Epilepsy & Behavior Reports 16 (2021) 100501

Contents lists available at ScienceDirect

Epilepsy & Behavior Reports

journal homepage: www.elsevier.com/locate/ebcr

Neurostimulation for the treatment of functional neurological disorder: A systematic review

Irene Gonsalvez [a,*], Primavera Spagnolo [b], Barbara Dworetzky [c], Gaston Baslet [a]

[a] Department of Psychiatry, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA
[b] Mary Horrigan Connors Center for Women's Health & Gender Biology, Department of Psychiatry, Brigham and Women Hospital, Harvard Medical School, Boston, MA 02115, USA
[c] Department of Neurology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

ARTICLE INFO

Article history:
Received 31 August 2021
Revised 28 October 2021
Accepted 4 November 2021
Available online 9 November 2021

Keywords:
FND
Functional seizures
TMS
tDCS

ABSTRACT

Functional Neurological Disorder (FND), also known as conversion disorder, is characterized by neurological symptoms that are incompatible with any known structural disorder and best explained by a biopsychosocial model. Evidence-based treatments for FND are limited, with cognitive behavioral therapy (CBT) and physiotherapy being the most effective interventions [1]. In recent years, functional neuroimaging studies have provided robust evidence of alterations in activity and connectivity in multiple brain networks in FND. This body of evidence suggests that neurocircuitry-based interventions, such as non-invasive brain stimulation techniques (NIBS), may also represent an effective therapeutic option for patients with FND.

In this systematic review, we outline the current state of knowledge of NIBS in FND, and discuss limitations and future directions that may help establish the efficacy of NIBS as a therapeutic option for FND.

Contents

* Corresponding author.
E-mail address: igonsalvez@bwh.harvard.edu (I. Gonsalvez).

https://doi.org/10.1016/j.ebr.2021.100501
2589-9864/

Introduction

FND: From a psychological explanation to a neurocircuitry disease model

Functional neurologic disorder (FND), also known as conversion disorder, is characterized by the presence of '*one or more symptoms of altered voluntary motor or sensory function which clinical presentation must provide evidence of incompatibility between the symptoms and the recognized neurological or medical condition*', according to the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM–5) [2]. FND comprises a myriad of different symptoms, including motor symptoms (from hyperkinetic- movement disorders- to loss of motor function- paresis), cognitive symptoms, sensory pathology (including vision, hearing, etc.) and seizures. Functional seizures are one of the most common clinical manifestations of FND. Little has been known regarding the underlying pathophysiology of FND. The original conversion disorder hypothesis suggested that psychological factors (i.e., traumatic and/or stressful events) are converted into neurological symptoms [3]. This has been abandoned in favor of a more comprehensive biopsychosocial framework that considers predisposing, precipitating and perpetuating risk factors [4–7].

A growing number of neuroimaging studies in patients with FND has provided evidence of dysfunction in activity and connectivity in brain networks implicated in cognitive and motor control, emotion regulation, self-awareness and agency [8,9]. Clinical studies have led to the identification of positive neurological signs specific for these disorders (e.g., Hoover's sign) [10–12], facilitating the diagnostic process. Furthermore, epidemiological studies have shown that a history of trauma or provoking stressor are not necessary but are considered risk factors for FND [13]. This improved understanding of the pathophysiology of FND has not yet been translated into effective treatments. Currently, evidence-based treatments available for FND include physical and psychological therapies, particularly cognitive-behavioral therapy (CBT)- which represents the most effective evidence-based treatment for patients with FND [1,14–16]- along with reassurance and a compassionate explanation of the diagnosis, which are also critical for recovery [17,18]. Interestingly, efficacy of CBT and motor retraining in patients with FND has been associated with changes in the activity and connectivity of several brain regions implicated in FND [19,20]. This evidence suggests that interventions aimed at targeting neurocircuitry dysfunctions, such as non-invasive brain stimulation (NIBS), may be a promising therapeutic strategy for FND.

Transcranial magnetic stimulation (TMS) and transcranial direct current stimulation (tDCS) are two NIBS interventions increasingly studied for clinical use. Both techniques are safe and well-tolerated when delivered according to existing guidelines [21–24] as they do not require general anesthesia, and both have fewer potential side effects when compared with other neuromodulatory techniques such as electroconvulsive therapy (ECT). ECT was the first electrical stimulation technique used to treat neuropsychiatric disorders, including FND [25], however ECT- related side effects and lack of spatial specificity of this intervention limits its efficacy [see Box 1 for overview of neuromodulatory techniques]. Both TMS and tDCS have demonstrated modulation of brain networks and change in clinical and behavioral domains relevant to FND, in both healthy controls and patients with neuropsychiatric disorders [26–33]. In this study, we review the literature on investigations of NIBS as a therapeutic intervention in patients with FND and discuss the implications that study design, stimulation protocols, patient population and treatment outcomes have in determining the efficacy of NIBS for FND.

Methods

A systematic literature search was performed using PubMed for reports published until July 20, 2021. Two sets of search terms were used: one to identify articles on TMS and FND, and the other to identify articles on tDCS and FND. The terms used in each search can be found in Appendix A and Appendix B.

For study on TMS, our initial search was further refined by selecting those articles that used TMS and repetitive TMS (rTMS) – including also accelerated stimulation protocols such as intermittent theta burst stimulation (iTBS) - as a treatment tool for any FND phenotype. To ensure accuracy, the literature search was performed at four different time points by the first author (IG). We excluded review/update articles, manuscripts that were not in English, and non-therapeutic studies (including reports that used TMS as a diagnostic tool for FND and/or other disorders as well as those that used TMS to measure cortical excitability). We excluded studies that used other neuromodulation treatments (tDCS, vagus nerve stimulation-VNS, ECT). Another article was excluded as presented duplicate subject data [34] that was incorporated in a later report already included in our review [35]. We also examined previously published reviews [14,36–40] and identified three further studies [41–43] that met our inclusion criteria, which were included in the final data collection. Two of these 3 articles were not originally published in English [41,43] and the third one was an abstract not available through PubMed and localized through a different search engine, WebofScience [42]. Thus, data from these articles were extracted from reviews [36,38,44], instead of the original publications. The selection process is illustrated in Fig. 1.

The same procedure was followed to identify publications on tDCS in FND (Fig. 2). We excluded articles not in English, those that used tDCS for pathologies other than FND and reports that did not evaluate tDCS as a therapeutic intervention. Our search led to a single article that used tDCS as a treatment tool for a patient with functional seizures [45]. Additionally, we identified another article describing potential therapeutic benefit of one tDCS session in FND, although the study was not designed to test the efficacy of this intervention [46].

Of note, our search was not limited by age range. No studies were identified that use/studied TMS/rTMS or tDCS in children with functional neurological disorder diagnosis. However, both neurostimulation techniques have been studied in children and adolescents with other neuropsychiatric disorders and determined to be feasible and safe [47–50].

Results

Following our methodology, we divided our results in 2 sections to describe in detail each NIBS technique studied in our review (TMS and tDCS) separately.

1. TMS in FND

We identified a total of 21 studies that investigated the efficacy of TMS/rTMS in FND patients (Fig. 1). Study characteristics are summarized in Table 1.

1.1. Study design

Of the 21 studies identified, 4 were randomized, controlled trials (RCTs) that aimed to assess the efficacy of TMS as a potential treatment for FND, 8 were open label studies /case series and 9 were individual case reports. A total of 82 patients participated in the 4 RCTs (n = 21 [51], n = 33 [52] , n = 17 [53] and n = 11

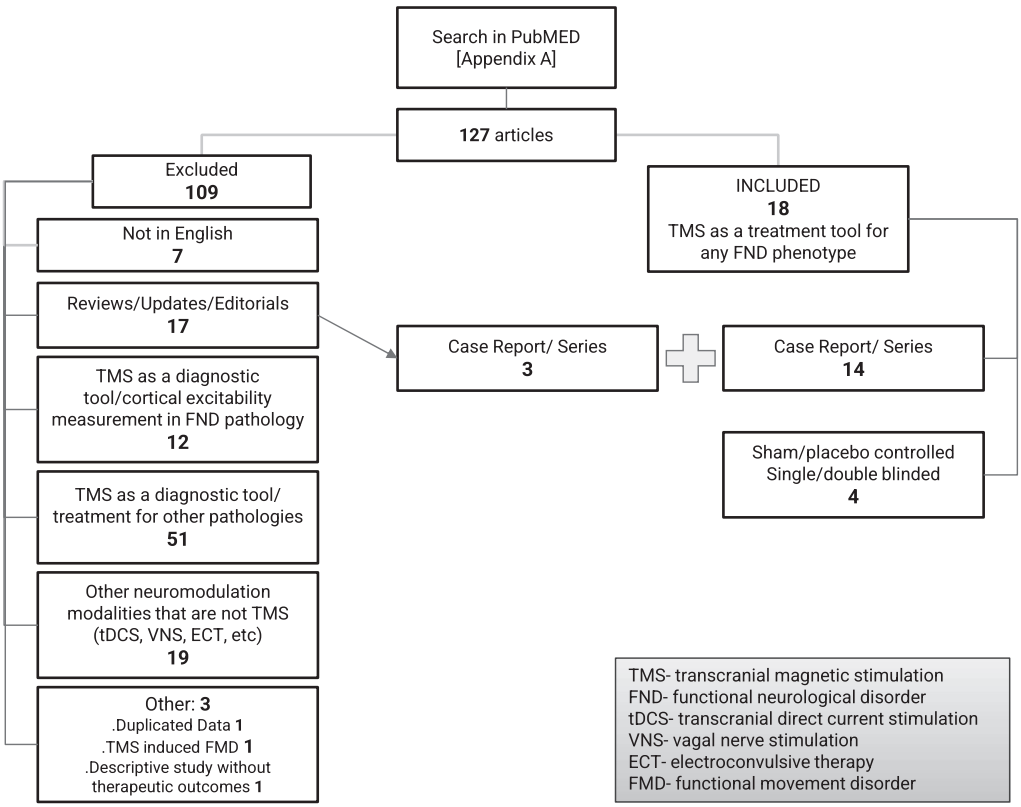

Fig. 1. TMS articles' selection process flowchart.

[54]), while a total of 138 patients were enrolled in open label studies. A total of 11 patients were included in the individual case reports.

Of note, two of the RCTs identified used sham TMS as the control intervention [53,54], while root magnetic stimulation (RMS) [52] and low-intensity stimulation (below motor threshold) [51] were used as control interventions in the other two RCTs.

