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EMOTIONAL AWARENESS, AND TMS AND tDCS

The modulation of emotional awareness using non-invasive brain stimulation techniques: a literature review on TMS and tDCS

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Abstract

The emotional awareness defined as the conscious experience of emotions is the ability to regulate emotions, to attribute them an unambiguity denomination, and to identify their causes. In the current review we included studies examining those alterations in emotional awareness elicited by non-invasive brain stimulation techniques, specifically by the transcranial magnetic stimulation (TMS), and the transcranial direct current stimulation (tDCS). The anodal tDCS stimulation over the dorsolateral prefrontal cortex (DLPFC) increases the ability to discriminate facial expressions and the associated emotions. TMS over the dorsomedial prefrontal cortex (DMPFC) significantly interfered with the effect of minimal group-membership on emotion recognition, reducing participants' ability to differentiate emotions expressed by *in-group* members; therefore, it is associated to closed people and self-related concepts. Similarly, the ventrolateral prefrontal cortex (VLPFC) contributes to emotional elaboration and - whether stimulated by cathodal and anodal tDCS – it may influence the monitoring of negative emotions. Stimulation by repetitive TMS (rTMS) over the right intraparietal sulcus, improves the emotion identification. Anodal stimulation over the right orbitofrontal cortex (OFC), the right posterior superior temporal sulcus (pSTS), and the right temporoparietal junction (rTPJ), contributes to enhance emotion recognition abilities. On the contrary, rTMS over the somatosensory cortex and the frontotemporal anterior insular network seems to alter the emotion appraisal. The cerebellum plays an important role in managing emotion recognition and emotional (self) evaluation probably modulated by the DMPFC activity. The current literature review aimed to shed light on effects of non-invasive brain stimulation techniques over several brain areas involved in the emotional awareness.

Keywords: emotional awareness, emotion dysregulation, non-invasive brain stimulation techniques, TMS, tDCS.

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Introduction

The emotional awareness consists in the cognitive ability to recognize, identify and communicate emotions experienced related to themselves or to others (Lane & Schwartz, 1987). The emotional awareness is based on cognitive schemas influencing emotional experiences and it associates with reflection, understanding, detection of emotions, and recognition of psychological needs (Bajgar et al., 2005; Dizén et al., 2005; Lane & Garfield, 2005; Lane & Schwartz, 1987). The emotional awareness consists of two components: the *emotional clarity* and the *attention to emotions* (Mankus et al., 2016). The emotional clarity, in turn, includes the *type clarity* and the *source clarity*. The type clarity consists in the ability to identify and to denominate different emotions as a sort of an emotional metacognitive capacity (Boden et al., 2013); the source clarity is characterized by the awareness of emotions' causes (Boden & Berenbaum, 2011). Aware experiences of emotions are implicated in emotion regulation (Thompson & Calkins, 1996) consisting in understanding and accepting emotions, in managing impulsive behaviors, in using strategies to regulate emotional states and negative affective experiences that can hamper goals' achievement (Gratz & Roemer, 2004).

Emotional awareness and emotion regulation represent the essential requirements to mental health allowing to cope with stressful situations and psychophysical well-being (Gohm & Clore, 2002; Monti & Rudolph, 2014; Salovey et al., 2002); whether emotional awareness and emotion regulation would present alterations, the risk of psychopathology may increase: in fact, mental disorders (such as post-traumatic stress, somatoform, eating and personality disorders) are characterized by a lacking emotional awareness and anomalies in expressing and regulating emotions (Boden & Thompson, 2015).

Several brain areas are associated to the emotional awareness. The anterior insula plays a key role, especially for the awareness of bodily sensations and sensory experiences (Craig 2002; Craig, 2009). The right anterior insula is also responsible for evaluating feelings. Also, the

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1
2 evaluation of feelings involves the right anterior temporal lobe and, even though marginally, the
3
4 subgenual anterior cingulate cortex (a visceromotor regulation site; Lindquist et al., 2012). The
5
6 orbitofrontal cortex, instead, integrates *exteroceptive and interoceptive*¹ sensory information and,
7
8 with the dorsolateral prefrontal cortex, orients purpose-directed behaviors (Corbetta & Shulman
9
10 2002; Corbetta et al., 2008; Lindquist et al., 2012). The ventrolateral prefrontal cortex is implicated
11
12 in explicit attention directed to emotional stimuli and in the inhibition of impulsive responses to
13
14 emotions (Aron et al., 2004).
15

16
17 By using the brain stimulation techniques, several studies (e.g., Fan et al., 2018; Ferrucci et al.,
18
19 2012; Mattavelli et al., 2011; Nitsche et al., 2012; Pitcher et al., 2008; Riva et al., 2015; Vonck et
20
21 al., 2015; Willis et al., 2015) have investigated the brain activity and neural correlates related to
22
23 levels of the emotional awareness. Non-invasive brain stimulation methods elicit temporary
24
25 changes in the brain activity and, consequently, (observable) behavior modifications (Rossi et al.,
26
27 2009).
28
29

Transcranial magnetic stimulation (TMS)

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32
33
34 Transcranial magnetic stimulation by a coil² placed on the human head generates a magnetic
35
36 that, in turn, induces an electric field in the brain. The electric field induces ionic flow, modifying
37
38 the electrical charge on both sides of cell membranes and, consequently, the neuron depolarization
39
40 or hyperpolarization (Rossi et al., 2009); the duration of the neuronal facilitation effect depends on
41
42 the intensity of stimulation (Miniussi et al., 2013; Epstein & Rothwell, 2003). There are several
43
44 stimulation's protocols: *single pulse TMS* (spTMS), *paired pulse TMS*, *repetitive TMS* (rTMS),
45
46 and *continuous* (cTBS) or *intermittent* (iTBS) *theta burst stimulation* (TBS). In particular, SpTMS
47
48 is a stimulation with a brief duration (less than 1 ms; Rossi et al., 2009; Sacco, 2013); spTMS is
49
50 used to study motor responses after the stimulation, to ascertain temporal parameters of nerve signal
51
52
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57
58 ¹Exteroceptive information concerns environmental stimuli (e.g. visual, acoustic or tactile stimuli); while interoceptive
59 information refers to bodily internal states, signals arising from physiological condition (Craig 2002; Craig & Craig,
60 2009; Critchley et al., 2004; Sherrington, 1906).

