Ethical Aspects of Transcranial Magnetic Stimulation for Neuroenhancement

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Aspectos éticos de la estimulación magnética transcraneal para la mejora neuronal

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ISSN 1989-7022

Abstract: The non-invasive stimulation techniques are already recognized as technology that allows neuroenhancement, specifically the Transcranial Magnetic Stimulation (TMS) can be applied following potentiation protocols in order to enhance both cognitive and motor systems. Hand in hand with this capacity arises the ethical problem of its application. The objective of this contribution is to describe and discuss what ethical aspects have been established in relation to this current phenomenon. Thus, we will describe the mechanisms and results of non-invasive technology in relation to neuroenhancement, focusing on TMS enhancing protocols. Next, we will make a brief historical review of the ethical aspects established around the application of TMS and its ability to result in neuroenhancement. Finally, we will discuss the ethical aspects that have been described, developing new debates and concluding on a broad vision of neuroenhancement ethical factors.

Keywords: Non-invasive Stimulation, Transcranial Magnetic Stimulation, Neuroenhancement, Safety issues, Disruptive Technology

Resumen: Las técnicas de estimulación no invasiva son ya reconocidas como una tecnología que permite la potenciación neuronal, concretamente la Estimulación Magnética Transcraneal (EMT) puede ser aplicada siguiendo protocolos de potenciación con el fin de potenciar tanto los sistemas cognitivos como los motores. De la mano de esta capacidad surge el problema ético de su aplicación. El objetivo de esta contribución es describir y discutir qué aspectos éticos se han establecido en relación con este fenómeno actual. Así, describiremos los mecanismos y resultados de la tecnología no invasiva en relación con la neuropotenciación, centrándonos en los protocolos de potenciación de la EMT. A continuación, haremos un breve repaso histórico de los aspectos éticos establecidos en torno a la aplicación de la EMT y su capacidad para dar lugar a la neuropotenciación. Finalmente, discutiremos los aspectos éticos que se han descrito, desarrollando nuevos debates y concluyendo en una visión amplia de los factores éticos la neuromejora.

Palabras clave: Estimulación no invasiva, estimulación magnética transcraneal, neuromejora, cuestiones de seguridad, tecnología disruptiva

Arantzazu San Agustín & Juan Camilo Moreno: "Ethical Aspects of Transcranial Magnetic Stimulation for Neuroenhancement", en Jon Rueda (ed.): *Tecnologías socialmente disruptivas*
ILEMATA, Revista Internacional de Éticas Aplicadas, nº 34, 121-132

1. Introduction

Neurological interventions such as brain stimulation techniques are part of the most frequently mentioned branches when it comes to define neuroenhancement (Clark, V. P., 2014; Chatterjee, A., 2013). Since it has been shown that the stimulation in optimal time and brain location is giving as a result the improvement of both cognitive as well as motor nervous systems and therefore an improvement in behavioral capacity, the ethical issues regarding the technique have been addressed.

The aim of this contribution is to discuss the ethical aspects of the neuroenhancement focusing on the brain process potentiation that results from the Transcranial Magnetic Stimulation (TMS) technique.

Therefore, we will begin by describing the basic mechanisms of brain stimulation and the differences between invasive stimulation, such as Deep Brain Stimulation (DBS), and non-invasive brain stimulation (NIBS), such as transcranial Direct Current Stimulation (tDCS) and Transcranial Magnetic Stimulation (TMS), in order to understand how these techniques are influencing neuromodulation of the nervous system. Through this study, we will focus on TMS application as a technique that modify the excitability of the nervous system and therefore neuromodulate its activity.

Received: 06/12/2020
Accepted: 24/12/2020

ISSN 1989-7022

We will describe the TMS electrophysiological mechanisms and the neuroenhancement results in experimental research in regards of neuropsychiatric diseases and motor disorders. Then, we will review the addressed ethical aspects throughout the history of TMS in relation to its safe application, to its description of what is considered an ethical therapy and to its definition of neuroenhancement as a point to mention in the ethical considerations of the TMS application guidelines.

