



Can we rewire criminal mind via non-invasive brain stimulation of prefrontal cortex? Insights from clinical, forensic and social cognition studies

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Accepted: 10 May 2022

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Abstract

Non-compliance with social and legal norms and regulations represents a high burden for society. Social cognition deficits are frequently called into question to explain criminal violence and rule violations in individuals diagnosed with antisocial personality disorder (APD), borderline personality disorder (BPD), and psychopathy. In this article, we proposed to consider the potential benefits of non-invasive brain stimulation (NIBS) to rehabilitate forensic population. We focused on the effects of NIBS of the prefrontal cortex, which is central in social cognition, in modulating aggression and impulsivity in clinical disorders, as well as in forensic population. We also addressed the effect of NIBS on empathy, and theory of mind in non-clinical and/or prison population. The reviewed data provide promising evidence on the beneficial effect of NIBS on aggression/impulsivity dyscontrol and social cognitive functions, suggesting its relevance in promoting reintegration of criminals into society.

Keywords Non-invasive brain stimulation · APD · BPD · Aggression · Impulsivity · Social cognition · Empathy · Theory of mind

Introduction

The acceptance of and/or the compliance with social and legal norms and rules are essential for social cohesion and prosperity. In contrast, the lack of adherence with such norms and regulations, that is, antisocial behavior, causes a high

economic and social cost (Buckholtz, 2015; Foster, 2010). Despite the growing awareness of the relevance of neurobiology to explain and predict antisocial and illegal conducts, the extent to which such knowledge is used to advance research in criminology as well as to contribute to the development of respective scientific theories and interventions remains limited. A prototypical example of contempt for social rules and legality with a strong neurobiological characterization is offered by antisocial personality disorder (APD), a clinical condition characterized by behavior potentially harmful to themselves or others, and a general attitude against the law, dishonesty, aggression, and low empathy (Gibbon et al., 2020; Koenigs, 2012). A recent example of the association between antisocial personality and rule violations comes from research reporting that individuals with antisocial traits (e.g., low in empathy and high in callousness, deceitfulness, and risk taking) are less compliant with containment measures to prevent the spread of COVID-19, which bears consequences on the pandemic spread and thus on society (Miguel et al., 2021). Similar results were found on people with aversive personality (Ścigała et al., 2021). Moreover, individuals with APD are affected by deficits in emotional

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processing, such as recognizing facial expressions (Igoumenou et al., 2017; Marsh & Blair, 2008; Yoder et al., 2015) and in understanding other people's social inputs, which are essential for normal socialization.

The aim of this article is to provide a narrative review to explore the hypothesis that non-invasive brain stimulation (NIBS) of the prefrontal cortex, which is central in social cognition, can be a relevant cortical target to rehabilitate forensic population.

The Role of Prefrontal Cortex in Non-normative Behavior

Research in neuroscience and clinical psychology has repeatedly documented abnormal structural and functional activity of the prefrontal cortex in APD. For example, a reduced activity in the dorsolateral prefrontal cortex (DLPFC) was found in individual affected by high psychopathy traits when viewing harmful compared with helpful social interactions (Buckholz, 2015; Yoder et al., 2015). Moreover, neuroimaging evidence highlighted the malfunctioning of two regions of the prefrontal cortex, namely the ventromedial prefrontal cortex (VMPFC) and the anterior cingulate cortex (ACC) in psychopathy (Blair, 2013; Koenigs, 2012). Finally, reduced cortical thickness of several regions of frontal lobes such as the superior frontal gyrus (SFG), the orbitofrontal cortex (OFC) and the middle frontal gyrus (MFG) were found in APD (Jiang et al., 2016) and psychopathic individuals (Anderson & Kiehl, 2012). Behavioral data are consistent with the neurobiological evidence. Offenders with APD have shown impaired abilities in neuropsychological tasks involving planning, set-shifting, and response inhibition, for which the DLPFC seems to be implicate (Chen et al., 2021; Dolan, 2012). These results have usually been interpreted in terms of APD individuals' inhibitory control deficits (Chamberlain et al., 2016; Dolan, 2012; Patrick et al., 2012), that is, a «braking failure» which would lead them to rule violations (Buckholz, 2015). Impulsivity, aggression and reduced emotional empathy/emotional regulation and recognition are also typical of the borderline personality disorder (BPD) (Daros et al., 2013; Hanegraaf et al., 2021; Roepke et al., 2013), a clinical condition frequently reported in female criminals (Sansone & Sansone, 2009). Both APD and BPD are DSM-5 Cluster B personality disorders (Diagnostic and Statistical Manual - 5th ed.; Psychiatric Association(2013)) and individuals can present a comorbidity of APD and BPD (Bateman & Fonagy, 2008; McCloskey et al., 2009). As for APD, also in the case of BPD, the frontal lobe seems to be critically involved (Nenadić et al., 2020; Völlm et al., 2004). For instance, Soloff et al. (2003) reported reduced metabolism of the medial orbital frontal cortex (mOFC) in BPD, in line with earlier reports (De la Fuente et al., 1997) documenting bilateral relative hypometabolism in large