² The magnetic field is generated by a short current pulse that passes through a coil (Rossi et al., 2009).

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1
2 transmissions to muscles, or to determine when exactly a cognitive event occurs as recorded by the
3
4 brain activity (Miniussi et al., 2013). Paired pulse TMS provides for different coils and it allows
5
6 estimating the interconnection degree between two areas or getting the facilitation or inhibition
7
8 measure of intra-cortical activity (Shirota et al., 2016). rTMS consists in rapid -repeated pulses
9
10 associated a) to low frequencies (no more than a pulse per second) in order to inhibit the activity of
11
12 a specific cortical region (Andò et al., 2018; or b) to high frequencies (5-25 Hz) facilitating the
13
14 neuronal activity (Kluger & Triggs, 2007). TBS high frequency and low intensity discharges are
15
16 repeatedly induced, interleaved by short pauses; TBS permits a more prolonged activation of brain
17
18 areas than rTMS (Di Lazzaro et al., 2008; Huang et al., 2010).
19
20
21

22
23 TMS is used for the treatment of neurological and psychiatric disorders, such as bipolar
24
25 disorders, hallucinations, acute mania, panic, catatonia, post-traumatic stress disorder, compulsions,
26
27 obsessions, depression, schizophrenia, drug craving, Parkinson's disease, dystonia, stuttering,
28
29 tinnitus, spasticity, epilepsy, tics, aphasia, hand function after stroke and pain syndromes, in
30
31 particular neuropathic pain, visceral pain and migraine (Couturier, 2005; Devlin & Watkins, 2006;
32
33 Fregni, et al., 2005; George et al., 2007; Gershon et al., 2003; Hallett, 2007; Hoffman et al., 2005;
34
35 Kobayashi & Pascual-Leone, 2003; Lefaucheur, 2004; Málly & Stone, 2007; Ridding & Rothwell,
36
37 2007; Rossi et al., 2004; Rossini & Rossi, 2007; Tassinari et al., 2003; Wassermann & Lisanby,
38
39 2001).
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42

Transcranial electric stimulation (tES)

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44
45 Transcranial electric stimulation induces low intensity (1-2 milliAmps) electrical currents
46
47 through two electrodes (*anode* and *cathode*) that cause modifications in the cortical excitability, in
48
49 discharge frequencies and in permeability of membrane, facilitating neuronal activity and synaptic
50
51 connections (Fertonani & Miniussi, 2017). Effects of tES depend on the activity of several factors,
52
53 such as the brain region, the task characteristics and the type of electrical current, and the duration
54
55 and intensity of the stimulation. The most used tES is the transcranial direct current stimulation.
56
57
58

Transcranial direct current stimulation (tDCS)

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tDCS is a continuous stimulation which modulates synaptic and neuronal spontaneous activity and it does not induce action potentials (unlike the TMS). tDCS is characterized by lower spatial and temporal resolution if compared to TMS. In tDCS the electrode is applied over the area of interest and the other electrode (i.e., *reference* electrode) over a remote site on the scalp (George & Aston-Jones, 2010; Priori et al., 1998). After-effects by tDCS can persist for over 30 minutes after stimulation and it is presumed that they are due to increasing or decreasing cortical excitability (Bindman et al., 1979; Bindman et al., 1962; Bindman et al., 1964; Purpura & McMurtry, 1965). Positive effects have been observed in treatment for aphasia (Monti et al., 2008), major depressive disorder (Berlim et al., 2013; Kalu et al., 2012), schizophrenia, and substance use disorder (in particular craving from tobacco, food, alcohol and cannabis). tDCS is a method that usually does not imply discomforts (Priori et al., 2009). However, tDCS can imply some side effects, such as a sensation of itch or heat according to stimulation intensity and dependent on the exposure time (Bikson et al., 2009), reddening of the skin under the electrode, an increase of local temperature proportional to intensity and superficial vasodilation which can cause an arterial pressure reduction (-10 mmHg) if applications are more extensive (Palm et al., 2008) and a metallic or a sharp taste.

Transcranial alternating current stimulation (tACS)

tACS induces a specific frequencies stimulation at low-intensity electrical current (0.1-1000 Hz) which modulates cortical oscillatory rhythms (Herrmann et al., 2013). Although it does not cause a depolarization, tACS modifies neuronal activity, synchronizing neural networks (Antal & Paulus, 2013). It improves, thus, the transfer and elaboration for information (Butts et al., 2007), with after-effects of alpha tACS persisting for 30-70 minutes (Kasten et al., 2016; Neuling et al., 2013). tACS has been used for treatment-resistant glioblastoma (Kirson et al., 2007) and optic-nerve injury (Gall et al., 2010; Sabel et al., 2011); also, it seems to improve motor performances (Joundi, et al., 2012) and several cognitive functions (Antal & Paulus, 2013; Fröhlich et al., 2015; Herrmann et al., 2013).

Transcranial random noise stimulation (tRNS)

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tRNS involves a random electrical oscillation spectrum over the cortex (0.1-640 Hz). It is hypothesized that the repeated administration of subthreshold stimulations potentiates neuronal activity and facilitates neuronal communication, according to a temporal summation mechanism (Fertonani et al., 2011). Another explanation to tRNS functioning is that the stimulation may increase the ratio between the signal and the noise, conferring to neurons more sensitivity to weak stimuli, through the stochastic resonance mechanism³ (Miniussi et al., 2013). It has been proposed also that tRNS can induce a repetitive activation of sodium channels, with an increase in the sodium inflow and, thus, a longer depolarization that may produce a long term potentiation⁴ (Fertonani et al., 2011; Terney et al., 2008). Also, it was observed that tRNS provides an enhancement in motor and visual perceptual learning tasks (Fertonani et al., 2011; Terney et al. 2008). tRNS' effects seem to be sufficiently tolerated (Ambrus et al., 2010; Curado et al., 2016; Curatolo et al., 2017; Terney et al., 2008).