Finally, we will put on the table the discussion of the previously described concepts, exposing a possible technological development of TMS and its relationship with the ethical application in the private sphere, as well as debating the effects that neuroenhancement can have in patients and in healthy subjects, opening a broader approach for further discussion.

2. Neuroestimulation Technologies: Basic Mecanisms and Therapeutic Application

Throughout human history, the different technologies of electrical or magnetic stimulation have emerged with a desire to modify the nervous systems state to palliate possible ailments and discomfort in the human body, with the aim of finding a better quality of life.

Nowadays, technically we call these changes by the name of neuromodulation, understood as the potentiation, inhibition, modification, regulation or therapeutic alteration of nervous activity, whether of the autonomic, peripheral or central nervous system (Krames, E. S. et al., 2009). The International Neuromodulation Society (INS) defines it as the technology, either electrical or pharmaceutical agents, applicable directly to the nervous system, which affects every area of the body and treat nearly every disease (The International Neuromodulation Society, 2020). Thus, for INS, neuromodulation is an industry that could have great growth for the next decade.

The idea that the nervous system could be altered by external stimuli arose as early as 43 CE, treating pain with baths in which electric torpedo fish were swimming, or applying them directly to the affected body region (Pascual-Leone, A., & Wagner, T., 2007). The electrical shocks that resulted from this practice appeared to have an effect on the activity of the spinal cord and brain, producing temporary pain relief. Later, over the centuries, this purpose has been applied with more sophisticated technologies that involve devices with current intensity control and its application was performed by electrodes in specific locations.

The modern era of neuromodulation began in the 1950s with the use of DBS, the application of intracerebral electrodes, in order to alleviate the symptoms of chronic pain (Nardone, R. et al., 2014). Later, in 1974, a less invasive technique was developed, in which the collocation of electrodes was outside the subarachnoid tissue, one of the meninges that cover the brain. This avoided the secondary effects of invasive stimulation risks, such as spinal cord compression and leakage of cerebro-spinal fluid (The International Neuromodulation Society, 2020). [For a more extensive review of the history of neuromodulation see Gildenberg, P. L. (2005)].

Thus, there are different varieties of stimulation of the nervous system as a technique to neuromodulate the excitability of a tract or a nervous system. These techniques can be classified in two groups: invasive and non-invasive stimulation, which today both versions are used, depending on the needs of the patient, their disease or the basic research target.

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On one hand, invasive stimulation techniques are those that require surgery to implant the electrodes. The intra-brain implanted electrodes enable the stimulation in deep areas of the brain, which currently are not possible to reach from an external region of the head with precision. The most popular electrical stimulation of this type is the aforementioned DBS.

The DBS technique involves the implantation of a battery-operated medical device (neurostimulator) by a surgical treatment that stimulate specific areas of the brain (Nardone, R. et al., 2014). The therapeutic application of DBS has shown notable benefits for patients in treatment resistant state in motor disorders and cognitive-affective impairments, such as chronic pain, Parkinson's disease, tremor, dystonia and obsessive or compulsive disorders. Yet the precise action mechanism of DBS remains uncertain (Kringelbach, M. eta al., 2007).

On the other hand, there are NIBS techniques (non-invasive), such as tDCS and TMS. In this neurostimulation modality, the electrodes are located in the skin of the head without the need for any type of intervention that requires surgery. Thus, their use avoids the postoperative recovery phase of the patient and allows the application of stimulation in healthy subjects, being a benefit for the investigation of basic physiology of the cerebral systems.

The tDCS application require a small direct current through the brain between two electrodes placed on the scalp, usually one over the target cortical area and the other one over the contralateral area of the head. The stimulation can be either cathodal tDCS or anodal tDCS, depending on the discharging direction. Not seizure is induced due to the weak (usually ≤1 mA) current and the brain has time to accommodate to it (Higgins, E. S. et al., 2019). The application of tDCS has been proved beneficial in a wide range of motor and cognitive disorders, such as stroke, refractory epilepsy, chronic depression, drug cravings and chronic pain conditions like fibromyalgia and traumatic spinal cord injury (Stagg, C. J., & Nitsche, M. A., 2011).