1.2. Stimulation parameters

The majority of the TMS studies reviewed used low-frequency (<1Hz) rTMS –considered inhibitory– (9 studies: 3 RCTs and 6 case reports). Five studies (1 RCT, 2 case series and 2 case reports) used high-frequency (>5Hz) rTMS –generally considered excitatory–; and 6 studies (5 case series and 1 case report) used single pulse

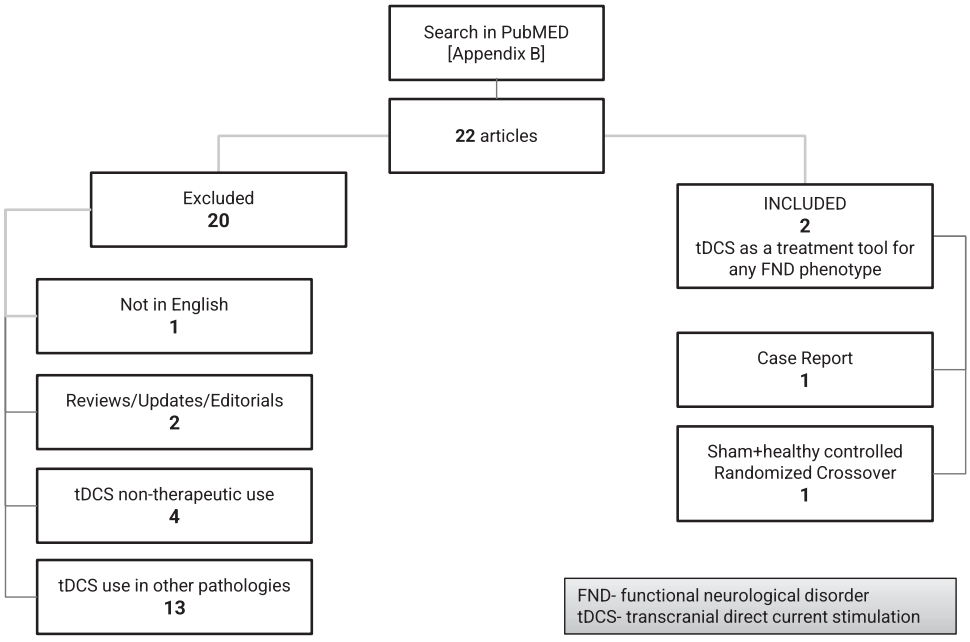

Fig. 2. tDCS articles' selection process flowchart.

Table 1
- TMS- study characteristics' description.

Table 1.1. Randomized Trials

Study (author/ year)	FND Phenotype	Design	N	Parameters of stimulation					Results		
				Anatomical Target	Frequency*	Intensity (% MT)	Total pulses/ session	# Sessions	Outcome Measures	Outcome Time point 1**	Outcome Time point 2***
Randomized Controlled Trials											
Pick et al. [65]	Paresis (unspecified laterality)	Randomized Inactive treatment controlled (rTMS above/below MT) Single blinded	21	MC	rTMS 1Hz	Active arm: 120% RMT Inactive arm: 80% RMT	120 pulses	2 sessions 4 weeks apart	CGI by patient CGI-InvestigatorFIM/ FAM (Psychosocial functioning) Barthel Index (Disability)	Both groups showed improvement-non- significant further improvement in the active vs inactive treatment groups Before and immediately after 2nd TMS session- 67% active group vs 20% inactive group reported "much improvement"	3 months after the first TMS session - 44% active group vs 20% inactive group reported "much improvement" 2 subjects lost of follow-up
Taib et al. [53]	Movement disorder -tremor (unilateral and bilateral)	RandomizedSham controlled (sham rTMS) Double-blinded 2nd phase open label	17	MC(hand+leg areas) .Contralateral in unilateral tremor .Bilateral in bilateral tremor	rTMS 1Hz	90% MT	800 pulses	Phase 1 (controlled trial): 5 sessions in 1 day (either arm)Phase 2 (open label): 3sessions in 3 weeks (rTMS+1 hour hypnosis)	PMDRS CGI-Investigator	Statistically significant improvement in PMDRS tremor subscores and CGI-I in active group only, at 1 month after study inclusion.	Maintained decrease in PMDRS in active rTMS group at M2, M6 and M12.No change in PMDRS or tremor subscore at M6 and M12 in control intervention group
Garcin et al. [52]	Movement disorder -unspecified (all unilateral)	RandomizedSham controlled (RMS) Single blinded Cross-over	33	TMS: MC-Contralateral (legs +arms area) RMS: Spinal Roots-Homolateral (cervical + lumbar)	rTMS 0.25HZ250 microsec (each pulse)	120-150% MT	Average 50 pulses (30-80 pulses)	2 sessions on consecutive days (interval minimum 18 hours) in cross-over design by group	CGI by patientNeurological evaluation (blind) FMD score	Both groups showed improvement (60% of subjects were improved by day 3) No difference between TMS and RMS groups.	Sustained improvement in 56% of all subjects at 1 year Recurrence in 12 subjects at 6 months who responded to single TMS booster session.
Broersma et al. [54]	Paresis (all unilateral)	Randomized REMP-controlled Single Blinded Cross-over	11	MC Contralateral	rTMS 5Hz 2 sec train ITI 4sec	80% MT	9,000 pulses	10 sessions in 2 weeks .Cross-over: separated conditions by 2 monthsRepetition of same protocol (10 sessions in 2 weeks)	.Dynamometry .Subjective change in muscle strength.	Significant increase in objective muscle strength in active group; no significant difference in sham group after 1st 10 sessions (for 8 subjects completing both treatments, increase was larger after active rTMS). No difference in subjective change between the placebo and active rTMS group	No data available

Frequency: if data not included, information was not provided in the original article
**Time Point 1: Assessments performed during the TMS treatment course
***Time Point 2: Assessments performed as follow up after TMS treatment- goal to assess durability of improvement
AC: Anterior Cingulate; CGI: clinical global impression; FMD: Functional Movement Disorders; FIM/FAM: Functional Independence Measure/ Functional Assessment Measure; ITI: inter-train interval; MC: (primary) Motor Cortex;
MT:Motor Threshold; M2,M6,M12: month; PMDRS: Psychogenic Movement Disorders Rating Scale; REMP: real electromagnetic placebo; RMS: Root Magnetic Stimulation; RMT: Resting Motor Threshold.

Table 1.2
Open Label Studies

Table 1.2. Open Label Studies

Study (author/year)	FND Phenotype	Design	N	Parameters of stimulation					Results		
				Anatomical Target	Frequency*	Intensity (% MT)	Total pulses/ session	# Sessions	Outcome Measures	Outcome Time point 1**	Outcome Time point 2***
Open label											
Spagnolo et al. [56]	Movement disorder -unspecified	Open label	6	Left DLPFC Individualized fMRI imaging guided	iTBS	120%RMT	3600pulses	total of 6 sessions 2 visits- 24h interval 3 iTBS sessions each visit, >20min between sessions	Functional MRI data S-FMDRS	Decrease functional connectivity between the left amygdala and DLPFCSignificant FMDRS decrease within each stimulation visit (pre and post treatment)	Significant FMDRS decrease between baseline (pre TMS) and 24h after last stimulation
Peterson et al. [62]	Functional seizures	Open label	7	Right TPJ	rTMS 10Hz 5 sec trains ITI 30sec	110% MT	3000pulses	30 sessions in 3 weeks 2 sessions/day- 15min between sessions	Functional seizures count	Decrease in weekly functional seizures frequency in all subjects throughout treatment.	All participants sustained improvement up to 3 months post-treatment. 4 out of 7 subjects remained seizure free at 3 months.
McWhirter et al. [58]	Upper limb weakness (all unilateral)	Open label	10	MC Contralateral	Single pulses Up to 0.3Hz Sets of 4–5 pulses 3–4 sec interval	120-150% MT depending on subject tolerance	46-70 single pulses	1 session	.Measures of disability (SF-12 and MRS).Self-reported symptom severity (5-point Likert Scale) .Grip strength hand dynamometer .Tapping frequency	Significant reduction in self-report symptoms severity in 4 out of 10 subjects.No differences in objective measures.	Improvement not sustained After 3 months all subjects' symptoms had recurred
Shah et al. (2015)	Movement disorder -unspecified (bilateral)	Open label Phase1:TMS MC; assessment at 2weeks; Phase2:TMS PMC if no change after last assessment.	6	Phase1: MC- Dominant Phase2: Dorsal PMC-Dominant	Single pulses 0.33Hz 150 sec	90% MT	50 pulses	Phase1: 5 sessions Phase2:10 sessions total	WHOLQOL-BREF	Improvement in physical symptoms after both phase 1 and phase 2 Improvement in psychological symptoms only after phase 2. No changes in the social relationship and environmental domains in either phase.	Data only available in 2 subjects who reported sustained improvement after "many months"
Garcin et al. [57]	Movement Disorder -unspecified (9 unilateral; 15 bilateral)	Open label	24	MC Contralateral-unilateral FMD Bilateral-bilateral FMD	Single pulse 0.25Hz	120% MT	20 pulses (average)	1 session	.AIMS (modified). Burke-Fahn-Marsden scale (walking disability subscore).CGI-Improvement (by patient)	75% of subjects improved by >50% immediately after TMS (a third with complete resolution of motor symptoms)	Sustained improvement in 71% of subjects at 1-year follow-up (4 subjects returned to work). 10 subjects relapsed during f/u period but all improved again after boost TMS

(*continued on next page*)

Table 1.2 (*continued*)