The aim of the current review

Brain stimulation techniques have shown an evident utility for the treatment of major depressive disorder, anxiety and for other mental disorders (Modirrousta et al., 2015). Understanding how these techniques can improve the awareness of emotions related to accept emotions, to manage impulsive behaviors, to use strategies to regulate emotional states and negative affective experiences (Gratz & Roemer, 2004) would be extremely relevant from a clinical point of view. Feelings of anger and sadness may easily increase by developing deficits in the implementation of a *long-term repertoire* of emotion regulation strategies, and such deficits may confirm the sense of ineffectiveness and impotence observed in depression or anxiety. Therefore, this review focuses on alterations (and its consequences) produced by non-invasive brain stimulation techniques, on emotional awareness.

³ The stochastic resonance refers to the amplification of signals extremely weak to exceed a threshold, adding noise (McDonnell & Abbott, 2009; Wiesenfeld & Moss, 1995)

⁴ The long-term potentiation (LTP) is a learning-based hypothesized mechanism (Rioult-Pedotti et al., 2000).

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Specifically, we investigated the role that TMS and tDCS play in influencing the emotional awareness and its related constructs (i.e., *emotion regulation*, *emotion recognition*, and *emotion discrimination*; Bajgar et al., 2005; Lane, 2000). As mentioned before, emotion regulation consists in the modulation of *which*, *when* and *how* an individual experiences and expresses his/her own emotions (Thompson & Calkins, 1996). Emotion recognition refers to the perception and processing of emotional stimuli, detecting emotions (Lane et al., 1996). Emotion discrimination is the ability to categorize emotional information (Gamond & Cattaneo, 2016).

Method

Data sources and Study selection

Titles, abstracts and topics were searched using the following terms: “*transcranial magnetic stimulation (TMS)*” OR “*repetitive transcranial magnetic stimulation (rTMS)*” OR “*transcranial direct current stimulation (tDCS)*” OR “*continuous theta burst transcranial magnetic stimulation (cTBS)*” OR “*cerebellar stimulation*” OR “*neurostimulation*” AND “*emotions*” OR “*facial expressions*” OR “*facial expression recognition*” OR “*facial emotion*” OR “*emotional processing*” OR “*affective processing*” OR “*affective flexibility*” OR “*cognitive control*” “*emotion recognition*” OR “*emotion regulation*” OR “*emotional control*” OR “*attentional control*” OR “*memory*” OR “*working memory*” OR “*empathy*” OR “*embodied cognition*” OR “*cognitive reappraisal*” OR “*emotion discrimination*”. The electronic research literature database included the PubMed and Psychinfo from 2008 to 2019. Scientific articles were considered to be eligible whether included: 1) non-invasive brain stimulation methods; 2) studies with no clinical subjects ranging in age from 18 to 64 years. Limits were set to humans and English language. Additional studies were searched manually. Search was conducted independently by two investigators (A.A. & M. L.V).

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Results

Thirty-nine studies met our inclusion criteria and were included in the present review (see Table 1). The most consistent findings were that: (i) the dorsolateral prefrontal cortex plays a role in emotion processing and regulation; the stimulation over the dorsolateral prefrontal cortex produced an “antidepressant effect”; (ii) the medial prefrontal cortex and its regions seem to respond to those emotions elicited by close people and self- perception and attributions; (iii) the stimulation over the ventrolateral prefrontal cortex induces effects on regulation and memorization of negative emotions; (iii) the right orbitofrontal cortex, right temporoparietal junction, right posterior superior temporal sulcus, right intraparietal sulcus and somatosensory cortices are involved in emotion identification and appraisal; (iv) the stimulation over the cerebellum can influence abilities related to emotional identification. All details are discussed below.

Discussion**1. The role of the dorsolateral prefrontal cortex in the emotional elaboration: the discrimination of facial expressions**

The prefrontal cortex contributes to the elaboration, modulation and evaluation of emotional states, regulation of emotional reactions, and goal-directed behaviors (Dixon et al., 2017). The role of the prefrontal cortex in emotion processing can be inferred from several studies which included brain stimulation methods. The experimental study by Lapate and colleagues (2017) including TMS, highlighted the role of the left lateral prefrontal cortex in evaluations of emotional states. Nitsche and collaborators (2012) observed an increased ability in discriminating facial expressions (in particular, positive facial expressions) as a result of tDCS stimulation over the left dorsolateral prefrontal cortex (DLPFC). Anodal stimulation of the left DLPFC changed less negatively those emotions perceived - before the stimulation - as negative (Peña-Gómez et al., 2011). Furthermore, this effect varied if related to the extraversion-introversion personality features: down-regulation

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1
2 was stronger in those subjects with a higher subclinical introversion scores⁵. These findings are in
3
4 line with Pripfl and Lamm (2015) who reported that negative emotions were considered as more
5
6 positively after anodal tDCS over the right DLPFC. Vanderhasselt and colleagues (2013), using
7
8 anodal tDCS over the left DLPFC, reported a higher cognitive control and more rapid inhibitory
9
10 responses to an emotional cue characterized by a positive value. Likewise, Wiegand, Sommer,
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12 Nieratschker and Plewnia (2019) observed - following anodal tDCS over the left DLPFC - an
13
14 increase of cognitive control abilities. In stressful conditions, the neuro-stimulation improved mood
15
16 and performance. A facilitation of cognitive reappraisal, downregulating or upregulating emotions,
17
18 after anodal tDCS over the right DLPFC, as noted by Feeser and collaborators (2014).
19
20
21 Nevertheless, observations of Nord and colleagues (2017) seem to be in contrast, since the anodal
22
23 tDCS over the left DLPFC did not produce more accurate responses during exposures to facial
24
25 emotion categorizing tasks; therefore, researchers supposed that tDCS had an overall effect on the
26
27 emotional face identification. Sanchez et al. (2016) reported the presence of impairments in the
28
29 attentional disengagement from both positive and negative faces, following anodal tDCS over the
30
31 right DLPFC. These results have strengthened the theory of hemispheric lateralization of emotional
32
33 processes in general rather than emotion-specific ones. Hemispheric lateralization hypothesis was
34
35 supported by Weigand and colleagues (2013), since tDCS and (subsequent) rTMS over the right
36
37 DLPFC improved accuracy - but not reaction times - in working memory tasks with fear-related
38
39 words. A possible explanation is that the neuro-stimulation, by inhibiting the right DLPFC,
40
41 influenced the elaboration of fear-related cues, giving priority to the task-relevant information and,
42
43 consequently, increasing the accuracy. On the contrary, with neutral words it was observed only a
44
45 reaction time reduction, due to the decrease of the cortical excitability (the performance improved
46
47 for focusing effects); with anger-related words, instead, anodal tDCS and active rTMS enhanced
48
49 both accuracy and reaction times (the accuracy decreased after cathodal tDCS).
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59 ⁵ These findings are in line with Eysenck's research (1981) which has gathered that introvert individuals are more
60 sensible to low or moderate levels of stimulation