Another NIBS is the magnetic one, called TMS. This technique is not applied with electrodes, but rather approaches the area of interest in the brain through a coil, which rest by the subject's scalp. An electric current runs through this coil, and by the Faraday's law of magnetism induction, short high intensity magnetic fields are generated, which trespass the cranium and elicit electric currents in the cerebral cortex. The triggered current induce a depolarization in neurons of the reached brain regions (Hallett, M., 2000) and thus, its activation. The TMS has two applications. On one hand, the assessment of the excitability state of the motor nervous system, by measuring the amplitude of the muscle potentials that it induces. These are called Motor Evoked Potentials (MEP). On the other hand, TMS can trigger in the nervous system neuromodulation mechanisms. The application of a single pulse of TMS by itself does not have a neuromodulatory effect. Its application has to follow a series of time and location configuration so that the promotion of plastic changes in the nerve pathways is possible. There are different protocols that promote a change, and specifically an enhancement, which is reflected on a greater excitability of cellular electrical activity and further behavioral functions.

The potentiation protocols can be classified in two broad subgroups: 1. Repetitive TMS (rTMS): a train of high frequency TMS pulses, typically between 1Hz and 50Hz, applied at a constant intensity and brain area (Rotenberg, A. et al., 2014). 2. Paired Associative Stimulation (PAS): the synchronization of a single TMS pulse with another exogenous or endogenous stimulus that induce an activation paired at the same or interconnected nervous localization.

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The Hebb's principles explain the effectiveness of PAS application, due to the description of the plastic mechanisms involved in synaptic efficacy changes when the activation of two close in location neuros happens synchronously in a repetitive basis (Hebb, D. O., 1949). Thus, PAS protocols are based on the cooperativity among coactive afferents mechanisms; when concurrent fibers are high frequency activated, an activity enhancement is produced, whereas the same fiber stimulation separately failed to be effective in potentiation (McNaughton, B. L. et al., 1978).

The stimulus that is applied for the activation of nervous system and coupled with the TMS activation can be of different nature. The original PAS protocol was administer pairing a TMS single pulse in motor cortex synchronized with a peripheral electrical stimulus in the medial nerve of the arm with an Inter Stimulus Interval (ISI) of 25ms (Stefan, K. et al., 2000). Subsequently, other protocols converging diverse stimuli have emerged. The convergence of two TMS pulses, one in each hemisphere, also called Paired Bihemispheric Stimulation (PBS) has been developed for its application (Rizzo, V. et al., 2008). As well as the pairing of TMS pulse with a endogenous activation of motor cortex triggered by the performance of a movement while carrying out a motor task, called task-related PAS protocol (Thabit, M. N. et al., 2010; San Agustín, A., et al., 2018).

The configuration of pairing an endogenous activation opens the way to PAS application in cortical areas that do not connect with an afferent peripheral pathway to be excited by an electrical stimulus, like sensory-motor cortex do. By this configuration approach, the areas related to higher processes can be activated by a cognitive task and paired with a TMS pulse if their location allows it, for the enhancement of their synaptic plasticity and their behavioral function (San Agustín, A., & Pons, J. L., 2019).

The therapeutic application that TMS provides has already been tested in different combinations for the benefits of neuropsychiatric diseases such as depression disorder and drug-resistant major depression, as an alternative to pharmaceutical therapy. In addition, it is also emerging as a therapy in other diseases such as posttraumatic stress disorders, auditory hallucinations (schizophrenia disorder), chronic pain, epilepsy, aphasia, and there are new anatomic-functional targets for the treatment of obsessive compulsive disorder. The benefits for motor disorders have also been shown already in acute stages of stroke patients (Rossini, P. M., & Rossi, S., 2007).