Table 1.2. Open Label Studies

Study (author/year)	FND Phenotype	Design	N	Parameters of stimulation					Results		
				Anatomical Target	Frequency*	Intensity (% MT)	Total pulses/ session	# Sessions	Outcome Measures	Outcome Time point 1**	Outcome Time point 2***
Dafotakis et al. [43] [Nicholson [38], Garcin [44]]	Movement Disorder -tremor (3 unilateral; 8 bilateral)	Open label	11	MC Laterality not specified	Single pulse 30pulses 0.2Hz	120%MT-15 pulses 140%MT-15 pulses	30 pulses	1 session	Kinetic Motion Analysis	Immediate reduction of symptoms in 97% of subjects	Sustained recovery in 4 subjects at 8-12months Remaining subjects had recurrence
Chastan and Parain [60]	Paresis (paraparesis 40; monoparesis 26; quadriparesis 2; hemiparesis 2)	Open label	70	MC .Contralateral in unilateral paralysis .Bilateral in bilateral paralysis	Single pulse 30 pulses 4-5 sec interval	100% max stimulator output (2.5 Tesla)	30 pulses	1-2 sessions in 1day (2nd session performed if 1st resulted in incomplete improvement)	None reported	Effective in 89% of subjects (total recovery in 59 subjects) immediately or within hours after rTMS.	Sustained improvement in most patients. Recurrence in 8 subjects at 6 months; 6 received and responded to rTMS booster sessions
Schönfeldt-Lecuona et al [35]	Paresis (3 unilateral; 1 bilateral)	Case Series	4	PMC .Contralateral to paralytic limb .Laterality not specified for subject with bilateral paresis	rTMS 15Hz 2 sec train ITI 4 sec	110% MTx2weeks 90%MTx4-12weeks	4000 pulses	25-70 sessions in 5-14 weeks as dictated by symptomatic recovery	None reported	3 of 4 cases improved by week 2-3 and recovered or improved significantly by week 5-12	Sustained improvement after 1 year

Frequency: if data not included, information was not provided in the original article
**Time Point 1: Assessments performed during the TMS treatment course
***Time Point 2: Assessments performed as follow up after TMS treatment- goal to assess durability of improvement
AC: Anterior Cingulate; AIMS: Abnormal Involuntary Movement Scale; CCI: clinician's clinical impression; CGI: clinical global impression; DLPFC: Dorsolateral Pre-Frontal Cortex; FMD: Functional Movement Disorders; ITI: inter-train interval;
MC: (primary) Motor Cortex; MRS: Modified Rankin Scale; MT: (resting) Motor Threshold; PMC: Premotor Cortex; PMDRS: Psychogenic Movement Disorders Rating Scale; SF-12:

Table 1.3
Case Reports

Table 1.3. Case Reports

Study (author/ year)	FND Phenotype	Design	N	Parameters of stimulation					Results		
				Anatomical Target	Frequency*	Intensity (% MT)	Total pulses/ session	# Sessions	Outcome Measures	Outcome Time point 1**	Outcome Time point 2***
Case Reports											
Bottemanne et al. [66]	Tetraparesis Mixed Tremors Functional Seizures	Case report	1	MC	rTMS 1Hz	150%	300 pulses	20 sessions 2 sessions/day 10 days	MRC	Symptoms improved between 8th and 12th session, with paresis improving first.	At 2 months - resolution of all functional neurological symptoms
Naro et al. [61]	Functional myoclonus	Case report	1	Left PMC	rTMS 1Hz	115% RMT	1,200 pulses	30 sessions 6 weeks 5 sessions/ week	EEG EMG	Magnitude and frequency of the myoclonus were strongly reduced based on EMG data	Patient-reported improvement in myoclonus severity after 2 weeks of rTMS treatment. This improvement consolidated at the end of the rTMS paradigm and persisted up to 2 months later.
Blades et al. [63]	Functional seizures, Functional dystonia -head and neck Dissociative PTSD	Case report	1	Primary target: AC Secondary target: SMA + PMC Laterality not specified	rTMS 1Hz	Not reported	Not reported	36 sessions in 2 months.multiple locations in each session: 36 cingulate, 2 PMC (right+left) , and 32 SMA	BDI-2 GAD-7 PHQ-9 BAI TWSTRS	Improvement in speech, motor twitching, mood and global change after all TMS treatments	Sustained improvement after 2 months leading to return to active duty.
Agarwal [55]	Functional seizures	Case report	1	Right TPJ 1 cm lateral to CP4	iTBS "excitatory" No other specifics given	80% MT	600 pulses	10 sessions in 7 days 2sessions/day	PNES scale HAM-D HAM-A	Decrease functional seizures frequency and in all scales immediately after treatment.	Sustained improvement in all scales one week after treatment and functional seizures remission 2 weeks after treatment.
Yeo et al. [64]	Visual loss	Case report	2	Central occipital cortex	rTMS 10Hz 10 trains 10 sec trains	Not specified "increasing amplitude until phosphenes and tolerance of facial twitching"	Not specified [1000 pulses by TMS parameters]	Case 1: 3 sessions over 3 months Case 2: 6 sessions over 1 year (frequency not specified)	None reported	Improvement in sight in both cases	Complete recovery at 12 (sudden recovery after 8 months) and 15 months in each case (improvement attributed to head injury) .
Portaro et al. [67]	Flaccid paraparesis	Case report	1	MCBilateral (hand+leg area)	rTMS 1Hz	100% maximum output	100 pulses	36 sessions in 12 weeks	Psychological evaluation Gait analysis	Improvement in mood, weakness, pain and gait immediately after rTMS.	No data available
Gaillard et al. [41] (in French) [Schonfeldt-Lecuona et al. [36]]	Quadriplegia	Case report	1	MC Bilateral limb areas	rTMS 1Hz	Not Reported	1,000pulsesxregion total 4,000 pulses	40 sessions in 8 weeks initially-then 2sessions/ week *total duration of treatment not specified	CCI-CGI	Progressive improvement (CGI-I = 1.5), two subsequent recurrences responded to booster treatment (CGI-I = 2.5 and 2 respectively)	Recurrence at f/u (timeline not specified) with medical complications (phlebitis, PE and pressure soars)

(*continued on next page*)

Table 1.3 (*continued*)

Table 1.3. Case Reports

				Parameters of stimulation					Results		
Study (author/ year)	FND Phenotype	Design	N	Anatomical Target	Frequency*	Intensity (% MT)	Total pulses/ session	# Sessions	Outcome Measures	Outcome Time point 1**	Outcome Time point 2***
Kresojevic et al. [42] (Abstract) [Schonfeldt-Lecuona [36]), Nicholson [38]]	Hemiparesis (1-compromising ability to walk) ; ; Movement disorder (1-unspecified)	Case report	2	Vertex	Single pulse 12 pulses	30% maximum output- increasing by 10% stepwise up to 80%	12 pulses	1 session	CCI rating	Immediate response-recovery in both patients	Mild return of symptoms after 6 months
Chastan et al. [59]	Aphonia	Case report	1	Session 1: left PFC; Session 2: right MC	rTMS 0.33Hz 150 sec	100% maximum output (2.5Tesla)	50 pulses	2 sessions 1 week apart	None reported	Dramatic improvement after 2nd session with full recovery within few days	Sustained recovery at 6 months

Frequency: if data not included, information was not provided in the original article
**Time Point 1: Assessments performed during the TMS treatment course
***Time Point 2: Assessments performed as follow up after TMS treatment- goal to assess durability of improvement
AC: Anterior Cingulate; BAI: Beck Anxiety Inventory; BDI-2: Beck Depression Inventory 2; CCI: clinician's clinical impression; CGI: clinical global impression; CP4: central parietal 4 (EEG electrode position); EEG: electroencephalogram; EMG: electromyography; GAD-7: Generalized Anxiety Disorder 7; HAM-A: Hamilton Scale-Anxiety; HAM-D: Hamilton Scale-Depression; MC: (primary) Motor Cortex; MT: (resting) Motor Threshold; PFC: Prefrontal Cortex; PHQ-9: Patient Health Questionnaire 9; PNES: psychogenic non-epilectic seizures; PMC: Premotor Cortex; SMA: Supplementary Motor Area; TPJ: Temporoparietal Junction; TWSTRS: Toronto Western Spasmodic Torticollis Rating Scale

TMS. Lastly, 2 studies (a case report and a proof-of-concept study) used iTBS – an accelerated excitatory protocol using short bursts of stimulation at high frequencies [55,56].

We observed great heterogeneity among studies in terms of duration of the stimulation session, total number of sessions and total duration of the study (including the time period between pre- and post- treatment measurements). Four studies entailed a single session and applied single pulse TMS [42,43,57,58], while the remaining studies using either high or low frequency rTMS used multiple sessions, ranging from 2 [59,60] up to 70 sessions [35]. There was a wide range of pulses depending on the frequency: 12–70 pulses in one session of single pulse TMS, 30–4,000pulses in low frequency rTMS, and 1,000–9,000 in high frequency rTMS. The 2 studies using iTBS applied a total of 600 pulses and 3600 pulses respectively. Some studies reported patients receiving additional TMS session(s) between end of treatment and follow-up visit due to incomplete response, which could impact the outcome at the follow up timepoints [41,52,60].

1.3. Stimulation targets and study population

The majority of the studies included in our review evaluated TMS effects on functional motor disorders (FMD) with negative symptoms (paresis, weakness, paralysis, myoclonus) (see Table 1). In these trials, the primary motor cortex contralateral to the symptom (bilateral in the case of bilateral motor symptoms) represented the most frequently selected anatomical target, with the exception of 2 studies in which the premotor cortex – contralateral to the affected limb [35,61] – and the vertex [42] were stimulated.

Five studies investigated TMS efficacy on FMD with hyperkinetic motor symptoms (2 RCTs, 1 pilot study and 2 case series – Table 1), and they all used the primary motor cortex as the stimulation site, except for one study using an individualized, functional neuroimaging-guided stimulation target within the left dorsolateral prefrontal cortex [56]. Although the TMS protocol used was different between studies (single pulse TMS, low frequency rTMS and iTBS), all reported positive outcomes that persisted through their follow-up timepoint.

Three further studies evaluated the efficacy of TMS on functional seizures. Peterson et al (2018) [62] and Agarwal et al (2019) [55] used right temporo-parietal junction (TPJ) as the anatomical stimulation target, whereas Blades et al (2020) [63] used the anterior cingulate cortex as the target. Although all three studies used different TMS protocols (rTMS excitatory, rTMS inhibitory and iTBS excitatory respectively) and different parameters of stimulation, all three reported positive outcomes with significant improvement after treatment and sustained improved in symptoms at subsequent follow-up timepoints.

There were two studies on other FND phenotypes: one case report that described a case of aphonia, which targeted the left prefrontal cortex and right motor cortex with an inhibitory protocol [59] and another report with 2 cases of visual loss, which stimulated (excitatory rTMS) the central occipital cortex[64].