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1
2 However, these findings were not repeated by Ferrari and colleagues research (2017). After
3
4 TMS over the DLPFC, indeed, the authors did not identify either alterations in a positive emotion
5
6 evaluation, or alterations in the identification of negative emotions. In the experimental study by
7
8 Allaert et al. (2019) evidences of functional lateralization were found: the authors using anodal
9
10 tDCS over the left DLPFC observed an increased pupil dilatation (that is an index of arousal and
11
12 cognitive resource allocation) when negative pictures were shown. The authors considered that,
13
14 likely, the major cognitive resource allocation increased top-down regulation of emotional stimuli.
15
16 Differently, anodal tDCS over the right DLPFC reduced the pupil dilatation, while individuals
17
18 observing both negative or positive images. The hemispheric lateralization hypothesis was
19
20 investigated also in a previous work by Sanchez-Lopez and colleagues (2018). The tDCS caused an
21
22 improvement of top-down attentional control to emotional stimuli, when the stimulated area was the
23
24 left DLPFC, as is it inferred from faster gaze disengagement from emotional faces. Vice versa,
25
26 stimulation of the right DLPFC implied a slowing of emotional disengagement, as previously
27
28 observed (Sanchez et al., 2016). De Raedt et al. (2010) conducted a study with participants exposed
29
30 to an emotional modification of the spatial cueing task: left prefrontal HF-rTMS resulted in
31
32 attentional disengagement from angry faces associated with increased activity within the right
33
34 DLPFC, dACC, right superior parietal gyrus and left orbitofrontal cortex; authors' observations
35
36 support the presence a functionally interactive network of cortical-limbic pathways that play a
37
38 central role in emotion regulation. Similar findings were found in a former study (Leyman et al.,
39
40 2009) in which one session of HF-rTMS over the right DLPFC induced alterations in the inhibition
41
42 of negative emotions; but, unlike the other research (De Raedt et al., 2010), no significant
43
44 attentional control modifications were noted after HF-rTMS on the left DLPFC. A further study
45
46 (Zwanzger et al., 2014) supported the role of DLPFC in emotional attention regulation: the authors
47
48 using rTMS over the right DLPFC observed an amplification of visual processes in bilateral
49
50 parietal, temporal and occipital regions, a major activation of the right temporoparietal junction
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52 (TPJ) area with threatening cues and, consequently, slower reaction times to fear faces and not to
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neutral ones. Lantrip and colleagues (2019) repeated these findings, confirming the *antidepressant* effect of HF-rTMS over the left DLPFC, since they remarked an improvement in emotion regulation (the modification not reported after right DLPFC stimulation). In another study by Balconi and Canavesio (2015) was confirmed the role of left DLPFC in emotion identification and the relation between face expressions and score at the Balanced Emotional Empathy Scale (BEES), a questionnaire investigating the empathy capacity. Neuro-stimulation through rTMS over the left DLPFC, actually, facilitate the discrimination of happy faces more difficult, especially for high-BEES subjects. Furthermore, from their research emerged the relevance of the behavioral activation system (BAS⁶; e.g., Gray, 2007) and its correlation to BEES: participants with high-BAS had also high scores in BEES showing a worse performance in positive emotions recognition as result of TMS.

2. The involvement of regions of medial prefrontal cortex in processing emotions and emotions recognition

The medial prefrontal cortex (MPFC) plays a key role in (subjectively) experiencing emotions (Smith et al., 2014). Indeed, MPFC is associated to recognition, representation, evaluation and attention to emotional experiences. In Mattavelli, Cattaneo and Papagno's study (2011) participants were exposed to the single-pulse TMS over the MPFC and over the right somatosensory cortex (rSC) during a task consisting in discriminating happy and angry facial expressions. Facial expressions were preceded by *prime* words that could refer to emotions of happiness or anger and that could be congruent or not with the target face. After TMS on the MPFC Mattavelli, Cattaneo and Papagno, observed a significantly interference with the priming effect, in case of congruence between the prime and target stimuli. These findings have supported the existence of different neural representations for anger and happiness which include a lexical

⁶ The BAS is a system of behavior control, based on positive emotions, such as conditioned reinforce stimuli and rewarded cues, which has the left FC as neural substrate. The BAS, referring to personal attitudes toward emotions, explains the different orientation, among individuals, to positive or negative emotions.