areas of frontal cortex including DLPFC. Furthermore, Völlm et al. (2004) found that both APD and BPD patients showed a wider and more bilateral prefrontal and temporal network of brain activations compared to a healthy control group in a Go/No-Go task. This is a neuropsychological task that entails an individual's ability to inhibit responses and it is usually used to assess the VMPFC and DLPFC function. The authors' interpretation of these differential brain activations in patients compared to controls is that APD and BPD patients might require more cortical responses than healthy controls to successfully achieve response inhibition.

A link between frontal lobe and criminal behavior is supported by the research on empathy (Beadle et al., 2018) and moral decision-making and reasoning (Anderson & Kiehl, 2012; Blair, 2007; Decety & Cacioppo, 2012), which are compromised in several clinical populations affected by lesion and/or abnormal activity of the prefrontal cortex (Fumagalli & Priori, 2012; Vicario et al., 2017, 2021), and frequently linked with a deficit of executive functions (Lucifora, Grasso, et al., 2021c). Finally, alterations in the frontal lobe have been associated with negative clinical outcomes such as suicide (Auerbach et al., 2021), which is frequently associated with BPD and APD (e.g. Kaurin et al., 2022; Links et al., 2013) and can be predicted by affective temperament, for its role on impaired problem solving, decision-making and self-harm (Baldessarini et al., 2017). For a discussion see also Solano et al. (2016).

A Promising Intervention: Non-invasive Brain Stimulation

No compelling evidence of successful and cost-effective prevention (Foster, 2010) and treatment of such maladaptive conducts with the application of standard (i.e., psychological and/or pharmacological) interventions and therapies is documented so far (Gibbon et al., 2020). Therefore, new approaches are advisable to promote current efforts for rehabilitation and reintegration of these individuals in the society. The evidence of functional and structural abnormalities of frontal lobe in APD and BPD, as outlined above, suggests that maladaptive plasticity of frontal lobe may contribute to the origin and stability of antisocial and criminal attitude.

Non-invasive brain stimulation (NIBS) may represent a relevant treatment option to modulate this maladaptive plasticity and promote a substantial – long-lasting attenuation of the main factors responsible for persistent and severe antisocial and criminal conduct. This is promoted by its modulatory effect on neural activity (Kronberg et al., 2017; Ziemann, 2017) by acting on synaptic plasticity (Fritsch et al., 2010; Kronberg et al., 2017; Nitsche et al., 2012) via long-term potentiation (LTP) and long-term depression (LTD) (Bliss & Cooke, 2011; Monte-Silva et al., 2013; Nitsche et al., 2003) mechanisms.

A growing amount of evidence has demonstrated that NIBS is an effective approach to ameliorate a wide range of neurological and psychiatric disorders (Alizadehgoradel et al., 2020; Flöel, 2014; Kuo et al., 2014; Marković et al., 2021; Martin et al., 2017; Salehinejad et al., 2019, 2020; Vicario et al., 2019; Vicario, Nitsche, et al., 2020b; Vicario, Salehinejad, et al., 2020a) including those affecting pediatric populations (Vicario & Nitsche, 2013a, b, 2019; Rivera-Urbina et al., 2017).

In the current article, we provide an overview of the literature exploring the potential beneficial effects of NIBS of the prefrontal cortex for the treatment of clinical conditions (APD and BPD) that might experience difficulties to comply with social and legal rules. We also include a summary of the literature on the effects of NIBS on empathy and Theory of Mind (ToM) in non-clinical populations, as these social cognition abilities are considered reliable predictors of criminal conduct and/or people compliance with social and legal rules (Gómez, 2021; Huesmann et al., 2002; Swogger et al., 2015). We did not include the literature on the effects of NIBS on morality given that several recent and exhaustive review articles are available in the field (Darby & Pascual-Leone, 2017; Yuan et al., 2017).