1.4. Outcome measures

Study outcome measures varied significantly among studies. Some studies used validated outcome scales (e.g., clinical global impression scales [CGI]) to measure change in symptom severity, while others provided a descriptive report. Study outcomes were measured immediately after patients received rTMS and at follow-up in the majority of the studies (Table 1). The interval between the last stimulation session and the follow-up was highly variable among studies, ranging from 24 hours to 12 months. None of the studies consistently incorporated the core outcome measures outlined by the FND-COM group– Clinical Global

Impression-Improvement scale (CGI-I): core FND symptoms change; Patient Health Questionare-15 (PHQ-15): other physical symptoms; Hospital Anxiety and Depression Scale/ Beck Depression Inventory (HADS/BDI): psychological symptoms; Short Form-36 Health Survey Questionnaire/ Work and Social Adjustment Scale (SF-36/WSAS): life impact; Health economics: healthcare resource use [65] – although it is worth noting that many studies were published prior to the FND-COM group recommendations.

Several studies also assessed secondary outcome measures related to mood, pain, functioning, and cognitive complaints. Imaging and/or physiological measures (e.g., functional MRI, EEG) to evaluate target engagement were not included in the studies identified, with the exception of a recent pilot study which used resting-state functional connectivity data to identify an individualized stimulation target and evaluate neurocircuitry engagement [56].

1.5. Efficacy measures

Two of the 4 RCTs evaluated TMS efficacy in terms of objective improvement in muscle strength between subjects receiving active versus sham TMS [53,54]. In the other two RCTs, efficacy was measured as between-group differences in subjective improvement based on patient- and/or investigator-rated CGI scale. Garcin and colleagues [52] found improvement in both active and control (RMS) groups, with no statistical difference between them. Similarly, Pick et al.[51] found subjective improvement within both active and inactive treatment groups. Efficacy from open label studies and case series were reported as a decrease in symptom severity and frequency, as well as complete resolution of symptoms in some cases [55,59,64,66]. In addition, nineteen out of 21 studies included reported results from follow-up assessments. Of these studies, only 2 described no TMS effects on study outcomes at follow-up [54,67], and 16 reported prolonged effects of TMS on primary and/or secondary study outcomes. However, it is important to note that time at follow-up varied greatly among studies (from 24 hours to 1 year after last TMS session). In some of the studies with positive follow-up outcomes, patients received further TMS sessions if exhibiting symptoms at follow-up [52,57,60], thus affecting the validity of follow-up data at a later timepoint.

2. tDCS in FND

We identified 2 studies investigating the effects of tDCS on FND (Fig. 2). Study characteristics are summarized in Table 2. The first study is a case report describing the effects of 30 sessions of anodal (excitatory) tDCS stimulation over the F3 EEG position (left dorsolateral prefrontal cortex-DLPFC), over 15 consecutive working days, with a duration of 30 minutes per session. Interestingly, the stimulation target was selected using a FDG-PET(fluorodeoxy glucose-positron emission tomography) guided approach; which in this case showed hypometabolism in the frontal region [45]. The authors reported reduction in functional neurological symptoms as well as mild improvement in psychiatric symptoms. Symptom improvement was observed for 8 weeks after treatment, although the patient required additional tDCS sessions within those 8 weeks due to incomplete response.

As mentioned above, we included a further case-control study that aimed to measure improvement in interoceptive sensitivity and spatial attention and used tDCS as a neurocircuitry probe [46]. The authors investigated the effects of one anodal tDCS session (20 minutes) over the posterior parietal cortex on interoceptive sensitivity (by a heart rate detection task) and spatial attention (using the Posner paradigm [68]). There was a significant decrease in interoceptive sensitivity in the FND group after the tDCS session, while no significant difference was found in the healthy control group. The authors suggest a potential translation of these positive results to a hypothetical therapeutic effect of tDCS in FND. The authors also demonstrated a negative correlation between interoceptive sensitivity and scales measuring alexithymia, depression, and anxiety in the active but not in the control group. There was no effect of tDCS on spatial attention in either group, which could be due to the study's small sample.

Discussion

In this systematic review we examined a total of 23 studies investigating the therapeutic potential of tDCS and rTMS for FND: 21 used TMS/rTMS and 2 used tDCS. These studies were small in sample size, variable in design, and differed in terms of stimulation protocols, FND phenotype, and outcome measures.

In terms of stimulation paradigms, most studies used rTMS, with sessions ranging between 10 and 20 minutes. The majority of the studies used high frequency stimulation, but overall the frequency varied from 1 to 20 Hz. The intensity, measured as a percentage of resting motor threshold, ranged from 80% to 140% and the motor threshold was usually determined visually and only in a few cases using electromyography (EMG), which is more accurate and reproducible. The total number of pulses, an essential parameter for rTMS efficacy [69], varied between 600 and 2000 in most trials.

A further critical source of variability was represented by the stimulation target. In the majority of studies, the motor cortex was selected as target site, despite lack of motor cortex abnormalities in patients with FND based on a large body of neurophysiological and neuroimaging studies (for a review see Spagnolo, Garvey and Hallett, 2021 [56]). Current evidence suggests that functional neurological symptoms are associated with abnormalities in activity and connectivity in motor-limbic circuitry (i.e., amygdala, insula, supplementary motor area) as well brain areas implicated in agency (right temporoparietal junction – rTPJ– and precuneus) [60,61]. Therefore, modulation of these areas via NIBS may represent a novel and effective therapeutic strategy for FND. Furthermore, studies targeting these regions via NIBS may allow to directly probe a causal link between dysfunction in distinct brain networks and clinical and behavioral manifestations of FND. Neuroimaging studies alone do not provide such causal connections. As our understanding of the neurobiological basis of FND grows, NIBS may play a pivotal role in facilitating the translation of this knowledge into neurobiologically-informed therapeutic interventions for FND.

In addition to the rationale for choosing a given brain region, the procedure to identify the specific stimulation site within said region needs to be considered. The majority of previous TMS studies in FND selected the target areas using scalp landmarks or skull coordinates based on an EEG electrode system. These approaches can lead to inaccurate targeting compared to MRI-based neuronavigation methods [70] and do not account for the complex functional organization of the brain and for disease-specific alterations in neurocircuitry. Neuroimaging-guided target selection currently represents the gold standard for NIBS studies, as this method allows for an accurate and reproducible identification of the stimulation site. Importantly, mounting evidence indicates that clinical response to NIBS, particularly rTMS, relates to the functional connectivity between the cortical stimulation site and distal brain regions, which are part of the same neurocircuitry. For example, in patients with depressive disorders, the connectivity

Table 2
- tDCS – study characteristics' description.

Study (author/year)	FND Phenotype	Design	N	Location	Current	Electrode size	Duration	# Sessions	Outcome Scales	Outcome Time point 1*	Outcome Time point 2**
Leroy et al. 2019	Functional Seizures	Case report	1	PET-guided Anode F3 Cathode FP2	2 mA	Anode 35cm2 Cathode 35 cm2	30 min	30 sessions in 15 working days	.AIMS .Seizure episodes .MADRS .TAS	Proggresive decrease of involuntary movemenrs beginning at week 2 of treatment. Mild improvement in psychiatric symptoms overall. After 5 weeks: .AIMS < 63%; PNES < 80% .MADRS < 20%; TAS < 8%	Booster treatements for 1 week at 5 wks post-treatment due to incomplete response. Improvement remained stable over 8 weeks
Demartini et al. 2019	FMS .Tremor .Parkinsonism .Dystonia .Weakness	Randomized Double blind Cross-over Sham + healthy control	9FMS 7Healthy controls	Anode:R-PPC Cathode: Supraorbital (laterality not specified)	1.5 mA	Anode 25cm2 Cathode 35 cm2	20 min	1 tDCS 1 sham tDCS (2 day minimun interval)	.Heartbeat Detection Task (interoceptive sensitivity) .Posner Paradigm (spatial attention) .HAM-A .HAM-D .TAS-20	Significant decrease in Interoceptive sensitivity in the FND group vs healthy control No significant change in spatial attention task after intervention in either group	No follow up

*Time Point 1: Assessments performed during the tDCS treatment course.
**Time Point 2: Assessments performed as follow up after tDCS treatment- goal to assess durability of improvement.
AIMS: abnormal involuntary movement scale; FMS: functional movement symptoms; HAM-A: Hamilton Rating Scale for Anxiety; HAM-D: Hamilton Rating Scale for depression; mA:milliampere; MADRS: Montgomery-Asberg Depression Rating Scale; PNES: psychogenic non-epileptogenic seizures; PPC: posterior parietal cortex; TAS:Toronto Alexithymia Scale; tDCS: transcranial direct current stimulation.

between the stimulation target in the left dorsolateral prefrontal cortex and the subgenual cingulate cortex has been shown to predict clinical response to rTMS. These observations have prompted the investigation of a novel, individualized connectivity-based targeting strategy, which allows to tailor the stimulation target to each patient. This approach has already been used in several studies, including a study in patients with Alzheimer' disease and a recent study in patients with FMD [56,71].

Interpretation of the results of rTMS and tDCS is also limited by the size and characteristics of the sample. The majority of the reviewed trials consisted of small sample sizes with clinically heterogeneous populations. Patients enrolled in these studies were affected by different phenotypes within the FND spectrum, such as FMD and functional seizures; and within the FMD group, studies evaluated patients with both positive and negative motor symptoms, raising the question whether NIBS in FND should be approached considering the specific FND phenotype. Studies on the neurobiology of FND usually consist of small samples of patients with similar FND symptoms [9,72]. Therefore, our current understanding of the neurobiology of FND is based on samples that at least share some phenotypic resemblance. Note that this may be overcome if, as suggested above, anatomical targets can be individualized based on functional neuroimaging, allowing for more flexible anatomical target and protocol selection.

A further source of variability is represented by psychiatric comorbidities. Functional seizures, for example, are associated with high frequency and severity of depression, anxiety, posttraumatic stress, dissociation, and somatic distress [73]. Many of these comorbid disorders have well-established neurocircuitry dysfunction that may converge (or not) with the proposed neurocircuitry dysfunction in FND, such as brain areas involved in emotion regulation and cognitive control [74]. Understanding the overlap in neurocircuitry alteration between FND and comorbid conditions could potentially further reinforce target selection. This suggestion should be cautiously considered, as evidence already exists that well-proven therapies for comorbid psychopathology do not automatically translate into improvement in FND symptoms [75] and vice versa [76].