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1
2 knowledge of facial expressions. Stimulation of the rSC, differently, did produce few impairments
3
4 in emotion recognition, suggesting its general involvement in the face expressions recognition, but
5
6 not in the elaboration of emotional words. De Pisapia, Barchiesi, Jovicich and Cattaneo (2019)
7
8 asserted the MPFC is implicated in affective coding of negative stimuli, rather than an exclusive
9
10 elaboration of self, as well as proved by increased reaction times in negative adjectives elaboration
11
12 both when attributes referred to oneself or to close people after low frequency rTMS over the
13
14 MPFC. Also, rTMS over the MPFC settled the tone of other cerebral areas, modulating blood
15
16 oxygen level-dependent (BOLD) of the posterior cingulate cortex, left angular gyrus and temporal
17
18 cortex, but only for negative attributes elaboration. The MPFC contributes also to emotions control,
19
20 as highlighted by Riedel research group (2019), who observed, following rTMS over the right
21
22 MPFC, a modification of functional connectivity with the right amygdala after the high-frequency
23
24 stimulation and vice versa. It is supposed that such modifications were due to neurotransmitter
25
26 release or changes in trans-synaptic connections among different areas. Likewise, Dedoncker and
27
28 collaborators (2019) noted, in women with high perceived criticism, a reduction of medial
29
30 prefrontal neural connectivity, as an effect of the tDCS.
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37 The role of the dorsomedial prefrontal cortex (DMPFC) in emotion recognition, social
38
39 categorization and self-related concepts was investigated also by Gamond and Cattaneo (2016);
40
41 TMS over the DMPFC reduced the accuracy for *in-group* faces (task) and interfered with the *in-*
42
43 *group* advantage in emotion recognition tasks. In their experimental study, using TMS over the
44
45 right temporo-parietal junction (rTPJ; a brain region involved in mentalization) a marginal decrease
46
47 of accuracy and a delay in participants' performances were observed both for *in-group* and *out-*
48
49 *group facial expressions* (see also Donaldson et al., 2019). The DMPFC is related also to empathy
50
51 associated, in turn, with the responsiveness to emotional faces⁷: in Balconi and Bortolotti (2013),
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58
59 ⁷The empathy can be defined as the ability to acquire the point of view of another person, discover the origin of oneself
60 and someone else's emotions, self-regulate and share to other emotional states (Batson et al., 1997; Decety & Jackson, 2004; Harmon-Jones & Winkielman, 2007; Hooker et al., 2008; Ickes, 1997; Preston & De Waal, 2002).

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rTMS over the DMPFC, during a facial detection task in fact, impaired performances and increased errors and reaction times, above all in association to the exposure to anger and fear faces.

The ventromedial prefrontal cortex (VMPFC) plays an important role in processing emotions and metacognitive abilities; Abend and colleagues (2019) after tDCS stimulation observed an increased activation of VMPFC, subgenual anterior-cingulate cortex (sgACC) and ventral striatum (a part belonging to the limbic system) and, thus, a decrease of stress and of negative emotions intensity watching unpleasant films. Lastly, Winker et al. (2018) found association between the VMPFC, positive emotions and reward, for its connection to the dopaminergic reward circuit. Neuro-stimulation, indeed, caused an increase of the VMPFC activity with the presentation of happy faces when tDCS was excitatory, while the opposite occurred in presence of the inhibitory tDCS. Another effect of excitatory tDCS was that ambiguous facial expressions needed a higher degree of fearful expressions to be considered fearful, but a lower happiness degree to define them as *happy*. Besides, for the most ambiguous expressions related to happiness reaction times were lower, whereas reaction times were greater for the fearless ambiguous faces, as a result of excitatory tDCS. It seemed, therefore, that an excitatory stimulation would facilitate recognition of happiness in ambiguous expressions and a decrease of recognition of fearful faces one. On the contrary the inhibition of VMPFC facilitated identification of fear in ambiguous expressions and reduced the overall emotional arousal.

3. Brain areas involved in awareness and distinction of emotions

Apart from the DLPFC and the MPFC there are several brain regions involved in emotions processing, including the right ventrolateral prefrontal cortex (rVLPFC). As a matter of fact, stimulation of the rVLPFC induces more negative emotions, reacting to difficult situations (such as the social exclusion) (Riva et al., 2015). The implication of rVLPFC in emotion regulation is reported also by Vergallito, Riva, Pisoni and Romero Lauro (2018), given the fact that anodal tDCS reduced the negative emotions valence. Nevertheless, anodal tDCS, modulated only anxiety, fear and, almost significantly, sadness, unlike anger and disgust. Different emotions response to

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neurostimulation is due to presence of two motivational systems: an approach-related system, to which anger belongs, linked to the left anterior cortex and an avoidance-related one, that includes anxiety, fear and sadness, associated to right anterior regions. VLPFC is implicated also in the emotion enhancement of memory (EEM), as suggested by Weintraub-Brevda and Chua (2018) that used the cTBS. In emotions processing also the orbitofrontal cortex (OFC) is involved, as well as proved by the improvement in emotion identification, in terms of efficiency and reaction times, after anodal tDCS over the right OFC (Willis et al., 2015).

Emotions recognition implicates the activity of the posterior superior temporal sulcus (pSTS). In line with this Vonck, Swinnen, Wenderoth and Alaerts (2015), an enhancement in the identification of negative bodily emotions (sadness and anger) occurred following anodal tDCS over the right pSTS, compared to cathodal tDCS; no results were found for positive bodily emotions. Sliwinska and Pitcher research (2018) focused on the contribution of the pSTS in emotions elaboration. TMS on the right pSTS, in fact, caused a higher impairment in an emotion recognition task, than stimulation over the left pSTS. The rpSTS has, thus, a domination role in this process. In spite of this for an optimal performance both left and right sPTS were needed. Sliwinska and Pitcher observed, also an inter-individual variability in TMS effects, because some subjects presented an increased activation of the left than the right pSTS. Emotion identification needed the activation of the right occipital face area (rOFA) with the contribution of the right somatosensory cortex (rSC). rTMS over rOFA and rSC, actually, causes an impairment in emotion discrimination, impeding the somatic simulation of faces. Such impairment is sequential, because it occurs at 60-100 ms for the rOFA and at a longer period (100-140 and 130-170 ms) for the rSC after double-pulse TMS (Pitcher et al., 2008). Therefore, a hierarchical process of emotional faces elaboration and early involvement of nonvisual regions can be inferred. The experimental study of Mai, Braun, Probst, Kammer and Pollatos (2019) adds strength to the involvement of the somatosensory cortices in emotions processing, since rTMS with a cTBS protocol produced more positive evaluations of negative pictures, finding that may show a specificity to aversive stimuli. After rTMS over the

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frontotemporal anterior insular network, instead, both positive and negative cues were rated as more neutral, maybe for the conflict between predicted and experienced interoceptive signals.

