

Transcranial Direct Current **Stimulation**

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Introduction

Over the last decades, we have witnessed an explosive advancement in noninvasive technologies for interacting in a safe and painless way with the brain and inducing direct and indirect changes in cortical excitability (George and Aston-Jones [2010;](#page-10-0) Fox [2011\)](#page-10-0). Among these techniques, transcranial direct current stimulation (tDCS) (Nitsche and Paulus [2011\)](#page-12-0) has become recognized as a promising tool in neuroscience research not only for understanding the relationship between brain and behavior but also as cognitive enhancer (Filmer et al. [2014\)](#page-10-0). Similarly, to tACS, see Chapter "Transcranial Alternating Current Stimulation", tDCS is a "top-down" technique that indirectly modulates subcortical activity through primary network changes in

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cortical activity. Several studies have provided converging evidence showing that tDCS is suited to modulate and enhance cognitive (Kuo and Nitsche [2012;](#page-11-0) [2015;](#page-11-0) Cohen-Kadosh [2015;](#page-9-0) Shin et al. [2015](#page-12-0)) and sensory-perceptual functioning (Costa et al. [2015\)](#page-10-0). See also Chapter "The Application of Brain Stimulation and Neural Entrainment in Sport", if you are interested in the practical application of tDCS in enhancing motion perception and motor learning, crucial functions in sport science. However, by comparison, only a limited number of studies have investigated the enhancing effects of tDCS on socialcognition. Although the scarceness of research in this area, there is sufficient evidence to anticipate the potential of this technique to enhance social functioning and social decision-making.

In the present chapter, adapted from Sellaro et al. [\(2016](#page-12-0)), we intend to review the currently available findings stemming from recent studies that have successfully applied tDCS to enhance social behavior in healthy individuals. By providing this systematic overview, our goal is to help gain a better understanding of the potential of tDCS as a (social) cognitive enhancer. First, we will describe the mechanism of action of tDCS. Second, we will outline the recent available studies investigating the effect of tDCS on self-other representations. The studies point out that tDCS has promising potential for promoting social abilities. Last, we will identify potential modulators and individual differences in determining response to tDCS.

Mechanism of Action

In the classical protocols, tDCS delivers a low-intensity constant current, varying between 1 and 2 mA, via relatively large $(25-35 \text{ cm}^2)$ electrodes that are applied on the participants' scalp above brain regions of interest for a few minutes (5–20 min). At least two electrodes with opposite polarities, a positively charged anode and a negatively charged cathode, are needed, with the resulting current flowing from the anode toward the cathode (see Fig. [1](#page-3-0)). A limited but sufficient portion of the applied current enters the brain and is capable of altering spontaneous neural activity and excitability (Nitsche et al. [2008\)](#page-11-0). During the last years, new protocols have been developed, which are assumed to deliver more focal effects, or network stimulation, by aid of smaller electrodes, or multi-electrode arrangements, often based on computational modeling (Nitsche et al. [2007;](#page-11-0) Edwards et al. [2013](#page-10-0); Ruffini et al. [2014\)](#page-12-0).

The current applied to the brain via tDCS is not of sufficient magnitude to generate action potentials (Nitsche et al. [2008](#page-11-0)). Rather, tDCS causes a sub-threshold modulation of the resting membrane potential of cortical neurons, altering their likelihood of firing, and thereby affecting spontaneous cortical activity (Bindman et al. [1964;](#page-9-0) Purpura and McMurtry [1965;](#page-12-0) Nitsche and Paulus [2000\)](#page-12-0). The tDCS-induced shifts in the resting membrane potential are largely, although not entirely (see below) determined by the polarity of the stimulation. Anodal stimulation causes a slight depolarization of the resting membrane potential, which increases the probability of neural firing and, consequently, cortical excitability (Bindman et al. [1964;](#page-9-0) Purpura and McMurtry [1965](#page-12-0); Nitsche and Paulus [2000\)](#page-12-0).