Non-invasive Brain Stimulation for the Treatment of Aggressiveness and Impulsivity in Clinical Disorders and Crime Populations

Aggressive behavior generally refers to actions that use physical force with the intention to cause physical or psychological harm to another individual or object (Stanford et al., 2003). The origin of aggressive behavior is very complex and encompasses environmental and neurobiological factors. An aggressive personality style is often associated with problems of impulse control and reduced regulation of emotions in which the frontal lobes play a fundamental role (Hoffmann, 2013). Impulsiveness has been reported in many clinical conditions (Black, 2022; Moeller et al., 2001; Vicario et al., 2021) and it includes deficits in executive functions such as attention, inhibitory control (Lucifora, Grasso, et al., 2021c). Many studies have shown that NIBS modulate prefrontal cortex activity and functions involved in impulsivity, inhibitory control, and risk taking with promising results (Brevet-Aeby et al., 2019). A series of social neuroscience studies have shown the modulatory role of ventrolateral prefrontal cortex (VLPFC) in relation to aggression. For example, a study using transcranial direct current stimulation (tDCS, a non-invasive technique that applies a weak electrical current through two electrodes attached to the scalp) found that increasing the cortical excitability of the right ventrolateral pre-frontal cortex (rVLPFC) reduced behavioral aggression (operationalized in terms of hot sauce allocation to an interaction partner) after an episode of social

exclusion in an online ball-tossing game (Riva et al., 2015). In another study, the anodal stimulation to the rVLPFC reduced the unprovoked (but not the provoked) aggression that followed playing violent video games (Riva et al., 2017). A more recent study focused on one of the main causes of aggression: frustration, which was induced in participants by means of an unsolvable task on number sequences (Gallucci et al., 2020). Aggression was then measured by means of three behavioral tasks (e.g., giving noise blasts in the headphones to a partner in a competitive task). The authors found that anodal stimulation to the left ventrolateral prefrontal cortex (lVLPFC) increased frustration-induced aggression compared to the sham (control) stimulation. The authors also found a gender difference following sham stimulation: Male participants were more aggressive than female participants. However, this difference disappeared following left- and right-side tDCS stimulation. Furthermore, the authors did not find the hypothesized modulatory effect on the rVLPFC in terms of decreased aggression after anodal stimulation, which was instead found in previous studies (Riva et al., 2015, 2017). This discrepancy was explained by the authors in terms of the different nature of the tasks used in the different studies: when approach is involved (as in their study, in which frustration and aggression were received/acted from/against a computer-controlled partner), negative emotions would be related to a greater activity in the left hemisphere, while when affective valence is involved (as in the case of emotion ratings required after the experimental manipulation (Riva et al., 2012), then negative emotions would be associated with a greater activity in the right hemisphere.

According to DSM-5 (Diagnostic and Statistical Manual - 5th ed. (2013), a key feature of APD is a pervasive pattern of non-compliance and violation of the rights of others. There are seven main characteristics of this disorder and include: criminal behavior, deception, impulsiveness, aggressiveness, violence, reckless disregard for safety, irresponsibility, and lack of remorse.

While no research is currently available on the effects of NIBS on APD, the literature provides preliminary evidence on the potential benefits of this approach for the treatment of APD. A tDCS study (Weidacker et al., 2016) on healthy participants reported that - compared to sham stimulation - 1.5 mA cathodal tDCS of the right DLPFC improved performance in a response inhibition task in participants scoring high on cold-heartedness, a personality trait which reflects an absence of feelings of guilt and empathy.

In a more recent report (Lisoni et al., 2020), the effects of tDCS were tested on a sample of patients affected by BPD, another personality disorder characterized by marked impulsivity and aggression as described above (Bateman & Fonagy, 2008; Völlm et al., 2004). Patients were randomized to receive active-2 mA or placebo tDCS, once a day for 15 sessions. Anode electrode (excitatory) was placed on the

right DLPFC, cathode electrode on the left DLPFC. Impulsivity and aggression measures were significantly reduced only in patients treated with real DCS. Moreover, Wolkenstein et al. (2021) recently found that anodal tDCS to the left DLPFC ameliorates deficient cognitive control over emotional distraction of BPD, which is a central characteristic of these individuals (Soloff et al., 2015).