Nevertheless, no effects on arousal were observed, because of the attenuation of emotional valences or for the nature of the material used. Fan and collaborators (2018) reported the role of the right intraparietal sulcus (rIPS) in perception and attention to emotional expressions. rTMS over the rIPS produced an improvement in emotion identification but only in relation to the left visual field. A possible explanation is that rTMS increased the functional connectivity between rIPS, visual cortex and superior temporal sulcus that are areas implicated in facial perception and in orienting attention according to specific stimuli.

4. The role of cerebellum in emotion identification

The cerebellum is involved in processing of emotional stimuli, in particular identification of negative emotions, since its connections to the amygdala. It contributes to attribution of a meaning to external signals (e.g., Ferrucci and al., 2012); as a result of both anodal and cathodal cerebellar tDCS, an improvement in the elaboration of negative facial expressions occurred. Ferrucci and colleagues (2014) stimulated also the right prefrontal cortex and did not observe any significant effects, suggesting the presence of at least two dissociable systems (Ferrucci & Priori, 2014). Effects of TMS in the decrease of emotional identification accuracy highlighted the role of cerebellar activity (even when emotions are irrelevant for the task) (Ferrari et al., 2018) supporting the hypothesis of the cerebellar involvement in emotional perception and appraisal, probably modulating by MPFC. Cerebellum, indeed, is linked with several regions, being part of the mirror neuron system, such as the ventral prefrontal cortex, the inferior parietal lobule and the inferior frontal gyrus.

In conclusion the DLPFC is involved in discrimination and regulation of both negative and positive emotions, while the VLPFC influences regulation and memorization of negative emotions. Furthermore, and overall, the MPFC responds to *in-group* emotions and self-related concepts. In emotion identification are implicated also the right orbitofrontal cortex, right posterior superior

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temporal sulcus, right temporoparietal junction, and the right intraparietal sulcus. The somatosensory cortex and the frontotemporal anterior insular network, instead, contribute to the overall evaluation of emotions. In addition, the cerebellum has a main role in emotions recognition and appraisal.

Clinical implications of this work

The investigation of brain activity using brain stimulation techniques may allow us to find answers to several questions still unsolved. The knowledge of how brain stimulation techniques act in improving aspects related to emotional awareness can facilitate the overall psychological well-being and the effectiveness of treatment/psychotherapy addressed individuals with psychopathology. It could be extremely useful to focus on how the improvement in emotional awareness can contribute to mitigate those discomforts caused by mental disorders/psychological problems. For example, in anxiety the brain stimulation techniques with their effects may play an important role in reducing the tendency to emotional dysregulation and the consequent impairment in the development of strategies coping or defense mechanisms capable of containing normal fears. Also, during a psychological treatment/psychotherapy, a lacking emotional awareness and regulation could make the therapist as the target of attention seeking and behaviors impulsive, and therefore we may suppose that TMS effects would be useful for improving emotional awareness/emotional regulation abilities, that may increase the overall therapeutic alliance.

Interventions, both pharmacological, psychological and brain stimulation techniques, are often planned and developed as *monotherapies* and we believe that further studies in the combined use of them could be potentially helpful. Recently psychological research has begun to invoke the need for new studies aimed at investigating the potential synergistic effects of multi-modal therapies (e. g., Aakash et al., 2019). This review can represent a first contribute for evidence regarding efficacy of brain stimulation techniques, aimed to support their application combining with, cognitive interventions and or psychotherapies for offering a new approach to treating neuropsychiatric and mental disorders.

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Limitations

This review not included experimental studies included tACS or tRNS.

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Table 1. Literature review on brain stimulation techniques (TMS and tDCS) and emotional awareness/its related components.

Study	Brain stimulation technique	Brain region	Main findings
1. Abend et al. 2019	tDCS	MPFC	MPFC seems to modulate subjective emotional states by facilitating implicit emotion regulation. tDCS facilitates brain activation in MPFC regions underlying implicit regulation of emotions. Accordingly, tDCS contributes to modulates subjective emotional experiences.
2. Allaert et al. 2019	Anodal tDCS	DLPFC	There were evidences of functional lateralization, as with anodal tDCS over the left DLPFC pupil dilatation (an index of arousal and cognitive resource allocation) increased when negative pictures were shown. The major cognitive resource allocation increased the top-down regulation of emotional stimuli. Anodal tDCS over the right DLPFC, instead, reduced the pupil dilatation, observing both negative or positive images.
3. Balconi & Bortolotti 2013	rTMS	DMPFC	rTMS over the DMPFC, during a facial detection task, impaired performance and increased errors and reaction times, above all for anger and fear faces. Besides, empathy resulted linked to responsiveness to emotional faces.
4. Balconi & Canavesio 2015	rTMS	Left DLPFC	The study confirmed the role of left DLPFC in emotion identification, and the relation between face expressions and the BEES, a questionnaire to investigate the empathy capacity. Neuro-stimulation through rTMS over the left DLPFC, actually, rendered discrimination of happy faces more difficult, especially for high-BEES subjects. Participants with high-BAS showed high-BEES and had worse performance in positive emotion recognition as result of TMS.
5. De Pisapia et al. 2019	rTMS	MPFC	The MPFC is implicated in affective coding of negative stimuli, rather than an exclusive elaboration of self, as proved by increased reaction times in negative adjectives elaboration (both when attributes referred to oneself or to close people) after low frequency rTMS over the MPFC. rTMS on the MPFC set the tone of other cerebral areas, modulating BOLD of the posterior cingulate cortex, left angular gyrus and temporal cortex, but only for the elaboration of negative attributes.