Fig. 1 During tDCS, a weak constant current (1–2 mA) is delivered to the brain via (at least) two electrodes with opposite polarities: a positively charged anode and a negatively charged cathode. Current is delivered for a few minutes (10–20 min) via a DC stimulator and it flows from the anode to the cathode tDCS stimulator

In contrast, cathodal stimulation leads to a slight hyperpolarization of the resting membrane potential, and hence to decreased probability of neural firing and excitability (Bindman et al. [1964;](#page-9-0) Purpura and McMurtry [1965](#page-12-0); Nitsche and Paulus [2000\)](#page-12-0). Changes in neural activity are observed during the stimulation period and, when the current is delivered for a sufficient period of time (i.e., at least 9–10 min), such changes can remain for longer than 1 h after the stimulation (Nitsche et al. [2008;](#page-11-0) Nitsche and Paulus [2000,](#page-12-0) [2001](#page-12-0); Nitsche et al. [2003\)](#page-11-0). This makes it possible to assess the cortical and behavioral effects of tDCS both during (online) and after (offline) the stimulation. Although online and offline tDCS-induced anodal and cathodal changes in cortical excitability are associated with similar neurophysiological effects, they seem to depend on different mechanisms (Stagg and Nitsche [2011\)](#page-13-0). Broadly speaking, the primary effects of both anodal and cathodal tDCS during stimulation appear to solely depend on sub-threshold membrane polarization (Nitsche et al. [2003,](#page-11-0) [2005\)](#page-12-0). Conversely, the aftereffects of tDCS seem to depend more on synaptic modulation, which is assumed to depend on strengthening (anodal tDCS) or weakening (cathodal tDCS) glutamatergic synapses, and reduction of GABAergic activity independent from stimulation polarity (Nitsche et al. [2003](#page-11-0), [2005;](#page-12-0) Stagg et al. [2009\)](#page-12-0). However, activity of neuromodulators including dopamine, acetylcholine, and serotonin seems to play a role as well (Kuo et al. [2007;](#page-11-0) Monte-Silva et al. [2009;](#page-11-0) Nitsche et al. [2009,](#page-11-0) [2012](#page-11-0)).

The tDCS-induced changes in cortical excitability have been found to result in corresponding behavioral effects, whose direction is assumed to depend on the relation between the effects of stimulation polarity and task-dependent alterations of brain physiology (Shin et al. [2015;](#page-12-0) Nitsche et al. [2008](#page-11-0)). However, it is worth noting that all what we know about the physiological effects of tDCS, including the aforementioned link between tDCS-induced cortical and behavioral changes, comes primarily from studies that have focused on motor cortex excitability. Therefore, these principles do not necessarily apply one-to-one to stimulation of nonmotor areas, as the available evidence in fact suggests (Jacobson et al. [2012](#page-10-0)).

Besides the polarity of the stimulation, similarly to tACS (see Chapter "Transcranial Alternating Current Stimulation"), the tDCS-induced physiological and behavioral effects depend on a variety of other factors, such as electrode montage and size, current density, intensity and duration of the stimulation, but also state-dependency (i.e., the initial brain state) and inter-subject variability in terms of cortical anatomy, genetic polymorphisms, and psychological and motivational factors (Jacobson et al. [2012](#page-10-0); Datta et al. [2012;](#page-10-0) Batsikadze et al. [2013](#page-9-0); Tremblay et al. [2014;](#page-13-0) Li et al. [2015](#page-11-0)) (for further details, see Sect. "[Factors affecting tDCS](#page-7-0) [effects](#page-7-0)"). Among them, electrode montage is a crucial factor, and not just because it determines the polarity of the stimulation. As previously mentioned, tDCS needs at least two electrodes to work. Typically, one electrode (i.e., the target electrode) is placed over the brain area of interest and the other one (i.e., the return electrode) over another region (either cephalic or extracephalic). When both electrodes are placed on the scalp (i.e., bipolar cortical electrode montage) (Nasseri et al. [2015\)](#page-11-0), one needs to keep in mind that not just the target electrode but also the return electrode will have a functional effect on the area where it is placed, thus introducing an important confounding factor when such a functional effect is not desired. To avoid that, researchers may opt for the use of an extracephalic electrode (i.e., monopolar extrachepahlic electrode montage), or for the use of a larger cephalic return electrode. Indeed, the use of a larger return electrode has been shown to be an effective and easy way to allow a functional monopolar montage because of smaller current density, when current strength is kept constant (Nitsche et al. [2007\)](#page-11-0). Even in that case, however, the position of the return electrode will affect the physiological effects of tDCS, because it determines current flow direction through the brain. Current flow direction in relation to neuronal orientation is critical for the effects and direction of the effects of tDCS: for being effective, the electrical field has to meet the long axis of a neuron, and electrical field orientation in relation to neuronal orientation will determine excitability-enhancing or diminishing effects. This is the case because current has to enter and leave a given neuron to be effective. Because of higher receptor and ion channel density at the soma and axon hillock, it is assumed that current flow direction at these areas determines the effects of tDCS at the cellular level. In accordance, it was demonstrated that dependent on neuronal orientation, tDCS of identical current flow direction has antagonistic effects in hippocampal slices (Kabakov et al. [2012](#page-10-0)), and that in the human brain, return electrode positions anterior and posterior to a target electrode result in different effects with identical target electrode stimulation polarity (Antal et al. [2004](#page-9-0); Accornero et al. [2007](#page-9-0)).