Beneficial effects of DLPFC tDCS on aggression are also documented in another recent study (Molero-Chamizo et al., 2019) reporting a reduced scores in the Brief Aggression Questionnaire of violent inmates after bilateral anodal tDCS of the DLPFC. Finally, the recent report by Sergiou et al. (2021) found that the High Density (HD)-tDCS of a cortical region between the DLPFC and the VMPFC reduces violent behavior in forensic substance-dependent offenders.

Overall, the examined literature, although preliminary, suggests that NIBS of the prefrontal cortex is a promising tool to modulate aggression and impulsivity dyscontrol in APD, BPD and in forensic populations.

Effects of Non-invasive Brain Stimulation on Social Cognition

In this paragraph, we focus on the effects of NIBS as a tool to modulate social cognitive processes such as empathy, ToM and thus mentalizing, that is, the process of explaining a behavior based on a person's mental state rather than the environment (Bateman & Fonagy, 2008; Gallagher et al., 2002), which are abnormal in APD, BPD and psychopathy (American Psychiatric Association, Washington, DC, 2013; Bateman & Fonagy, 2008; Dolan & Fullam, 2004; Dziobek et al., 2011; Németh et al., 2018; Owens et al., 2018; Preißler et al., 2010).

Recent research has indicated the complexity of the relationship between the constructs of empathy, ToM and feigning mental illness (Di Girolamo et al., 2021). According to a criminological model, intentionally feigning about one's own physical or psychological symptoms to obtain an advantage or a reward (i.e., malingering), is more likely to be exhibited by individuals with antisocial or psychopathic traits (Di Girolamo et al., 2021; Rogers & Bender, 2018). Di Girolamo et al. (2021) found that healthy individuals with high levels of cognitive empathy were more successful in feigning psychopathology. The term empathy derives from the German word *Einfühlung* and indicates the ability to understand the subjective experience of another human being (Wispé, 1986). Scholars propose a general distinction between cognitive and affective empathy (Cuff et al., 2016). Affective empathy is related to emotional experience; cognitive empathy refers to the ability of understanding intentions and desires of others (Cuff et al., 2016). While the neural correlates of affective empathy includes the amygdala, the hypothalamus, and the orbitofrontal cortex, which are

involved in affective arousal, cognitive empathy is related to activity in anterior insula and a network of regions in the prefrontal cortex, which are involved in emotion awareness and regulation (Saladino et al., 2021). The result by Di Girolamo et al. (2021) indicates that the distinction between affective and cognitive empathy is relevant to get insights into the complexity of the relationship between empathy and behaviors such as malingering that have been associated with antisocial personality.

ToM is fundamental to understand the mental states of the self and others to explain behaviors, and it has been described in relation to mentalizing (Calarge et al., 2003; Sprung et al., 2022). Also, in the case of ToM it is useful to distinguish between the affective and the cognitive dimension (Sprung et al., 2022; Brothers & Ring, 1992). The first one refers to the ability of understanding the emotional state of other people, the second is related to the knowledge about beliefs of others (Shamay-Tsoory & Aharon-Peretz, 2007).

Empathy, ToM, and specifically inferring someone else's mental states all seem to be regulated by the activity of the prefrontal cortex (PFC) (Shamay-Tsoory et al., 2003). A PET study found that medial frontal cortex (mFC), within a widespread network of brain regions, was activated during a ToM task that required participants to make mental state attributions (i.e., to make up a story based on an encounter with a woman/man crying while sitting on a park bench, Calarge et al., 2003). The activation of mFC, with a left hemisphere predominance, found in this study echoed the results emerged from early studies on the neural correlates of ToM despite the methodological differences (e.g., attribution of intentions to comic strips' characters (Brunet et al., 2000; Fletcher et al., 1995; Gallagher et al., 2000; Goel et al., 1995) In a more recent study, Shamay-Tsoory et al. (2010) also found that patients with left PFC damage had a deficit in the affective condition of a ToM task (the "Yoni" task, in which participants have to indicate among four pictures the one Yoni, a cartoon face outline, is referring to based on a statement, and cues such as Yoni's eye gaze and facial expression) (Shamay-Tsoory et al., 2010). The same study found subtle deficits in affective ToM both in a sample of criminal offenders with psychopathic symptoms and in patients with OFC lesions. This result is in line with studies suggesting that a network of prefrontal regions, along with temporal-parietal areas, underlie ToM abilities. Indeed, an fMRI study by Schiffer et al. (2017) compared groups of violent offenders with and without schizophrenia and conduct disorder/antisocial personality disorder, and non-offenders with and without schizophrenia in a ToM task (the Reading-the-Mind-in-the-Eyes Task, RMET, which involves the attribution of a person's emotional state based on a picture of the person's eyes). They found an increased ToM task-related activation in brain regions that seem to be implicated in cognitive ToM (medial prefrontal cortex, mPFC, vPFC,

