects of their personality authentically their own by taking responsibility for them through protracted use is extremely plausible. This consideration would also reduce the force of the objection that enhancement constitutes cheating — gives the person an unearned and therefore unfair advantage — to the extent to which that worry rests on the thought that the enhanced ability comes to the person without requiring an investment of effort. It might also suggest that one of the most effective — and ethically controversial — ways of achieving effective enhancement is by intervening during early development and affecting learning and the acquisition and consolidation of cognitive abilities. In this respect, the attribution to TDCS of the label that it a ‘thinking cap’ [10] might be erroneous as it does not cause thinking per se, but depends primarily on the learning process.

## **Conclusions and future directions**

NIBS, and more specifically TDCS, could prove to be an important means of treating psychiatric disorders, neurological conditions, and currently intractable disorders of psychological development. It could also improve psychological processes in the healthy population, and thus offer benefits at the individual and societal level [18]. But there is a substantial risk that it could be utilized prematurely, before proper protocols are established, and potentially before unwanted side effects are well understood, especially with regards to children.

To overcome these obstacles, we suggest starting by translating established research findings from adults (which have shown TDCS to be safe and effective) to children. Both atypically and typically developing children may be justifiable subjects, although it could be that only one type of population might benefit from the usage of NIBS. However, the following safeguards are important: First, data about psychological side effects should be collected, including medium term (say, three to six months) and long term (say, one year) follow-ups after the initial intervention, using a variety of tests to assess potential long-term effects on the psychological processes of interest, as well as on other psychological functions. Because of the time constraints, it is only possible to examine children on a limited number of tests. We suggest that the particular tests should be decided based on the involvement of the stimulated brain area and nearby brain areas in other psychological functions. However, it is possible that psychological functions that are subserved by remote brain areas would be affected as a result of reallocation of blood flow and energy substrates (such as oxygen) to the stimulated brain area. Therefore, at the first stage a variety of tests should be used, and if there is no trend for psychological side effects, these tests should be replaced with other tests on the same type of population.

Second, experiments in children should start with small samples to avoid exposing a large population to potential risks. Once the desired effect of TDCS has been established, the experiments should be scaled up to larger randomized double-blinded controlled trials.

Third, the population should be recruited from different social-economic classes and ethnic groups, and barriers which would inhibit the recruitment of a wide spectrum of children should be eliminated.

Fourth, the developing brain should be monitored for possible neurochemical, anatomical, and functional changes that are associated with TDCS. This can be achieved by using non-invasive and safe neuroimaging methods such as magnetic resonance spectroscopy, diffusion tensor imaging, functional MRI, electroencephalography or near infrared spectroscopy. Assessment should focus not only on the intended induced neural alterations in the stimulated brain area, but also monitor for possible changes in remote brain areas that mediate other psychological functions.

Another issue is whether the effects shown by NIBS are clinically significant. What is the ecological validity of findings in a lab to everyday life? As with every new technology, most of the results so far are from controlled experiments in a lab setting. Therefore, the current results are based mainly on improvements at the level of milliseconds or percentage accuracy. However, some findings have shown that TDCS is able to improve performance not only quantitatively but also qualitatively by inducing a profile of behaviour that matches a more advanced developmental stage [2]. Others have shown that TDCS can be used to improve naming ability in patients with chronic aphasia [19]. The future use of NIBS, and its possible application in clinical settings or educational systems, should provide further evidence as to whether the current findings with NIBS have a real-world value as a therapy or enhancement in settings outside the lab.

There are also other pending questions that need to be addressed in the future such as: who should be funding this type of research, particularly if it might become obligatory for parents? Is it too risky for parents to permit their children to participate in NIBS experiments given the current state of knowledge? If yes, how is such participation different from other strenuous and risky things parents are allowed to do (such as crossing the road at a red light with their child or allowing a child at the beginning of primary school to have a mobile phone)? If there are unforeseen adverse side effects, how should we attribute responsibility and blame?

In sum, ethical obstacles can and should be overcome. If it is handled judiciously, TDCS could prove to be an inexpensive and widely-deployed technology with substantial benefits to individuals and society.

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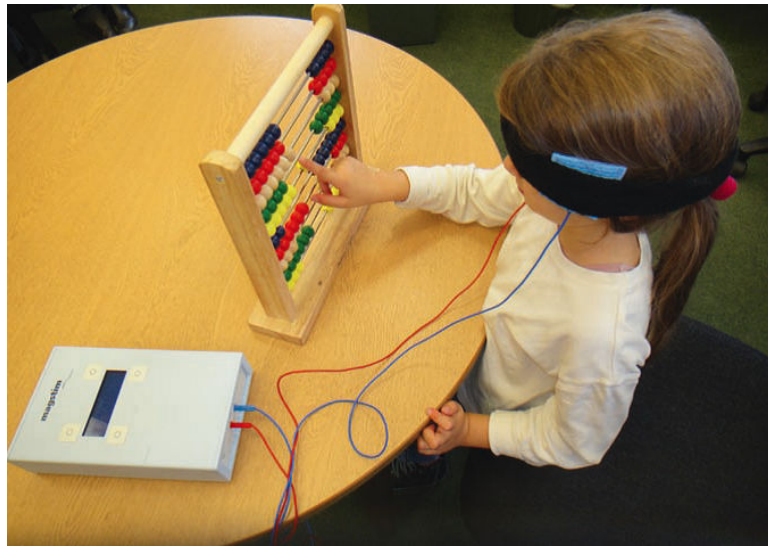
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**Figure 1.**

Ethics of using non-invasive brain stimulation in children. The usage of non-invasive brain stimulation in children to improve psychological functions raises many important scientific and ethical questions, such as: Which is the appropriate brain area to be stimulated? What is the effect of brain stimulation on the developing brain? Is there a possibility that cognitive enhancement of some abilities occurs at a cost to others? Might there be currently unknown safety and potential hazards at the psychological level and physiological level? The current picture is for demonstration purposes only. We discuss what necessary steps are needed in order to allow typically and atypically developing children to benefit from the usage of non-invasive brain stimulation.