Promoting Self-other Representations

In this section we describe recent studies that used tDCS to promote self–other representations.

By self–other representations we understand the ability to handle mental representations of both the self and other people—a fundamental ability for humans to engage in successful social interactions (Decety and Sommerville [2003](#page-10-0); Spengler et al. [2009](#page-12-0); Sowden and Shah [2014](#page-12-0)). Santiesteban et al. [\(2012](#page-12-0)) tested the role of the right temporoparietal junction (TPJ) in mediating the ability to distinguish and switch between concurrently activated self-related and other-related representations (i.e., self–other control) (Decety and Sommerville [2003;](#page-10-0) Spengler et al. [2009](#page-12-0); Brass et al. [2009\)](#page-9-0). In this study, anodal, cathodal, or sham tDCS was delivered over the right TPJ before participants executed three tasks, two of them requiring self-other control: a perspective-taking task (Keysar et al. [2000](#page-11-0)), which requires to inhibit one's own perspective and to enhance that of the other (Decety and Sommerville [2003\)](#page-10-0), and a imitation-inhibition task (Brass et al. [2000\)](#page-9-0), which instead requires to inhibit the other person's motor representations and to enhance the motor representations of one's own intended action (Spengler et al. [2009;](#page-12-0) Brass et al. [2009\)](#page-9-0). The third task was a mental state attribution task (Lombardo et al. [2010](#page-11-0)) that did not require self–other representations to be controlled. Results showed that anodal tDCS, compared to cathodal and sham tDCS, improved online control of self–other representations in both perspective-taking and control-of-imitation tasks, without affecting performance in the mental state attribution task. These findings therefore corroborate the hypothesis that stimulating the right TPJ may promote self–other control over coactivated representations by inhibiting one's own or the other person's representations depending on the task demands (Decety and Sommerville [2003;](#page-10-0) Spengler et al. [2009;](#page-12-0) Brass et al. [2009;](#page-9-0) Ruby and Decety [2004](#page-12-0)). Interestingly, these results were replicated in a follow-up study in which Santiestaban et al. [\(2015](#page-12-0)) obtained evidence that the assumed role of the TPJ in self-other control is not restricted to the right TPJ but extends to the left TPJ as well. Indeed, they found that, compared to anodal stimulation of a control area, anodal TPJ stimulation improved self-other control in both perspective-taking and control-of-imitation tasks, regardless of whether the right or left TPJ was stimulated. Again, they did not observe any tDCS-induced effect on performance in a task tapping the ability to infer other's mental states. Further converging evidence supporting the role of the right TPJ in the control of imitation was provided by Hogeveen et al. [\(2015](#page-10-0)). In this study, following anodal tDCS of either the right TPJ or the right inferior frontal

cortex (IFC), or sham stimulation, participants were confronted with two critical tasks: a imitation-inhibition task (Brass et al. [2000](#page-9-0)), in which better performance requires to inhibit imitative behavior, and a social interaction task (Chartrand and Bargh [1999\)](#page-9-0), in which higher mimicry levels signal better social interaction. Replicating the results observed by Santiesteban et al. ([2012](#page-12-0), [2015\)](#page-12-0), right TPJ anodal tDCS, compared to sham, improved online control over imitative behavior, without affecting the degree of mimicry in the social interaction task. Instead, anodal tDCS of the right IFC, compared to sham tDCS, was found to have a dissociable effect on both tasks: similarly to anodal right TPJ tDCS, it improved the ability to inhibit imitation, but it also increased imitative behavior in the social interaction task. These results support the hypothesis that the right IFC, compared to the right TPJ, has a more direct impact on imitation, leading to either inhibit or enhance imitation, depending on task demands (Iacoboni et al. [1999;](#page-10-0) Heiser et al. [2003;](#page-10-0) Brass et al. [2005](#page-9-0); Spengler et al. [2010](#page-12-0); Sowden and Catmur [2015](#page-12-0)).