left posterior superior temporal sulcus at temporoparietal junction, and precuneus) and a decreased activation of left amygdala (involved in affective ToM) in violent offenders with conduct disorder/antisocial personality disorder (with or without schizophrenia) compared to healthy non-offenders, non-violent schizophrenic patients, and violent offenders with schizophrenia and no conduct disorder. The authors interpreted this pattern of results in terms of a possible use of cognitive ToM in violent offenders with conduct disorder and antisocial personality disorder to compensate for their deficit in affective ToM.

In addition, mPFC has been identified as the distinct neural correlate of social cognition. An fMRI study by Mitchell et al. (2005) has shown that mPFC was involved in a specific aspect of impression formation: inferring someone else's mental states, that is, mentalizing, which is a core aspect of social cognition. In another fMRI study, mPFC showed reduced activation when participants reported the emotions felt toward pictures of outgroups such as homeless and drug addicted individuals, but not for other social groups (Harris & Fiske, 2006). Those outgroups are considered as extreme because they are perceived as both low in warmth and low in competence, thus suggesting that the reduced activity in mPFC may be a neural marker of dehumanization, that is, denying humanness to other human beings (Volpato & Andrighetto, 2015).

Therefore, several research teams explored whether it is possible to modulate these social cognition processes via NIBS of this brain region.

Balconi et al. (2011) asked a group of healthy participants to recognize the emotion and establish the emotional value of images of human faces representing the six basic emotions. Inhibitory rTMS was applied over the mPFC and psychophysiological measures (EMG) were recorded in the region of the zygomatic and corrugator muscle. The results showed that mPFC inhibition led to a reduction in the ability to recognize emotions and in the respective empathic response measured via facial EMG. On the other hand, in a further study by the same group (Balconi & Canavesio, 2013) it was shown that high frequency (i.e., excitatory) rTMS of the mPFC increased empathic behavior (i.e., increased prosocial attitude in case of the decision to support people).

The results from Boggio et al. (2009) extended the link PFC-empathy to the DLPFC. They showed that a single session of DLPFC excitatory (anodal) tDCS was sufficient to modulate empathy for pain, with reduced emotional distress at the sight of unpleasant images, compared to placebo stimulation and the stimulation of other cortical regions (M1 and V1). Similar results were also documented in a subsequent report by the same group (Rêgo et al., 2015).

Talking about the effects of NIBS on ToM, it is worth mentioning the study by Krause et al. (2012). The authors

applied deep (low frequency) rTMS over the mPFC of a group of neurotypical participants performing an affective (which involves the comprehension of others' emotional states) or cognitive (which involves the understanding of others' cognitive mental states such as beliefs and intentions) ToM task (Shamay-Tsoory et al., 2006). Deep rTMS disrupted affective ToM performance for those with high self-reported empathy but improved affective ToM performance for those with low self-reported empathy. Therefore, mPFC appears to play a role in affective ToM, but the stimulation outcomes are predicted by the empathic abilities of participants.

In a further study, Schuwerk et al. (2014) demonstrated a role of the posterior medial prefrontal cortex (pmPFC) in ToM. The authors inhibited the pmPFC, via low frequency rTMS, of a group of students performing the "Sally-Anne" false belief (cognitive ToM) task. Their results showed that pmPFC inhibition impaired the ability to distinguish the other's from one's own perspective and supported the pmPFC's causal role in establishing perspective differences.