6. De Raedt et al. 2010	HF-rTMS	DLPFC	After HF-rTMS over the right DLPFC, a significantly disengagement from angry faces occurred as a result of a reduced activation of the right DLPFC, dACC and left superior parietal gyrus and a major activation of the right amygdala. Following HF-rTMS over the left DPFC, an increased activation of the right DLPFC, right superior parietal gyrus, dACC and the left part of the OFC and consequently a diminished attentional engagement to angry faces, or rather an improvement of the spatial attention. HF-rTMS over the left prefrontal cortex may increase top-down regulation and influence subcortical networks implicated in affective processes.
7. Dedoncker et al. 2019	tDCS	MPFC	The researchers noted, in women with high perceived criticism, a reduction of medial prefrontal neural connectivity, as effect of tDCS after receiving critics.
8. Donaldson et al. 2019	Anodal HD-tDCS	rTPJ	After anodal HD-tDCS over the rTPJ it was noted an improvement of fear recognition, corroborating the role of rTPJ in emotional processing.
9. Fan et al. 2018	rTMS	rIPS	rTMS over the rIPS produced an improvement in emotion identifications but only those in the left visual field. A possible explanation is that rTMS increased the functional connectivity between rIPS, visual cortex and superior temporal sulcus, areas implicated in facial perception and in orienting attention according to stimuli. Thus, emotional cues got attentional resources and reached conscious awareness.
10. Feeser et al. 2014	Anodal tDCS	Right DLPFC	A facilitation of the cognitive reappraisal, downregulating or upregulating emotions, after anodal tDCS was reported with right DLPFC stimulation. It was accompanied by changes in arousal ratings and skin conductance responses.
11. Ferrari et al. 2017	TMS	DLPFC	Following TMS the authors not identified either alteration of positive emotions evaluation after stimulation of the left DLPFC, or compromise of negative emotions identification when the region stimulated was the right DLPFC.
12. Ferrari et al. 2018	TMS	Left cerebellum	TMS had effects in the decrease of emotional identification accuracy shedding light to the left cerebellar activity (even when emotions are irrelevant for the task). The findings support the hypothesis of cerebellar involvement in emotional perception and appraisal, maybe modulating MPFC activity. Cerebellum, indeed, is linked with several regions, being part of the mirror neuron system, such as the ventral prefrontal cortex, the inferior parietal lobule and the inferior frontal gyrus.
13. Ferrucci et al. 2012	tDCS	Cerebellum	As a result of both anodal and cathodal cerebellar tDCS, an improvement was observed in the elaboration of negative facial expressions.

14. Ferrucci & Priori 2014	tDCS	right PFC	After stimulation of the right PFC researchers did not observe any significant effect, suggesting the presence of at least two dissociable systems, including cerebellum one.
15. Gamond & Cattaneo 2016	TMS	DMPFC and rTPJ	TMS over the DMPFC reduced the accuracy for in-group faces and interfered with the in-group advantage in emotion recognition tasks. It was stimulated also the rTPJ, being part of the mentalizing neural network, observing a marginal decrease of accuracy and a delay in participant performances both for in-group and out-group facial expressions.
16. Lantrip et al. 2019	HF-rTMS	DLPFC	The experimental study confirmed the antidepressant effect of HF-rTMS over the left DLPFC, since it remarked an improvement in emotion regulation, modification not reported after right DLPFC stimulation.
17. Lapate et al. 2017	TMS	IPFC	TMS highlighted the role of the left lateral prefrontal cortex in evaluations, influenced by valence of cues previously showed.
18. Leyman et al. 2009	HF-rTMS	DLPFC	One session of HF-rTMS over the right DLPFC induced alterations in the inhibition of negative emotions; but no significant attentional control modifications were noted after HF-rTMS on the left DLPFC.
19. Mai et al. 2019	rTMS	Somatosensory cortices and frontotemporal anterior insular network	rTMS with a cTBS protocol over the somatosensory cortices produced more positive evaluations of negative pictures, finding that may show a specificity to aversive stimuli. After rTMS over the frontotemporal anterior insular network, instead, both positive and negative cues were rated as more neutral, maybe for the conflict between predicted and experienced interoceptive signals.
20. Mattavelli et al. 2011	Single-pulse TMS	MPFC and the right somatosensory cortex	The MPFC is connected to recognition, representation, evaluation and attention to emotional experiences, as this study proved using brain stimulation methods. Participants were subjected to single-pulse TMS over the MPFC and rSC during a task consisting in discriminating happy and angry facial expressions. Facial expressions were preceded by <i>prime</i> words that could refer to happiness or to anger, congruently or not with the target face. After TMS on the MPFC the researchers observed a significantly interference with the priming effect, in case of congruence between prime and target. These findings support the existence of different neural representations for anger and happiness which include a lexical knowledge of facial expressions. Stimulation over the rSC, instead, did not cause any modification on the priming effect.

21. Nitsche et al. 2012	tDCS	Left DLPFC	It was observed an increased ability in discriminating facial expressions (in particular positive facial expressions) as a result of tDCS stimulation over the DLPFC.
22. Nord et al. 2017	Anodal tDCS	Left DLPFC	Anodal tDCS on the left DLPFC did not produce more accurate responses and lesser reaction times in facial emotion categorizing tasks, rather a significant slowing and more uncertain; researchers supposed these data prove tDCS has not an emotion-specific, but a general effect on emotional face identification.
23. Peña-Gómez et al. 2011	Anodal tDCS	Left DLPFC	Anodal stimulation of the left DLPFC changes as less negatively those emotions perceived - before the stimulation - as negative. Furthermore, this effect varies in the extraversion-introversion personality dimension: down-regulation is stronger in subjects with higher subclinical introversion scores.
24. Pitcher et al. 2008	rTMS and double-pulse TMS	rOFA and rSC	rTMS over the right OFA and rSC caused an impairment in emotion discrimination, interfering with the somatic simulation of faces. A hierarchical process of elaboration of emotional faces and early involvement of nonvisual regions can be inferred.
25. Pripfl & Lamm 2015	Anodal tDCS	Right DLPFC	Negative emotions were evaluated more positively after anodal tDCS over the right DLPFC.
26. Riedel et al. 2019	rTMS	Right MPFC	Following rTMS over the right MPFC it was recorded a modification of functional connectivity with the right amygdala. It is supposed that such modifications were due to the neurotransmitter release or changes in trans-synaptic connections among different areas.
27. Riva et al. 2015	Cathodal tDCS	Right VLPFC	Stimulation of the rVLPFC induces more negative emotions, reacting to difficult situations (such as the social exclusion).
28. Sanchez et al. 2016	Anodal tDCS	Right DLPFC	Experimental subjects showed impairments in attentional disengagement from both positive and negative faces, following anodal tDCS on the right DLPFC. Such results strengthen the theory of hemispheric lateralization of emotional processes in general rather than emotion-specific ones.
29. Sanchez-Lopez et al. 2018	Anodal tDCS	DLPFC	The tDCS caused an improvement of top-down attentional control to emotional stimuli, when the stimulated area was the left DLPFC, as it inferred from faster gaze disengagement from emotional faces. Vice versa, stimulation of the right DLPFC implied a slowing of emotional disengagement.