Taken together, these studies provide converging evidence for the critical role of the right TPJ in enhancing the online control of concurrently activated self-related and other-related representations. Interestingly enough, such a role for the right TPJ has recently been proven to mediate the ability to detect lies as well (Sowden et al. [2015\)](#page-12-0). Indeed, using an offline protocol, Sowden et al. [\(2015](#page-12-0)) showed that anodal tDCS of the right TPJ, compared to anodal tDCS of a control area, improved lie-detection performance when participants were confronted with statements in which the to-be-judged opinions were in conflict with those held by the participants —a condition that in a previous experiment of the same study was found to significantly impair lie detection.

Other studies have provided evidence supporting the role of prefrontal cortex areas in promoting self-other representations. For instance, in another study the role of the anterior medial frontal cortex (AMFC) in self-other action discrimination was examined. Liepelt et al. [\(2016](#page-11-0)) delivered anodal, cathodal, or sham stimulation over either the AMFC or the right TPJ while participants performed a joint Simon task (Sebanz et al. [2003](#page-12-0); Hommel et al. [2009](#page-10-0); Dolk et al. [2013\)](#page-10-0)—a turn-taking paradigm requiring the participant and a confederate to perform complementary parts of the same task. A more pronounced joint Simon effect (i.e., reduced self-other action discrimination) was found during excitability-reducing cathodal tDCS of the AMFC but not of the right TPJ—a finding that supports the assumed role of the AMFC in enhancing the representation of self-generated actions (Spengler et al. [2009;](#page-12-0) Brass et al. [2005](#page-9-0), [2009](#page-9-0)). The absence of any tDCS effect during right TPJ stimulation instead further support the view that this area enhances online self-other control only when self-related and other-related representations are concurrently activated, as is the case in perspective-taking and control-of-imitation tasks (Decety and Sommerville [2003;](#page-10-0) Spengler et al. [2009;](#page-12-0) Brass et al. [2009;](#page-9-0) Ruby and Decety [2004\)](#page-12-0). As such, these results are in line with the results observed by Santiesteban and colleagues (Santiesteban et al. [2012](#page-12-0), [2015](#page-12-0)).

Finally, Sellaro et al. [\(2015](#page-12-0)) investigated the enhancing effect of tDCS over the medial prefrontal cortex (MPFC) in counteracting stereotypes activation resulting from in-group versus out-group categorization (Allport [1979;](#page-9-0) Greenwald and

Banaji [1995](#page-10-0))—a situation in which self and other representations can be seen as polarized on a positive versus negative dimension. In this study, increased cognitive control over stereotypes activation with a resulting reduced implicit negative bias towards a social out-group was found in the group of participants who received online anodal tDCS of the MPFC, compared to participants who received cathodal or sham stimulation—a finding that speaks in favor of the idea that the stimulation of the MPFC may promote self-regulatory and cognitive-control processes implemented to overcome unwanted responses driven by stereotypes activation (Amodio and Frith [2006](#page-9-0); Amodio et al. [2006](#page-9-0)). Interestingly, in the same sample of participants MPFC tDCS was not effective in enhancing interpersonal trust (Colzato et al. [2015\)](#page-10-0), although MPFC activity has been linked to the degree of mutual trust (McCabe et al. [2001](#page-11-0); Delgado et al. [2005](#page-10-0); Krajbich et al. [2009\)](#page-11-0).

Taken together, the studies reviewed in this section provide evidence supporting the role of tDCS over the TPJ and prefrontal cortex areas in enhancing several facets pertaining to the ability to handle self-other representations, and speak in favor of the possibility that the use of tDCS may represent a promising way to improve social abilities.

Factors Affecting tDCS Effects

In this section, we will consider the role of several factors that have been identified as playing a critical role in determining response to tDCS.