Future directions

Our review of the extant literature on NIBS for FND shows that efficacy and real indications for the use of tDCS and rTMS in this patient population need confirmation. Many critical questions remain unanswered, including the optimal stimulation parameters, the appropriate patient population, and the opportunity to combine other treatments. Larger studies are needed, and these should be based on specific, testable pathophysiological hypotheses and robust electrophysiological effects. Physiological measures, including EEG, PET and functional MRI, should be included in such studies to provide evidence of *target engagement*, that is that the stimulation protocol selected is able to modulate activity and/or connectivity in the selected site and related neurocircuitry. Furthermore, combining these measures with clinical outcomes can provide mechanistic insights and better characterize the neurocircuitry underlying FND.

To fully uncover the therapeutic potential of NIBS for FND, other aspects should also be considered and investigated. First, it will be important to assess the effects of NIBS combined with other therapeutic strategies. For instance, engagement in specific activities (for example, FND-specific physical therapy or CBT) or tasks (e.g., cognitive tasks, cue exposure tasks) immediately before, during or after neurostimulation has the potential to directly engage the neurocircuitry targeted by NIBS, thus reinforcing neuroplastic effects, as suggested by studies in depressed patients [74,75]. For example, CBT for functional seizures utilizes distraction, relaxation techniques, exposure to avoided or feared situations and development of more flexible thinking patterns [1]. Exposing patients to this learning around the time of neurostimulation would therapeutically exploit the neuroplastic changes induced by NIBS and could potentially solidify or amplify therapeutic gains from CBT. A similar approach may be considered for a treatment protocol pairing FND-informed physical therapy with NIBS [77]. Having the experience of moving a limb again, recovering speech, or decreasing a positive sensory symptom through neurostimulation could serve as a powerful "catalytic inducer of change," especially if coupled with behaviors and/or cognitions that help reinforce the positive experience. An equivalent mechanism has been described in phantom limb pain phenomena, where stimulating the motor cortex [78] or the sensory cortex [79] contralateral to the amputated limb can "reset" altered perception. A related approach using a virtual reality-delivered mirror and exposure therapy protocol, without neurostimulation, has been described in FND [80]. These studies support the hypothesis that exposure to a rectified motor or sensory experience (which may be facilitated by neurostimulation) offers therapeutic potential. More recently, this hypothesis was tested by Bottemanne and colleagues [76], who used a biofeedback protocol coupled with rTMS in which a patient visualized motor activity of her upper limbs during stimulation of the primary motor area, with promising results. It is also critical to consider the cognitive pre-conditioning that may occur before neurostimulation treatment (patients hear "TMS will most likely help you"). The therapeutic effect of a suggestion is well documented and participants in TMS studies and actual treatment are known to gain confidence in recovery due to guidance from study staff [64]. A placebo effect should be further examined, and therapeutically exploited in FND if beneficial, as it has been shown to be an influencing factor in treatment response in TMS studies for different pathologies [81–84]. Investigation of the added benefit of NIBS to proven therapies for FND would require properly designed powered sham-controlled studies.

Finally, future studies should use a reliable and widely validated set of outcomes measures, as recommended by the FND-COM group, to assess treatment response and to facilitate comparisons between NIBS studies using different stimulation targets or protocols [65]. These outcomes should be evaluated immediately after patients receive NIBS and at follow-up intervals to establish both the acute and long-term effects of NIBS.

Conclusions

In conclusion, the efficacy of rTMS and tDCS as potential treatments for FND still needs to be confirmed. Existing NIBS studies in FND are heterogeneous in design. Many critical questions regarding development of future NIBS treatment protocols remain unanswered, such as what the optimal stimulation parameters are, who the appropriate patient population should be, and how to combine NIBS with other treatments. More work and larger studies are needed, but these studies should be based on our current understanding of the neurobiology of FND and should be designed to assess both clinical and brain-level effects. Physiological measurements (functional MRI, EEG) should be associated with clinical outcomes, to provide evidence of target engagement, as well as to better characterize the neurocircuitry underlying FND. Ultimately, the future of NIBS for FND and other psychiatric disorders depends on the design of studies that will provide answers for these crucial questions.

Box 1
TMS and tDCS: an overview:

Transcranial Magnetic Stimulation (TMS) is a non-invasive technique that uses an electromagnetic coil to generate electrical activity in targeted brain regions through the application of magnetic pulses. It is used to study brain physiology and plasticity when delivered as a single pulse TMS, or to elicit neuromodulation and neuroplasticity throughout train of pulses, repetitive TMS (rTMS) [85,86]. Neurostimulation with rTMS increases cortical excitability when delivered via high frequency stimulation (≥5 Hz) or intermittent theta burst stimulation (iTBS- a variation of high frequency rTMS) or decreases cortical excitability when delivered via low frequency (1 Hz) rTMS or continuous theta burst stimulation [87–89]. All these variants of stimulation frequencies could translate into prolonged excitability that outlasts the stimulation period [85,90–92]. The different coil shapes and the strength of the field determine which brain structures the stimulation can reach. Classical figure-of-eight coil targets brain regions at a depth of 3–4 cm while newer coils (H-coil) could reach areas 5–7 cm deep [93]. Muscle pain surrounding the area of the stimulation along with self-limited scalp pain and headache following the stimulation are the main side effects reported in rTMS [86]. The most serious concern is the potential risk of inducing an epileptic seizure, which translates into a minimal risk once following proper screening processes (by medical professionals) and TMS guidelines [23,94]. In terms of therapeutic applicability, TMS has been approved by the FDA for the treatment of major depressive disorder (2008) [95], migraine (2013) [96] and most recently OCD (2018) [97], and will likely continue to expand as TMS continues to show benefit for the treatment of many other disorders including post-traumatic stress disorder (PTSD) [98] substance use disorders [99], schizophrenia [100], cognitive abilities in Alzheimer's Disease (AD) [101], etc.

Transcranial direct current stimulation (tDCS) is a non-invasive technique that uses a low-amplitude direct current (0.5–2 mA) through a pair of saline-soaked electrode pads placed directly over the scalp and connected to a battery device. It appears that tDCS modifies cortical excitability through subthreshold modulation of neuronal membrane potentials [102,103], and also can induce lasting plasticity changes [104]. Direction of cortical modulation (facilitation vs inhibition) depends on duration, intensity, and polarity of stimulation [105]. In addition, effects of tDCS could be altered depending on electrode positioning and configuration as well as skull thickness and composition [106]. tDCS's most common side effects are skin irritation and a sensation of burning [107].

It is important to note that both TMS and tDCS are overall safer and better tolerated than medications, especially in specific populations such as pregnant or women of child-bearing age, older adults, and those subjects with medical conditions impacting the absorption, distribution, or metabolism of drugs. To date, tDCS is not an FDA-approved treatment for any pathologies.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A .- terminology used for TMS study search

("functional neurological disorders"[Text Word] OR "functional neurological symptom disorders"[Text Word]) OR "conversion disorder"[Text Word]) OR "hysterical symptoms"[Text Word]) OR "psychogenic symptoms"[Text Word]) OR "psychogenic disorders"[Text Word]) OR "functional weakness"[Text Word]) OR "psychogenic weakness"[Text Word]) OR "conversion paralysis"[Text Word]) OR "psychogenic paralysis"[Text Word]) OR "functional movement disorder"[Text Word]) OR "functional movement disorders"[Text Word]) OR "psychogenic movement disorder"[Text Word]) OR "psychogenic movement disorders"[Text Word]) OR "functional gait"[Text Word]) OR "psychogenic gait"[Text Word]) OR "functional neurological paresis"[Text Word]) OR "psychogenic paresis"[Text Word]) OR "conversion paresis"[Text Word]) OR "functional motor"[Text Word]) OR "psychogenic motor"[Text Word]) OR "conversion motor"[Text Word]) OR "PNES"[Text Word]) OR "psychogenic nonepileptic seizures"[Text Word]) OR "nonepileptic seizures"[Text Word]) OR "dissociative seizures" [Text Word]) AND (((("TMS"[Text Word] OR "transcranial magnetic stimulation"[Text Word]) OR "rTMS"[Text Word]) OR "neuromodulation"[Text Word])

Appendix B .- terminology used for tDCS study search

("functional neurological disorders"[Text Word] OR "functional neurological symptom disorders"[Text Word]) OR "conversion disorder"[Text Word]) OR "hysterical symptoms"[Text Word]) OR "psychogenic symptoms"[Text Word]) OR "psychogenic disorders"[Text Word]) OR "functional weakness"[Text Word]) OR "psychogenic weakness"[Text Word]) OR "conversion paralysis"[Text Word]) OR "psychogenic paralysis"[Text Word]) OR "functional movement disorder"[Text Word]) OR "functional movement disorders"[Text Word]) OR "psychogenic movement disorder"[Text Word]) OR "psychogenic movement disorders"[Text Word]) OR "functional gait"[Text Word]) OR "psychogenic gait"[Text Word]) OR "functional neurological paresis"[Text Word]) OR "psychogenic paresis"[Text Word]) OR "conversion paresis"[Text Word]) OR "functional motor"[Text Word]) OR "psychogenic motor"[Text Word]) OR "conversion motor"[Text Word]) OR "PNES"[Text Word]) OR "psychogenic nonepileptic seizures"[Text Word]) OR "nonepileptic seizures"[Text Word]) OR "dissociative seizures" [Text Word]) AND (((("tDCS"[Text Word] OR "transcranial direct current stimulation"[Text Word])

References

[1] Goldstein LH, Robinson EJ, Mellers JDC, Stone J, Carson A, Reuber M, et al. Cognitive behavioural therapy for adults with dissociative seizures (CODES): a pragmatic, multicentre, randomised controlled trial. Lancet Psych 2020;7(6):491–505. https://doi.org/10.1016/S2215-0366(20)30128-0.

[2] American Psychiatric Association, editor. Diagnostic and statistical manual of mental disorders: DSM-5. 5th ed. Washington, D.C: American Psychiatric Association; 2013.

[3] Breuer J, Freud S. Studies in hysteria. In the standard edition of the complete psychological works of Sigmund Freud. London: Hogarth Press; 1895.

[4] Asadi-Pooya AA, Beghi M, Baslet G. Is sexual trauma a risk factor for functional (psychogenic) seizures? Neurosci. Biobehav. Rev. 2021;128:58–63. https://doi.org/10.1016/j.neubiorev.2021.06.019.