The study by Kalbe et al. (2010) documented a selective role of the right DLPFC in cognitive ToM. The authors found that 1 Hz (inhibitory) rTMS boosted reaction times in cognitive ToM (examined via the "Yoni" task, (Shamay-Tsoory et al., 2006), while no effect was found on affective ToM.

Overall, the literature examined above suggests that both empathy and ToM can be modulated by prefrontal NIBS. The mPFC seems especially relevant for affective empathy and affective ToM, which might be particularly important for the rehabilitation of APD, BPD and criminals with impulsivity dyscontrol, according to the suggestion that affective empathy and ToM reduce aggression and strengthen social ties (Aaltola, 2014). The DLPFC seems the most appropriate NIBS target to modulate empathy for pain and cognitive ToM.

A Trajectory for NIBS-Based Interventions in APD, BPD, and Incarcerated Offenders with Psychopathy

The take-home message coming from the examined literature (Table 1) is that NIBS can be a promising therapeutic tool to reduce symptoms severity in APD and BPD. The main implication of this work is the possibility to consider NIBS as a possible intervention to promote reintegration of prison population into society, which is estimated to be affected by psychopathic personality in a proportion between the 20% and the 30% (Hare, 2003). However, due to the limited number of studies, it is necessary to conduct further investigations before considering NIBS as a standard in the field of forensic rehabilitation.

Table 1 Effects of non-invasive brain stimulation on aggression and social cognition on clinical population, forensic population, and healthy individuals

Clinical/Forensic Studies									
Authors	NIBS type	Topic	Method	Sample	Gender MF	Mean Age	Stimulation site	Frequency/intensity	Duration
Lisoni et al. (2020)	tDCS	Aggression	Anodal tDCS	Clinical population	12\18	40.3	DLFPC left/right	0.06 mA	20 minutes
Molero-Chamizo et al. (2019)	tDCS	Aggression	Anodal tDCS	Forensic Population	4\10	36.2	DLFPC left/right	1.5 mA	15 minutes
Sergiou et al. (2021)	HD-tDCS	Aggression	Anodal tDCS	Forensic Population	5\00	37.4	VMPFC	2 mA	20 minutes
Wolkenstein et al. (2021)	tDCS	Emotional distraction	Anodal tDCS	Clinical population	0\40	29.25	dIPFC left	1 mA	20 minutes
Social Neuroscience Studies									
Authors	NIBS type	Topic	Method	Sample	Gender MF	Mean Age	Stimulation site	Frequency/intensity	Duration
Balconi and Canavesio (2013)	rTMS	Empathy and emotions	TMS	Healthy individuals	6\10	23.11	MPFC	10 Hz\50 pulses	5 seconds
Boggio et al. (2009)	tDCS	Emotions	Anodal tDCS	Healthy individuals	11\12	21.3	M1\DLFPC\VI	2 mA	5 minutes
Kalbe et al. (2010)	rTMS	Theory of Mind	rTMS on DLPFC	Healthy individuals	28\0	24	DLFPC right	1 Hz\900 pulses	15 minutes
Krause et al. (2012)	rTMS	Theory of Mind	Deep rTMS on mPFC	Healthy individuals	6\10	27.67\25.67	MPFC	1 Hz\900 pulses	15 minutes
Yuan et al. (2017)	tDCS	mPFC in Moral violations	Anodal tDCS	Healthy individuals	38\26	23.57	MPFC (Fpz-Fp1)	1.5 mA	N/A
Riva et al. (2015)	tDCS	Social Exclusion and Aggression	Anodal and cathodal tDCS	Healthy individuals	17\63	23.06	VLFFC right	1.5 mA	20 minutes
riva et al. (2017)	tDCS	Violent video games-induced aggression	Anodal vs. sham	Healthy individuals (university students)	48% female	21.73	rVLFFC	1.5 mA	20 minutes
GALLUCCI et al. (2020)	tDCS	Frustration-induced aggression	Anodal vs. sham	Healthy individuals	45\45	22.27	rVLFFC vs. lVLFFC	1.5 mA	20 minutes
Schuerk et al. (2014)	rTMS	Theory of Mind	rTMS	Healthy individuals	6\11	22.2	PMPPFC	1 Hz\200 pulses	33 minutes
Weidacker et al. (2016)	tDCS	Psychopathic traits	Cathodal tDCS	Healthy individuals	9\9	22.06	DLFPC right	1.5 mA	20 minutes

Legend. *tDCS* transcranial direct current stimulation, *rTMS* repetitive transcranial magnetic stimulation; **HD** High density; **BPD** Borderline Personality Disorder; **MPFC** Medial prefrontal cortex; **DLFPC** Dorsolateral prefrontal cortex; **VMPFC** Ventromedial prefrontal cortex; **VLFFC** Ventrolateral prefrontal cortex; **PMPPFC** posterior medial prefrontal cortex **MI** primary motor cortex **VI** primary visual cortex

In this section, we highlight the main caveats and challenges to address in order to exploit the potential of NIBS in antisocial behavior rehabilitation.