In addition, TMS is also applied in healthy subjects for the investigation of the basic neurological mechanisms of brain processes. Nowadays, it is pointed out by experts in the regulation of TMS practices that the effects on cognition are generally low or modest. As well as changes in motor behavior for example reaction times (RT), error rates, recall rates and motor accuracy has very short-lived results and rarely extend the time of stimulation for longer than tens of minutes when assessed (Rossi, S. et al. 2020). There are studies in which improvement is maintained in changes of Reaction Times of 30 minutes (Thabit, M. N. et al., 2010; San Agustín, A., et al., 2018).

In any case, it is being more and more utilized and more results are appearing from research in this framework. The configuration of what stimulus to pair, in what location apply it and in what specific time has an increasing development of information to result in a potentiation of the target nerve pathway. The enhancement of the brain pathways, in turn, leads to the alteration of behavior associated with the cognitive process in which the TMS therapy is being applied.

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3. Historical Approach to TMS Ethics

The application of TMS has gone hand in hand with a consensus on the ethics of its application since at least 1998, when a report and suggested guidelines were defined for the correct application of TMS (Wassermann, E. M., 1998). In this way, consensus conferences have been established on several occasions in 2008 and 2018 to update these guidelines, resulting in a series of ethical points around this stimulation. The most up-to-date guidelines at this time are those specified in the article "*Safety and recommendations for TMS use in healthy subjects and patient populations, with updates on training, ethical and regulatory issues: Expert Guidelines*" still in press, based on the meeting promoted and supported by the International Federation of Clinical Neurophysiology (IFCN), which took place in Siena (Italy) in October 2018 (Rossi, S. et al., 2020).

At this conference, new topics related to the practice of TMS that had arisen since the last meeting were discussed, leaving the recommendations that had already been described and debated in 2008 as valid. For example, the description of conventional or patterned TMS protocols, the screening of subjects and patients, the need of neurophysiological monitoring for new protocols, the utilization of reference thresholds of stimulation, the managing of seizures and the list of minor side effects (Rossi, S. et al., 2009; 2020). At that time, the ethical aspects of the application of TMS were focused on the risk that the patient could suffer and their ability to understand it. The proposal to do an ethical TMS therapy was based on the gain that the patients had in relation to the damages that they could suffer, which with the application of TMS were few although existing.

They described three fundamental ethical pillars on which the basic and clinical application of TMS is based. The first was based on **informed consent**, where the subject to whom the TMS is applied has to give voluntary consent when participating in the experimental procedures. In addition, the volunteer to be considered suitable to accept participation must be duly informed about the procedures to be carried out, as well as the possible risks and discomfort that she or he could feel. The researcher has to make sure that the experimental explanation is in terms that the subject can understand and that she or he has actually done so.

The second and third concepts are in regard of the **risk and benefit** of the application of TMS. Not only it is necessary that the subject is willing and has understood the risks involved in participating in brain stimulation processes, it is also a requirement the gain to be greater than the risk. In addition, there should be no other alternatives of scientific methodology by which to obtain the same data. This clinical policy is extrapolated to vulnerable populations due to various factors such as economic, social, or physical conditions, or patients with a specific type of disease, where the population itself should have more benefits than burdens as a result of the TMS application.

In the last review of the ethical issues of the TMS therapies application (Rossi, S. et al. 2020) we find a special mention to neuroenhancement, defined as "*Any augmentation of core information processing systems in the brain, including the mechanisms underlying perception, attention, conceptualization, memory, reasoning and motor performance*" (Luber, B., & Lisanby, S. H., 2014). In addition, they specified which improvements from a basal nervous system starting point (healthy state), have been performed in cognitive functions regarding specific brain areas stimulation: in Dorsolateral Prefrontal Cortex (DLPFC): planning and deceptive abilities,

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risk-taking and impulsivity, attention and logical reasoning; in inferior Frontal Cortex: deceptive abilities and attention; in posterior Parietal Cortex (PPC): attention; in Primary Motor Cortex (M1): motor control; and finally; in temporoparietal junction: working memory.