[5] Nicholson TR, Carson A, Edwards MJ, Goldstein LH, Hallett M, Mildon B, et al. Outcome Measures for Functional Neurological Disorder: A Review of the Theoretical Complexities. J Neuropsychiatry Clin Neurosci 2020;32(1):33–42. https://doi.org/10.1176/appi.neuropsych.19060128.

[6] Pick S, Goldstein LH, Perez DL, Nicholson TR. Emotional processing in functional neurological disorder: a review, biopsychosocial model and research agenda. J Neurol Neurosurg Psychiatry 2019;90(6):704–11. https://doi.org/10.1136/jnnp-2018-31920110.1136/jnnp-2018-319201.supp1.

[7] Sojka P, Paredes-Echeverri S, Perez DL. Are Functional (Psychogenic Nonepileptic) Seizures the Sole Expression of Psychological Processes? Curr Top Behav Neurosci 2021. https://doi.org/10.1007/7854_2021_225.

[8] Perez DL, Nicholson TR, Asadi-Pooya AA, Bègue I, Butler M, Carson AJ, et al. Neuroimaging in Functional Neurological Disorder: State of the Field and Research Agenda. NeuroImage Clin 2021;30:102623. https://doi.org/10.1016/j.nicl.2021.102623.

[9] Voon V, Cavanna AE, Coburn K, Sampson S, Reeve A, LaFrance WC. Functional Neuroanatomy and Neurophysiology of Functional Neurological Disorders

(Conversion Disorder). J Neuropsychiatry Clin Neurosci 2016;28(3):168–90. https://doi.org/10.1176/appi.neuropsych.14090217.
[10] Daum C, Gheorghita F, Spatola M, Stojanova V, Medlin F, Vingerhoets F, et al. Interobserver agreement and validity of bedside "positive signs" for functional weakness, sensory and gait disorders in conversion disorder: a pilot study. J Neurol Neurosurg Psychiatry 2015;86(4):425–30. https://doi.org/10.1136/jnnp-2013-307381.
[11] McWhirter L, Stone J, Sandercock P, Whiteley W. Hoover's sign for the diagnosis of functional weakness: a prospective unblinded cohort study in patients with suspected stroke. J Psychosom Res 2011;71(6):384–6. https://doi.org/10.1016/j.jpsychores.2011.09.003.
[12] Cock HR, Edwards MJ. Functional neurological disorders: acute presentations and management. Clin Med 2018;18(5):414–7. https://doi.org/10.7861/clinmedicine.18-5-414.
[13] Ludwig L, Pasman JA, Nicholson T, Aybek S, David AS, Tuck S, et al. Stressful life events and maltreatment in conversion (functional neurological) disorder: systematic review and meta-analysis of case-control studies. Lancet Psychiatry 2018;5(4):307–20. https://doi.org/10.1016/S2215-0366(18)30051-8.
[14] Gilmour GS, Nielsen G, Teodoro T, Yogarajah M, Coebergh JA, Dilley MD, et al. Management of functional neurological disorder. J. Neurol. 2020;267(7):2164–72. https://doi.org/10.1007/s00415-020-09772-w.
[15] LaFrance WC, Baird GL, Barry JJ, Blum AS, Frank Webb A, Keitner GI, et al. Multicenter pilot treatment trial for psychogenic nonepileptic seizures: a randomized clinical trial. JAMA Psychiatry 2014;71(9):997. https://doi.org/10.1001/jamapsychiatry.2014.817.
[16] Nielsen G. Physical treatment of functional neurologic disorders. Handb. Clin. Neurol., vol. 139, Elsevier; 2016, p. 555–69. Doi: 10.1016/B978-0-12-801772-2.00045-X.
[17] Espay AJ, Aybek S, Carson A, Edwards MJ, Goldstein LH, Hallett M, et al. Current Concepts in Diagnosis and Treatment of Functional Neurological Disorders. JAMA Neurol 2018;75(9):1132. https://doi.org/10.1001/jamaneurol.2018.1264.
[18] Stone J, Carson A. Functional neurologic disorders. Contin Minneap Minn 2015;21:818–37. https://doi.org/10.1212/01.CON.0000466669.02477.45.
[19] Espay AJ, Ries S, Maloney T, Vannest J, Neefus E, Dwivedi AK, et al. Clinical and neural responses to cognitive behavioral therapy for functional tremor. Neurology 2019;93(19):e1787–98. https://doi.org/10.1212/WNL.0000000000008442.
[20] Faul L, Knight LK, Espay AJ, Depue BE, LaFaver K. Neural activity in functional movement disorders after inpatient rehabilitation. Psychiatry Res Neuroimaging 2020;303:111125. https://doi.org/10.1016/j.pscychresns.2020.111125.
[21] Antal A, Alekseichuk I, Bikson M, Brockmöller J, Brunoni AR, Chen R, et al. Low intensity transcranial electric stimulation: Safety, ethical, legal regulatory and application guidelines. Clin Neurophysiol 2017;128(9):1774–809. https://doi.org/10.1016/j.clinph.2017.06.001.
[22] Hallett M, Di Iorio R, Rossini PM, Park JE, Chen R, Celnik P, et al. Contribution of transcranial magnetic stimulation to assessment of brain connectivity and networks. Clin Neurophysiol Off J Int Fed Clin Neurophysiol 2017;128(11):2125–39. https://doi.org/10.1016/j.clinph.2017.08.007.
[23] Rossi S, Antal A, Bestmann S, Bikson M, Brewer C, Brockmöller J, et al. Safety and recommendations for TMS use in healthy subjects and patient populations, with updates on training, ethical and regulatory issues: Expert Guidelines. Clin Neurophysiol Off J Int Fed Clin Neurophysiol 2021;132(1):269–306. https://doi.org/10.1016/j.clinph.2020.10.003.
[24] Rossini PM, Burke D, Chen R, Cohen LG, Daskalakis Z, Di Iorio R, et al. Non-invasive electrical and magnetic stimulation of the brain, spinal cord, roots and peripheral nerves: Basic principles and procedures for routine clinical and research application. An updated report from an I.F.C.N. Committee. Clin Neurophysiol Off J Int Fed Clin Neurophysiol 2015;126(6):1071–107. https://doi.org/10.1016/j.clinph.2015.02.001.
[25] Gilman SL. Electrotherapy and mental illness: then and now. Hist Psychiatry 2008;19(3):339–57. https://doi.org/10.1177/0957154X07082566.
[26] De Freitas DJ, De Carvalho D, Paglioni VM, Brunoni AR, Valiengo L, Thome-Souza MS, et al. Effects of transcranial direct current stimulation (tDCS) and concurrent cognitive training on episodic memory in patients with traumatic brain injury: a double-blind, randomised, placebo-controlled study. BMJ Open 2021;11(8):e045285. https://doi.org/10.1136/bmjopen-2020-045285.
[27] Edwards MJ, Talelli P, Rothwell JC. Clinical applications of transcranial magnetic stimulation in patients with movement disorders. Lancet Neurol 2008;7(9):827–40. https://doi.org/10.1016/S1474-4422(08)70190-X.
[28] Grami F, de Marco G, Bodranghien F, Manto M, Habas C. Cerebellar Transcranial Direct Current Stimulation Reconfigures Brain Networks Involved in Motor Execution and Mental Imagery. The Cerebellum 2021. https://doi.org/10.1007/s12311-021-01322-y.
[29] Ironside M, Browning M, Ansari TL, Harvey CJ, Sekyi-Djan MN, Bishop SJ, et al. Effect of Prefrontal Cortex Stimulation on Regulation of Amygdala Response to Threat in Individuals With Trait Anxiety: A Randomized Clinical Trial. JAMA Psychiatry 2019;76(1):71. https://doi.org/10.1001/jamapsychiatry.2018.2172.
[30] Rothwell J. Transcranial brain stimulation: Past and future. Brain Neurosci Adv 2018;2:2398212818818070. Doi: 10.1177/2398212818818070.
[31] Sudbrack-Oliveira P, Razza LB, Brunoni AR. Chapter One - Non-invasive cortical stimulation: Transcranial direct current stimulation (tDCS). In: Moro E, Polosan M, Hamani C, editors. Int. Rev. Neurobiol., vol. 159, Academic Press; 2021, p. 1–22. Doi: 10.1016/bs.irn.2021.01.001.
[32] Valero-Cabré A, Amengual JL, Stengel C, Pascual-Leone A, Coubard OA. Transcranial magnetic stimulation in basic and clinical neuroscience: A comprehensive review of fundamental principles and novel insights. Neurosci. Biobehav. Rev. 2017;83:381–404. https://doi.org/10.1016/j.neubiorev.2017.10.006.
[33] Zito GA, Anderegg LB, Apazoglou K, Müri RM, Wiest R, Holtforth MG, et al. Transcranial magnetic stimulation over the right temporoparietal junction influences the sense of agency in healthy humans. J. Psychiatry Neurosci. 2020:271–8. https://doi.org/10.1503/jpn.190099.
[34] Schönfeldt-Lecuona C, Connemann BJ, Spitzer M, Herwig U. Transcranial magnetic stimulation in the reversal of motor conversion disorder. Psychother. Psychosom. 2003;72:286–8. https://doi.org/10.1159/000071900.
[35] Schönfeldt-Lecuona C, Connemann BJ, Viviani R, Spitzer M, Herwig U. Transcranial Magnetic Stimulation in Motor Conversion Disorder: A Short Case Series. J. Clin. Neurophysiol. 2006;23:473–6. https://doi.org/10.1097/01.wnp.0000219004.69158.1e.
[36] Schönfeldt-Lecuona C, Lefaucheur J-P, Lepping P, Liepert J, Connemann BJ, Sartorius A, et al. Non-Invasive Brain Stimulation in Conversion (Functional) Weakness and Paralysis. A Systemat Rev Future Perspect Front Neurosci 2016;10. https://doi.org/10.3389/fnins.2016.00140.
[37] McWhirter L, Carson A, Stone J. The body electric: a long view of electrical therapy for functional neurological disorders. Brain 2015;138:1113–20. https://doi.org/10.1093/brain/awv009.
[38] Nicholson TRJ, Voon V. Transcranial magnetic stimulation and sedation as treatment for functional neurologic disorders. Handb. Clin. Neurol., vol. 139, Elsevier; 2016, p. 619–29. Doi: 10.1016/B978-0-12-801772-2.00050-3.
[39] Parain D, Chastan N. Large-field repetitive transcranial magnetic stimulation with circular coil in the treatment of functional neurological symptoms. Neurophysiol Clin Neurophysiol 2014;44(4):425–31. https://doi.org/10.1016/j.neucli.2014.04.004.
[40] Pollak TA, Nicholson TR, Edwards MJ, David AS. A systematic review of transcranial magnetic stimulation in the treatment of functional (conversion) neurological symptoms. J Neurol Neurosurg Psychiatry 2014;85(2):191–7. https://doi.org/10.1136/jnnp-2012-304181.
[41] Gaillard A, Gaillard R, Mouaffak F, Radtchenko A, Lôo H. Traitement par électroconvulsivothérapie d'une tétraplégie par conversion hystérique : à propos d'un cas. L'Encéphale 2012;38:104–9. https://doi.org/10.1016/j.encep.2011.06.005.
[42] Kresojevic N, Petrovic I, Tomic A, Svetel M, Radovanovic S, Kostic V. Transcranial magnetic stimulation in therapy of psychogenic neurological symptoms: Two case reports: 101. Mov Disord 2010;25.
[43] Dafotakis M, Ameli M, Vitinius F, Weber R, Albus C, Fink G, et al. Der Einsatz der transkraniellen Magnetstimulation beim psychogenen Tremor - eine Pilotstudie. Fortschritte Neurol Psychiatr 2011;79(04):226–33. https://doi.org/10.1055/s-0029-1246094.
[44] Garcin B. Motor functional neurological disorders: An update. Rev Neurol (Paris) 2018;174(4):203–11. https://doi.org/10.1016/j.neurol.2017.11.003.
[45] Leroy A, Beigné M, Petyt G, Derambure P, Vaiva G, Amad A. Psychogenic non-epileptic seizures treated with guided transcranial direct current stimulation: A case report. Brain Stimulat 2019;12(3):794–6. https://doi.org/10.1016/j.brs.2019.01.019.
[46] Demartini B, Volpe R, Mattavelli G, Goeta D, D'Agostino A, Gambini O. The neuromodulatory effect of tDCS in patients affected by functional motor symptoms: an exploratory study. Neurol Sci Off J Ital Neurol Soc Ital Soc Clin Neurophysiol 2019;40(9):1821–7. https://doi.org/10.1007/s10072-019-03912-5.
[47] Garvey MA, Gilbert DL. Transcranial magnetic stimulation in children. Eur J Paediatr Neurol EJPN Off J Eur Paediatr Neurol Soc 2004;8(1):7–19. https://doi.org/10.1016/j.ejpn.2003.11.002.
[48] Rajapakse T, Kirton A. NON-INVASIVE BRAIN STIMULATION IN CHILDREN: APPLICATIONS AND FUTURE DIRECTIONS. Transl Neurosci 2013;4. https://doi.org/10.2478/s13380-013-0116-3.
[49] Saleem GT, Crasta JE, Slomine BS, Cantarero GL, Suskauer SJ. Transcranial Direct Current Stimulation in Pediatric Motor Disorders: A Systematic Review and Meta-analysis. Arch Phys Med Rehabil 2019;100(4):724–38. https://doi.org/10.1016/j.apmr.2018.10.011.
[50] Minhas P, Bikson M, Woods AJ, Rosen AR, Kessler SK. Transcranial direct current stimulation in pediatric brain: a computational modeling study. Annu Int Conf IEEE Eng Med Biol Soc IEEE Eng Med Biol Soc Annu Int Conf 2012;2012:859–62. https://doi.org/10.1109/EMBC.2012.6346067.
[51] Pick S, Hodsoll J, Stanton B, Eskander A, Stavropoulos I, Samra K, et al. Trial Of Neurostimulation In Conversion Symptoms (TONICS): a feasibility randomised controlled trial of transcranial magnetic stimulation for functional limb weakness. Open Access n.d.:11.
[52] Garcin B, Mesrati F, Hubsch C, Mauras T, Iliescu I, Naccache L, et al. Impact of Transcranial Magnetic Stimulation on Functional Movement Disorders: Cortical Modulation or a Behavioral Effect? Front Neurol 2017;8. https://doi.org/10.3389/fneur.2017.00338.
[53] Taib S, Ory-Magne F, Brefel-Courbon C, Moreau Y, Thalamas C, Arbus C, et al. Repetitive transcranial magnetic stimulation for functional tremor: A randomized, double-blind, controlled study. Mov. Disord. 2019;34(8):1210–9. https://doi.org/10.1002/mds.v34.810.1002/mds.27727.