30. Sliwinska & Pitcher 2018	TMS	pSTS	TMS on the right pSTS caused a higher impairment in an emotion recognition task, than stimulation over the left pSTS. The rpSTS has, thus, a domination role in this process. In spite of this for an optimal performance both left and right sPTS were needed. The authors observed, also an inter-individual variability in TMS effects, because some subjects presented an increased activation of the left than the right pSTS.
31. Vanderhasselt et al. 2013	Anodal tDCS	Left DLPFC	Using anodal tDCS over the left DLPFC a higher cognitive control and more rapid inhibitory responses to emotional cue having a positive value were noticed.
32. Vergallito et al. 2018	Anodal tDCS	VLPFC	The implication of VLPFC in emotion regulation is evident in this research, given the fact that anodal tDCS reduced the negative emotions valence. Nevertheless, anodal tDCS, modulated only anxiety, fear and, almost significantly, sadness, unlike anger and disgust. Different emotions response to the neuro-stimulation is due to presence of two motivational systems, subtended by distinct neural networks: an approach-related system, to which anger belongs, linked to the left anterior cortex and an avoidance-related one, that includes anxiety, fear and sadness, associated to right anterior regions. Anodal tDCS over the VLPFC, therefore, had effect just on the emotions of the right-lateralized avoidance system.
33. Vonck et al. 2015	tDCS	Right pSTS	An enhancement in identification of negative bodily emotions (sadness and anger) occurred following anodal tDCS over the right pSTS, compared to cathodal tDCS; no results were found for positive bodily emotions.
34. Weigand et al. 2013	tDCS and rTMS	Right DLPFC	Hemispheric lateralization hypothesis is supported by this study, since tDCS and subsequent rTMS on the right DLPFC improved accuracy, but not reaction times, in working memory tasks with fear-related words. A possible explanation is that the neuro-stimulation, inhibiting the right DLPFC, influenced probably the elaboration of fear-related cues, giving priority to task-relevant information and, consequently, increasing the accuracy. On the contrary, with neutral words it was observed only a reaction times reduction, because cortical excitability decreased, compromising targets identification, but once recognized, performance improved thanks to focusing effect. With anger-related words, instead, anodal tDCS and active rTMS enhanced both accuracy that differently decreased after cathodal tDCS.

35. Weintraub-Brevda & Chua 2018	cTBS	VLPFC	Whilst cTBS over the right VLPFC decreased the EEM effect for “negative arousing” and “negative no arousing” stimuli under full attention; always under full attention, cTBS on the left VLPFC reduced it only for “negative no arousing” words, maybe as consequence to a reduced elaboration of low arousal cues. These data induced the researchers to affirm VLPFC needs sufficient attention to act on the EEM effect, action at all levels of arousal, in spite of the left VLPFC is specific for “negative no arousing”, but not for “negative arousing” words. Perhaps it denotes that the VLPFC function depends on cognitive control and not automatic processes, to which “negative arousing” words are related.
36. Wiegand et al. 2019	Anodal tDCS	Left DLPFC	Following anodal tDCS over the left DLPFC, an increase of cognitive control was observed. In stressful conditions the stimulation improved mood and performance.
37. Willis et al. 2015	Anodal tDCS	Right OFC	In emotions processing OFC is involved, as proved by the improvement in emotions identification, in terms of efficiency and reaction times, after anodal tDCS over the right OFC.
38. Winker et al. 2018	tDCS	VMPFC	Neurostimulation caused an increase of VMPFC activity with the presentation of happy faces when tDCS was excitatory, the opposite occurred with inhibitory tDCS. Another effect of excitatory tDCS was that ambiguous facial expressions needed a higher degree of fearful expressions to be considered fearful, but a minor happiness degree to define them happy. Besides, for the most ambiguous expressions related to happiness reaction times were lower, whereas reaction times were greater for the fearless ambiguous faces, as a result of excitatory tDCS. It seems, therefore, that excitatory stimulation facilitated the recognition of happiness in ambiguous expressions and the decrease of fearful faces one. On the contrary inhibition of VMPFC facilitated identification of the fear in ambiguous expressions and reduced emotional arousal.
39. Zwanzger et al. 2014	rTMS	Right DLPFC	The authors observed in facial expression identification task, as results of rTMS over the right DLPFC, an amplification of visual processes in bilateral parietal, temporal and occipital regions, a major activation of the right TPJ area with threatening cues and, consequently, slower reaction times to fear faces.

Note.

BAS=behavioral activation system

BEES= Balanced Emotional Empathy Scale

cTBS= continuous theta burst stimulation

DLPFC= dorsolateral prefrontal cortex

DMPFC= dorsomedial prefrontal cortex

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EEM= emotion enhancement of memory
HD-tDCS= high-definition transcranial direct current stimulation
HF-rTMS= high frequencies repetitive TMS
IPS= intraparietal sulcus
LPFC= lateral prefrontal cortex
MPFC= medial prefrontal cortex
OFA= occipital face area
OFC= orbitofrontal cortex
PFC= prefrontal cortex
rOFA= right occipital face area
rIPS= right intraparietal sulcus
pSTS= posterior superior temporal sulcus
rSC=right somatosensory cortex
rTMS= repetitive TMS
SC= somatosensory cortex
tDCS= transcranial direct current stimulation
TMS= transcranial magnetic stimulation
TPJ= temporo-parietal junction
VLPFC= ventrolateral prefrontal cortex
VMPFC= ventromedial prefrontal cortex