The TMS committee of experts on safety, ethical considerations and application already conceives this concept as a possible "brain-doping" that carries with it a social and ethical problem. This phenomenon will need to be addressed by focusing on the development of a safety policy that will require an analysis of the risks and benefits in both adults and children (Rossi, S. et al., 2020).

The debate on this ethical aspect of the TMS application for the possible induction of supernormal capacities of brain activity brings to the fore the debate of the Transhumanist current in philosophy. This philosophical current can be defined as "*Philosophies of life that seek the continuation and acceleration of the evolution of intelligent life beyond its currently human form and human limitations by means of science and technology, guided by life-promoting principles and values*" (More, M., 1990). In this debate, there is also the concern to prevent and recognize the risks, as well as to minimize the costs of the application of technologies for the improvement of human capacities, reaching the conclusion that applying this technology in a thoughtful and careful way we can become something describable as posthuman (More, M., 2013).

TMS has been proposed as a neuroenhancement device that today would be under control given that its results are still not on a scale as high as those that pharmacological agents can have (Rossi, S. et al., 2020), however the research of its neuroenhancement capability is growing and the discussion of its ethical application should be an actual concern in order to prevent unwanted future consequences. In relation to this concept IFCN has made a public statement (quoted in Wurzman, R. et al., 2016) that, NIBS should be applied only under medical supervision.

4. Discussion: Ethical Aspects of TMS Application

4.1. Regarding the directly to consumers and do it yourself use of TMS

The TMS technology is evolving. Right now it disposes of a static and heavy coil (flats and conical), which like all technology will adapt to new times until it will become wireless and lighter in order to be wearable. In addition, today's coils are not ergonomic; they cannot be adapted to the shape of the head. Other brain areas apart from the motor cortex are already being researched with this technique, and they are not as accessible as the frontal cortex, which basically allows the coil to be applied on top of the head. To reach brain regions like the occipitotemporal or parietotemporal lobe, the coils (especially with conic coils) would be much more efficient if they could be adaptable. Thus, this need will make its development run its course, the TMS would be easier to apply, and finally it could be used on a wireless state, facilitating its continuous use. In addition, a dynamic application of TMS would provide more forms of therapy, for example, motor therapies where the neurorehabilitation training could be done while the patient is walking. Along with mobility, we also have to relate cognitive processes such as spatial memory, or a series of processes that could be measured and neuromodulated in a more immersive environment and more related to the activities of daily living (ADL).

Nowadays, NIBS devices, especially tDCS, are being sold directly to consumers (DTC) for an application related to neuroenhancement in the field of health (cognitive or physical). However, the scientific explanation to consumers behind its sale in most cases was associated with general studies, not necessarily linked to the specific technology they sell, or literature that was irrelevant to the device (McCall, et al., 2019). In addition, the do it yourself (DIY) process to develop tDCS, not TMS (Dubljević, V., 2015), is relatively easy to build and therefore, it has attracted the attention of the non-specialized public (Jwa, A., 2015; Fitz, NS, & Reiner, PB, 2015).

This technology is already reaching private spheres without adequate regulation, without scientific control of its device-specific effects and without adequate consumer information. A regulation and supervision of neuro-devices is crucial, otherwise technology can come against us, since if they are not used properly, it can result in two scenarios: A) it will not give the expected results, which will cause frustration in users and an ineffective functionality notion of NIBS technology in society, and B) the users could be harmed and their use could be the opposite of what was expected.

Although NIBS has the potential to promote neuroenhancement, this technology is dependent on different precise factors for its effective application such as the stimulation frequency, the precise stimulation timing, user state when stimulating, the stimulated brain area or part of the body and, if paired pulse is applied, appropriate interstimulus time (ISI) and type of combination of stimuli. Currently, the specialists and neuroscientists in NIBS field are aware of them, however, it is not information that is broadly directed to user level.