[54] Broersma M, Koops EA, Vroomen PC, Maurits NM, van Beilen M. Can repetitive transcranial magnetic stimulation increase muscle strength in functional neurological paresis? A proof-of-principle study; 2015:8.
[55] Agarwal R, Garg S, Tikka SK, Khatri S, Goel D. Successful use of theta burst stimulation (TBS) for treating psychogenic non epileptic seizures (PNES) in a pregnant woman. Asian J Psychiatry 2019;43:121–2. https://doi.org/10.1016/j.ajp.2019.05.013.
[56] Spagnolo PA, Parker J, Horovitz S, Hallett M. Corticolimbic Modulation via Intermittent Theta Burst Stimulation as a Novel Treatment for Functional Movement Disorder: A Proof-of-Concept Study. Brain Sci 2021;11:791. https://doi.org/10.3390/brainsci11060791.
[57] Garcin B, Roze E, Mesrati F, Cognat E, Fournier E, Vidailhet M, et al. Transcranial magnetic stimulation as an efficient treatment for psychogenic movement disorders. J Neurol Neurosurg Psychiatry 2013;84(9):1043–6. https://doi.org/10.1136/jnnp-2012-304062.
[58] McWhirter L, Ludwig L, Carson A, McIntosh RD, Stone J. Transcranial magnetic stimulation as a treatment for functional (psychogenic) upper limb weakness. J Psychosom Res 2016;89:102–6. https://doi.org/10.1016/j.jpsychores.2016.08.010.
[59] Chastan N, Parain D, Verin E, Weber J, Faure MA, Marie J-P. Psychogenic aphonia: spectacular recovery after motor cortex transcranial magnetic stimulation. J Neurol Neurosurg Psychiatry 2009;80:94–94. Doi:10.1136/jnnp.2008.154302.
[60] Chastan N, Parain D. Psychogenic paralysis and recovery after motor cortex transcranial magnetic stimulation: Psychogenic Paralysis and rTMS. Mov. Disord. 2010;25(10):1501–4. https://doi.org/10.1002/mds.23187.
[61] Naro A, Pignolo L, Billeri L, Porcari B, Portaro S, Tonin P, et al. A Case of Psychogenic Myoclonus Responding to a Novel Transcranial Magnetic Stimulation Approach: Rationale, Feasibility, and Possible Neurophysiological Basis. Front. Hum. Neurosci. 2020;14:292. https://doi.org/10.3389/fnhum.2020.00292.
[62] Peterson KT, Kosior R, Meek BP, Ng M, Perez DL, Modirrousta M. Right Temporoparietal Junction Transcranial Magnetic Stimulation in the Treatment of Psychogenic Nonepileptic Seizures: A Case Series. Psychosomatics 2018;59(6):601–6. https://doi.org/10.1016/j.psym.2018.03.001.
[63] Blades R, Jordan S, Becerra S, Eusebio B, Heatwole M, Iovine J, et al. Treating dissociative post-traumatic stress disorder presenting as a functional movement disorder with transcranial magnetic stimulation targeting the cingulate gyrus. Neurol Sci 2020;41(8):2275–80. https://doi.org/10.1007/s10072-020-04433-2.
[64] Yeo JM, Carson A, Stone J. Seeing again: treatment of functional visual loss. Pract Neurol 2019;19(2):168–72. https://doi.org/10.1136/practneurol-2018-002092.
[65] Pick S, Anderson DG, Asadi-Pooya AA, Aybek S, Baslet G, Bloem BR, et al. Outcome measurement in functional neurological disorder: a systematic review and recommendations. J. Neurol. Neurosurg. Psychiatry 2020;91(6):638–49. https://doi.org/10.1136/jnnp-2019-322180.
[66] Bottemanne H, Imadache K, Pernet L, de La Forest Divonne T, English I, Barron E, et al. Psychothérapie augmentée par rTMS pour les troubles neurologiques fonctionnels. L'Encéphale 2021:S0013700621001172. Doi: 10.1016/j.encep.2021.02.017.
[67] Portaro S, Milardi D, Naro A, Chillura A, Corallo F, Quartarone A, et al. Chasing the Chameleon: Psychogenic Paraparesis Responding to Non-Invasive Brain Stimulation. Psychiatry Investig 2018;15(4):428–31.
[68] Posner MI. Orienting of Attention. Q J Exp Psychol 1980;32(1):3–25. https://doi.org/10.1080/00335558008248231.
[69] Gershon AA, Dannon PN, Grunhaus L. Transcranial magnetic stimulation in the treatment of depression. Am. J. Psychiatry 2003;160(5):835–45. https://doi.org/10.1176/appi.ajp.160.5.835.
[70] Fitzgerald PB, Maller JJ, Hoy KE, Thomson R, Daskalakis ZJ. Exploring the optimal site for the localization of dorsolateral prefrontal cortex in brain stimulation experiments. Brain Stimulat 2009;2(4):234–7. https://doi.org/10.1016/j.brs.2009.03.002.
[71] Bagattini C, Zanni M, Barocco F, Caffarra P, Brignani D, Miniussi C, et al. Enhancing cognitive training effects in Alzheimer's disease: rTMS as an add-on treatment. Brain Stimulat 2020;13(6):1655–64. https://doi.org/10.1016/j.brs.2020.09.010.
[72] Ospina JP, Jalilianhasanpour R, Perez DL. The role of the anterior and midcingulate cortex in the neurobiology of functional neurologic disorder. Handb. Clin. Neurol., vol. 166, Elsevier; 2019, p. 267–79. Doi: 10.1016/B978-0-444-64196-0.00014-5.
[73] Perez DL, LaFrance WC. Nonepileptic seizures: an updated review. CNS Spectr 2016;21(3):239–46. https://doi.org/10.1017/S109285291600002X.
[74] Perez DL, Dworetzky BA, Dickerson BC, Leung L, Cohn R, Baslet G, et al. An integrative neurocircuit perspective on psychogenic nonepileptic seizures and functional movement disorders: neural functional unawareness. Clin EEG Neurosci 2015;46(1):4–15. https://doi.org/10.1177/1550059414555905.
[75] LaFrance WC, Keitner GI, Papandonatos GD, Blum AS, Machan JT, Ryan CE, et al. Pilot pharmacologic randomized controlled trial for psychogenic nonepileptic seizures. Neurology 2010;75(13):1166–73. https://doi.org/10.1212/WNL.0b013e3181f4d5a9.
[76] Baslet G, Ehlert A, Oser M, Dworetzky BA. Mindfulness-based therapy for psychogenic nonepileptic seizures. Epilepsy Behav EB 2020;103:106534. https://doi.org/10.1016/j.yebeh.2019.106534.
[77] Nielsen G, Ricciardi L, Demartini B, Hunter R, Joyce E, Edwards MJ. Outcomes of a 5-day physiotherapy programme for functional (psychogenic) motor disorders. J Neurol 2015;262(3):674–81. https://doi.org/10.1007/s00415-014-7631-1.
[78] Malavera A, Silva FA, Fregni F, Carrillo S, Garcia RG. Repetitive Transcranial Magnetic Stimulation for Phantom Limb Pain in Land Mine Victims: A Double-Blinded, Randomized. Sham-Controlled Trial J Pain 2016;17(8):911–8. https://doi.org/10.1016/j.jpain.2016.05.003.
[79] Grammer GG, Williams-Joseph S, Cesar A, Adkinson DK, Spevak C. Significant reduction in phantom limb pain after low-frequency repetitive transcranial magnetic stimulation to the primary sensory cortex. Mil Med 2015;180(1):e126–8. https://doi.org/10.7205/MILMED-D-14-00236.
[80] Bullock K, Won AS, Bailenson J, Friedman R. Virtual Reality-Delivered Mirror Visual Feedback and Exposure Therapy for FND: A Midpoint Report of a Randomized Controlled Feasibility Study. J Neuropsychiatry Clin Neurosci 2020;32(1):90–4. https://doi.org/10.1176/appi.neuropsych.19030071.
[81] Hadi F, Soraya S, Bahramian A. The Enhanced Placebo Effect of Transcranial Magnetic Stimulation. Prim Care Companion CNS Disord 2020;22:19l02575. https://doi.org/10.4088/PCC.19l02575
[82] Mansur CG, Myczkowki ML, de Barros Cabral S, Sartorelli MdCB, Bellini BB, Dias ÁM, et al. Placebo effect after prefrontal magnetic stimulation in the treatment of resistant obsessive-compulsive disorder: a randomized controlled trial. Int J Neuropsychopharmacol 2011;14(10):1389–97. https://doi.org/10.1017/S1461145711000575.
[83] Paillère-Martinot M-L, Galinowski A, Plaze M, Andoh J, Bartrés-Faz D, Bellivier F, et al. Active and placebo transcranial magnetic stimulation effects on external and internal auditory hallucinations of schizophrenia. Acta Psychiatr. Scand. 2017;135(3):228–38. https://doi.org/10.1111/acps.2017.135.issue-310.1111/acps.12680.
[84] Bartlett J, Upshaw WN, Obregon D. Interactions of the Placebo Effect and Transcranial Magnetic Stimulation. Prim Care Companion CNS Disord 2021;23:20lr02874. https://doi.org/10.4088/PCC.20lr02874
[85] Paulus W, Peterchev AV, Ridding M. Transcranial electric and magnetic stimulation: technique and paradigms. Handb Clin Neurol 2013;116:329–42. https://doi.org/10.1016/B978-0-444-53497-2.00027-9.
[86] Rossi S, Hallett M, Rossini PM, Pascual-Leone A. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. Clin Neurophysiol 2009;120(12):2008–39. https://doi.org/10.1016/j.clinph.2009.08.016.
[87] Mix A, Benali A, Eysel UT, Funke K. Continuous and intermittent transcranial magnetic theta burst stimulation modify tactile learning performance and cortical protein expression in the rat differently. Eur J Neurosci 2010;32:1575–86. https://doi.org/10.1111/j.1460-9568.2010.07425.x.
[88] Peterchev AV, Wagner TA, Miranda PC, Nitsche MA, Paulus W, Lisanby SH, et al. Fundamentals of transcranial electric and magnetic stimulation dose: definition, selection, and reporting practices. Brain Stimulat 2012;5(4):435–53. https://doi.org/10.1016/j.brs.2011.10.001.
[89] Tse NY, Goldsworthy MR, Ridding MC, Coxon JP, Fitzgerald PB, Fornito A, et al. The effect of stimulation interval on plasticity following repeated blocks of intermittent theta burst stimulation. Neuroscience 2017. https://doi.org/10.1101/205781.
[90] Goldsworthy MR, Pitcher JB, Ridding MC. The application of spaced theta burst protocols induces long-lasting neuroplastic changes in the human motor cortex: The application of spaced theta burst protocols. Eur J Neurosci 2012;35:125–34. https://doi.org/10.1111/j.1460-9568.2011.07924.x.
[91] Nyffeler T, Wurtz P, Lüscher H-R, Hess CW, Senn W, Pflugshaupt T, et al. Extending lifetime of plastic changes in the human brain. Eur J Neurosci 2006; 24: 2961–6. Doi: 10.1111/j.1460-9568.2006.05154.x.
[92] Pascual-Leone A, Tormos JM, Keenan J, Tarazona F, Cañete C, Catalá MD. Study and modulation of human cortical excitability with transcranial magnetic stimulation. J Clin Neurophysiol Off Publ Am Electroencephalogr Soc 1998;15(4):333–43. https://doi.org/10.1097/00004691-199807000-00005.
[93] Roth Y, Pell GS, Chistyakov AV, Sinai A, Zangen A, Zaaroor M. Motor cortex activation by H-coil and figure-8 coil at different depths. Combined motor threshold and electric field distribution study. Clin Neurophysiol Off J Int Fed Clin Neurophysiol 2014;125(2):336–43. https://doi.org/10.1016/j.clinph.2013.07.013.
[94] Lefaucheur J-P, André-Obadia N, Antal A, Ayache SS, Baeken C, Benninger DH, et al. Evidence-based guidelines on the therapeutic use of repetitive transcranial magnetic stimulation (rTMS). Clin Neurophysiol Off J Int Fed Clin Neurophysiol 2014;125(11):2150–206. https://doi.org/10.1016/j.clinph.2014.05.021.
[95] O'Reardon JP, Solvason HB, Janicak PG, Sampson S, Isenberg KE, Nahas Z, et al. Efficacy and safety of transcranial magnetic stimulation in the acute treatment of major depression: a multisite randomized controlled trial. Biol Psychiatry 2007;62(11):1208–16. https://doi.org/10.1016/j.biopsych.2007.01.018.
[96] Lipton RB, Dodick DW, Silberstein SD, Saper JR, Aurora SK, Pearlman SH, et al. Single-pulse transcranial magnetic stimulation for acute treatment of migraine with aura: a randomised, double-blind, parallel-group, sham-controlled trial. Lancet Neurol 2010;9(4):373–80. https://doi.org/10.1016/S1474-4422(10)70054-5.
[97] Carmi L, Alyagon U, Barnea-Ygael N, Zohar J, Dar R, Zangen A. Clinical and electrophysiological outcomes of deep TMS over the medial prefrontal and anterior cingulate cortices in OCD patients. Brain Stimulat 2018;11(1):158–65. https://doi.org/10.1016/j.brs.2017.09.004.