Like tACS, see Chapter "Transcranial Alternating Current Stimulation", several studies have shown that variations in stimulation parameters (e.g., intensity and duration of the stimulation, online versus offline stimulation, electrode size and number, scalp placement), can cause different amounts of electrical current to be delivered and, thus, can produce different tDCS effects. For instance, there is evidence that prolonged stimulation duration and higher current intensity can invert the polarity of the stimulation (Batsikadze et al. [2013](#page-9-0)). Likewise, in some occasions, online and offline tDCS have been found to produce differential, and even opposite effects (Stagg and Nitsche [2011](#page-13-0); Pirulli et al. [2013](#page-12-0)). Also, although tDCS effects are not focal, electrode positioning is critical. Studies addressing tDCS-induced physiological changes and computational modeling studies of the expected current flow have found significant differences in the amount and distribution of current delivered to the brain depending on the relative positions of the electrodes (Minhas et al. [2012;](#page-11-0) Kessler et al. [2013;](#page-11-0) Woods et al. [2015\)](#page-13-0). For instance, it has recently been shown that a drift of just 1 cm in electrode position causes a significant alteration of the distribution of the current flow and of the intensity of stimulation delivered to the brain (Woods et al. [2015\)](#page-13-0). This is not surprising given that tDCS physiological and behavioral effects depend on the relation between current flow direction and neuronal orientation in the target area (Kabakov et al. [2012\)](#page-10-0) and, thus, variations in electrode position are likely to alter such a relation. Importantly, this means that undesired drifts in electrode position during stimulation, due to a

superficial or an inappropriate placement of the electrodes, can seriously undermine reproducibility of the effects. Therefore, more efforts should be made in the attempt to create optimized procedures that can guarantee a stable placement of the electrodes on the scalp.

Computational models have suggested that individual anatomical differences can affect the current flow through the brain during the stimulation (Datta et al. [2012;](#page-10-0) Truong et al. [2013](#page-13-0)). Moreover, hair thickness may contribute to the observed variability in response to tDCS, as it may lead researchers to use a large amount of saline solution to saturate thicker hair (Horvath et al. [2014](#page-10-0)). Oversaturation of the electrode sponges can cause saline solution to spill over the sponges, with the consequence that the entire area of the scalp that is covered in saline will receive stimulation. Obviously, this can severely undermine reproducibility of tDCS application and effects. Also, tDCS effects have been found to depend on the baseline status of the brain, which can substantially vary across individuals (Antal et al. [2007](#page-9-0); Benwell et al. [2015](#page-9-0)). Besides that, there is evidence that other factors such as age, gender, genetic polymorphisms, and psychological/motivational factors can influence the direction and the extent of the cortical and behavioral modulation (Krause and Cohen-Kadosh [2014\)](#page-11-0). Therefore, to improve our understanding of whether and to what extent tDCS can enhance social behavior, it would be necessary for future studies to consider the role of interindividual differences. This implies testing sufficiently large samples to enable a deeper investigation of tDCS effects that can take into consideration and control for the role of interindividual variability. Moreover, computer modeling of the current flow through the brain can provide valuable information to be used to create optimal electrode montages for a given target area and head anatomy (Ruffini et al. [2013\)](#page-12-0).

In sum, a detailed investigation of the factors that may influence tDCS-enhancing effects on social cognition in terms of both stimulation parameters and interindividual differences is highly advisable, especially given the recent controversy about the effectiveness of tDCS in modulating and enhancing cognitive processes (Horvath et al. [2015a,](#page-10-0) [b](#page-10-0)).

Conclusion

Transcranial direct current stimulation has the potential to enhance social cognitive functioning by modulating brain excitability through weak, direct electric currents. tDCS seems to be sensitive to individual differences suggesting the necessity to take into account these differences in order to predict the enhancing response to tDCS. In particular, anodal tDCS over TPJ and prefrontal cortex areas seems to enhance the online control of concurrently activated self-related and other-related representations and to promote the ability to handle self-other representations. However, optimal protocols of stimulation (e.g., intensity and duration of the stimulation, online versus offline stimulation, electrode size and number, scalp placement) still need to be identified. Further, in order to find straightforward evidence that tDCS

improves social cognition, homogeneity across different studies, also in terms of study design and the specific task/questionnaire used, should be advisable. It is important to point out that extensive research is needed to confirm whether the observed tDCS enhanced social cognitive effects are maintained over time. While previous studies have shown that repetitive sessions of tDCS can intensify the effects of stimulation for memory, visual perception, and motor learning (Nitsche and Paulus [2011](#page-12-0)), it still needs to be explored whether the same applies to social cognitive functions. Although more research is needed to fully understand the effects tDCS exert on social cognition, we conclude that tDCS is a promising tool to improve social abilities.

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