In addition, there are different problematic factors, apart from those basically recognized: possible skin burns due to heating, effects in the interaction with intracranial metal implants, drug or pharmacological treatments, or with pregnancy (Rotenberg, A., 2014). The DIY application may not take in consideration at the time of apply NIBS the following factors: the location where the stimulation is applied is interconnected with other brain regions where its physiology may be altering (Wurzman, R., et al., 2016), the brain compensation mechanism by which enhancing a cognitive process can suppose the weakening of another (Iuculano, T., & Kadosh, RC, 2013), the high inter-subject variability effects given the difference in anatomy and intrapersonal physiology, the polarity of the stimulators can reverse the stimulation into impairment, and the consideration of its effects can be long-lasting (Wurzman, R., et al., 2016; Fitz, NS, & Rei Ner, P. B., 2015).

Therefore, we believe that the use of NIBS in society for its neuromodulation should be regulated for its distribution and particular use, although the control over the application of these devices that can be relatively easy to develop, supposes a challenge. There are currently regulatory proposals such as the regulatory model of cognitive enhancement devices (CEDs), that proposed CEDs to be covered by the Medical Devices Directive (MDD), since these CEDs have similar mechanisms and risk-profiles to some medical devices (Maslen, H., et al., 2014). Other authors highlight the need to perform an in-depth analysis of the DIY users and their community, regarding how they use NIBS devices and the reason why they use it (Wexler, A., 2016). Besides the need for open communication and education, as the National Science

ISSN 1989-7022

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Advisory Board for Biosecurity wanted to promote, in order to develop a culture of responsibility by DIY practitioners (Fitz, NS, & Reiner, PB, 2015; National Science Advisory Board for Biosecurity, 2011). We believe that the combination of both approaches would be viable and desirable for the appropriate use of these devices in amateur users.

In addition, based on the previous discussion, we defined three essential elements that regulations and communications for DIY users should contemplate:

1. The NIBS devices use should conform a defined application protocol that encompasses the necessary characteristics (location, time, state of the subject, frequency, pairing and ISI) for a specific expected result.
2. For the application of market devices, a device-specific risk and damage control should be determined taking into account the user application frequency (e.g. every day for a year).
3. The action mechanisms of NIBS are not completely known, thus, it is crucial to promote further research on the neurophysiological aspects of NIBS to understand the complete cognitive alterations triggered by neuroenhancement.

Nevertheless, the conformation of the group to regulate the use in the private area must be integrated of both professionals in relation to the NIBS, and the extended community of DIY users. In addition, the reasons that society gives importance to the use of this technology should be taken into account and thus, analyze the trend that the use of NIBS devices will have in the future.

4.2. Regarding patient-to-healthy spectrum

In patients, the enhancement of brain processes is aimed at the rehabilitation of the system related to the patient's disease and to restore the symptoms that derive from its malfunction. Therefore, the desired result of the TMS application in these cases is the positioning of the patient to a basal state (a healthy or homeostatic state) and do not exceed the average ability baseline.

In this case, NIBS technologies for neuromodulation bring with them an improvement over invasive ones, which provides a decrease in the risk of the surgery inherent to invasive stimulation. Furthermore, this technique is an alternative to diseases in which the pharmacological route is not giving definitive results of improvement of symptoms or in the cases that the patient is not responding to them.

Therefore, in the case of the application of neuroenhancement using TMS in patients, the clinical application of TMS can be consider ethically applied given that risks are very low compared to the benefits, and the neuroenhancement is directed to reverse the symptoms of a disease.

The ethical dilemma in this framework would come when the improvement is applied on a subject with a condition that is difficult to define between the disease and a not desirable state in the healthy range, or a completely healthy subject. In this debate, the neuroenhancement implications of the NIBS can be found in different social spheres.

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In the academic world, like the pharmacology use to improve attention and concentration such as methylphenidate (Franke, A. G., 2015), the application of NIBS could be related to "brain-doping". This concept is related to acting in an illegitimate method to achieve a goal in an unequal way compared to other people against whom it is competed. Therefore, it could, be considered a misuse of technology in addition to opening the gap between low-access users compared to subjects with high purchasing power in competitive results. However, it has also been considered that given the low cost and the relatively easy development of technology using DIY techniques, the gap in access to this technology would be smaller (Pustovrh, T., 2014).