The main limitations of the available literature in the field, which should be addressed in future investigations, include: the low number of double blind, sham controlled studies; the absence of systematic protocols which combine NIBS with standard therapies; the absence of systematic titration of stimulation parameters such as cortical target for optimization, duration, repetition and intensity; the absence of simultaneous exposure to emotional stimuli/outcomes to make use of up-/downregulation properties of the PFC (Vicario et al., 2019).

Challenges for research in this field have also emerged from recent works that have highlighted the complexity of the neurobiological and behavioral underpinnings of antisocial behaviors. For example, Buckholz (2015) has argued for broadening the functional role commonly associated with DLPFC. This region is usually considered crucial for its inhibitory control functions. However, it is also involved in linking abstract rules with rewards, an aspect that can influence norm-based decision making and actions. For this reason, DLPFC should also be considered in relation to its projections to striatum, which is implicated in action selection (Buckholz, 2015). The specific localization targeted by an intervention should also be carefully considered given that the reviewed results from studies using tDCS suffer the limitation of this technique in terms of low spatial resolution (e.g., Gallucci et al., 2020; Riva et al., 2012). Thus, more focal techniques, such as rTMS, would provide more specific localizations. Relatedly, hemispheric lateralization should carefully be considered as the reviewed tDCS studies have highlighted some variability in the modulatory effects of anodal stimulations of rVLPFC, possibly due to the nature of the tasks that participants completed (e.g., Lisoni et al., 2020; Wolkenstein et al., 2021).

An additional caveat that future studies should take into account relates to the type of the neuropsychological tasks used to assess the DLPFC function/dysfunction. It would be important to use neuropsychological tasks that are high in the specificity of the brain regions they activate. This specificity would allow scholars to map individuals' performance in those tasks more precisely into specific neural functions/impairments (Dolan, 2012). As previously reviewed, it is also important to acknowledge the complexity of social cognitive constructs that are altered in APD and BPD, such as empathy and ToM. A differential assessment of the cognitive and affective components of empathy and ToM is key to understand how they relate to non-normative behaviors. Indeed, APD and BPD might rely on intact cognitive empathy to enact non-normative behaviors such as malingering (Di Girolamo et al., 2021) or to compensate for their deficits in empathy (Schiffer et al., 2017). Furthermore, scholars

should consider the specificity in the trait constructs the tasks map onto. For example, the Go/NoGo task might not fully capture the complexity of impulsivity, a trait shared by both APD and BPD (Völlm et al., 2004). Moreover, it might be useful adopting more ecological methodologies for assessing the effects of NIBS on social cognition in forensic populations. Virtual reality technology could represent a useful tool, as it allows scholars to make more realistic social cognition-related environments effective in promoting empathic and mentalizing experiences (Daher et al., 2021; Grasso et al., 2019, 2020; Lucifora et al., 2020; Lucifora, Angelini, et al., 2021b; Lucifora, Martino, et al., 2021a).

Rehabilitation interventions should also take into account individual differences in trait constructs that are relevant to antisocial behavior and which can reflect variations in both their neurophysiological bases and their associated behaviors ("neurobehavioral trait constructs" (Buckholz, 2015). Finally, screenings should consider individual differences based on gender as electrophysiological evidence about the neural mechanisms of empathy has shown some differences between psychopathic males and females (Saladino et al., 2021). Furthermore, as previously mentioned, gender differences in aggression were also found following sham stimulation, but not when following tDCS stimulation (to either hemisphere) in a sample of healthy adults (Gallucci et al., 2020).

Data Availability Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

Declarations

Conflict of Interest On behalf of all authors, the corresponding author states that there is no conflict of interest. No ethical approval is required for review articles, according to the regulation of the research ethics committee of the authors' department.

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