[98] Isserles M, Shalev AY, Roth Y, Peri T, Kutz I, Zlotnick E, et al. Effectiveness of Deep Transcranial Magnetic Stimulation Combined with a Brief Exposure Procedure in Post-Traumatic Stress Disorder – A Pilot Study. Brain Stimulat 2013;6(3):377–83. https://doi.org/10.1016/j.brs.2012.07.008.
[99] Steele VR, Maxwell AM. Treating cocaine and opioid use disorder with transcranial magnetic stimulation: A path forward. Pharmacol Biochem Behav 2021;209:173240. https://doi.org/10.1016/j.pbb.2021.173240.
[100] Baliga SP, Mehta UM. A Review of Studies Leveraging Multimodal TMS-fMRI Applications in the Pathophysiology and Treatment of Schizophrenia. Front Hum Neurosci 2021;15:662976. https://doi.org/10.3389/fnhum.2021.662976.
[101] Nardone R, Tezzon F, Höller Y, Golaszewski S, Trinka E, Brigo F. Transcranial magnetic stimulation (TMS)/repetitive TMS in mild cognitive impairment and Alzheimer's disease. Acta Neurol Scand 2014;129(6):351–66. https://doi.org/10.1111/ane.2014.129.issue-610.1111/ane.12223.
[102] Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. J Physiol 2000;527(3):633–9. https://doi.org/10.1111/tjp.2000.527.issue-310.1111/j.1469-7793.2000.t01-1-00633.x.
[103] Nitsche MA, Liebetanz D, Antal A, Lang N, Tergau F, Paulus W. Modulation of cortical excitability by weak direct current stimulation–technical, safety and functional aspects. Suppl Clin Neurophysiol 2003;56:255–76. https://doi.org/10.1016/s1567-424x(09)70230-2.
[104] Monte-Silva K, Kuo M-F, Hessenthaler S, Fresnoza S, Liebetanz D, Paulus W, et al. Induction of Late LTP-Like Plasticity in the Human Motor Cortex by Repeated Non-Invasive Brain Stimulation. Brain Stimulat 2013;6(3):424–32. https://doi.org/10.1016/j.brs.2012.04.011.
[105] Nitsche MA, Seeber A, Frommann K, Klein CC, Rochford C, Nitsche MS, et al. Modulating parameters of excitability during and after transcranial direct current stimulation of the human motor cortex. J Physiol 2005;568:291–303. Doi: 10.1113/jphysiol.2005.092429.
[106] Klooster DCW, de Louw AJA, Aldenkamp AP, Besseling RMH, Mestrom RMC, Carrette S, et al. Technical aspects of neurostimulation: Focus on equipment, electric field modeling, and stimulation protocols. Neurosci Biobehav Rev 2016;65:113–41. https://doi.org/10.1016/j.neubiorev.2016.02.016.
[107] Brunoni AR, Ferrucci R, Fregni F, Boggio PS, Priori A. Transcranial direct current stimulation for the treatment of major depressive disorder: a summary of preclinical, clinical and translational findings. Prog Neuro-Psychopharmacol Biol Psychiatry 2012;39(1):9–16. https://doi.org/10.1016/j.pnpbp.2012.05.016.