Nevertheless, there could be situations of selective discrimination, creating a gap between the population that could access the knowledge of building the technology compared to those that could not, partly possibly in relation to the socioeconomic condition of each person. For this reason, the ethical perspective of the application of these technologies should establish the foundations on which the next development of stimulation technologies for neuroenhancement is based.

In the workplace, increasing cognitive capacities is important for worker's function and productivity, which leads to the approach of scenarios where the coercion of the application of technologies due to the pressure to maintain competitiveness could be happen. As well as the possibility of extension of tasks and duties beyond those requested in an unimproved scenario (Pustovrh, T., 2014, Dubljević, V. et al., 2020). Therefore, the risks associated with this area could be derived from an abusive and coercive use of the devices in favor of the productivity of the market on the workers and its possible secondary effects of neurological fatigue and stress.

Beyond cognitive neurostimulation, NIBS technology could cause adverse social effects in relation to its affective enhancement aspect linked to changes in the user's personality. Affective enhancement is related to alterations in mood, motivation, removal or blunting unpleasant memories and the modification of personality (Erler, A., & Forlini, C., 2020). This neurostimulation, as cognitive neuroenhancement, has promising potential in use with patients with mental illness and in combination with psychotherapy (Bajbouj, M., & Padberg, F., 2014). However, when applied to healthy subjects, it raises an ethical problem in relation to the possibility of limiting personal autonomy or using it to coerce the user (Cabrera, LY, et al., 2014) and could affect authenticity and personal identity (Bublitz and Merkel, 2009). The use of NIBS for affective alteration could be coercive when applied towards unethical objectives such as marketing or political purposes.

We believe that this capacity is one more reason to promote research, analysis and discussion on the ethically appropriate use of this technology and its subsequent regulation.

Therefore, we conclude that the ethics of the application of TMS should be addressed, in addition to focusing on the subject in which it is applied (either because they have given their consent or because of the risks that it may carry), also focused on the results that it can bring to society. In addition to debating whether it could become a beneficial enhancer technology, and on what functional aspects it could be applied, we should already establish ethical foundations by analyzing the factors of its social and political impact.

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5. Conclusion

In this study, we have reviewed the neuroenhancement resulted by the different NIBS techniques, emphasizing the TMS, and its historical review of the ethical approach, specifically by the IFCN, focused on informed consent, and on the balance of risk- benefit.

We believe that like tDCS devices, users in private spheres will have access to the TMS application. We have currently reported that there is a commercialization of NIBS devices, especially tDCS, without clear information on the mechanisms of action and their risks. In addition, there is a significant community of DIY users of tDCS that is not regulated. For this reason, we believe that a policy of application of this technology together with a clear communication is necessary and should go hand in hand with indications about its device-specific protocol and risks, in addition to being aware that not everything that this technology triggers is still known.

Regarding the application of TMS on patients, through informed consent and the benefit/risk balance, it demonstrated that the ethical problems of the use of TMS for clinical purposes is limited and, on the other hand, has a potential for broad beneficial use.

However, there is an extensive and current debate on the ethical problems that may arise regarding the application in healthy subjects. In concrete, at the academic and work fields and in an affective level, in relation to the possible socioeconomic and political gaps. Therefore, we conclude that, apart from the regulation of its use and adequate technical application given the neurological risks, its social regulation of use in the areas described should be considered.

The policy established for the application of the NIBS in these areas will depend on its ethical evaluation, i.e., the morally accepted value of its use in society. However, the NIBS, such as tDCS and TMS, still do not have a consensus on their moral status since the academic debate we previously discuss is not resolved nor its social results fully described (Dubljević, 2020). Therefore, finally we conclude that the regulations made on both the clinical and private use of the NIBS will benefit from working to reach a consensus on the ethical debate and subsequently the regulation based on their ethical meanings.

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