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The impact of transcranial Direct Current stimulation on rumination: A systematic review of the sham-controlled studies in healthy and clinical samples

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ABSTRACT

Introduction: Broadly considered a transdiagnostic feature of psychological disorders, rumination is associated with lower treatment response, slower recovery rates, and higher relapse rates. Accordingly, research has focused on the development of interventions to alleviate rumination. Recently, transcranial Direct Current Stimulation (tDCS) has emerged as a promising tool to do so.
Methods: We performed a systematic review of sham-controlled tDCS studies targeting rumination among healthy participants or patients with psychiatric disorders, investigating the effectiveness of tDCS in reducing rumination, and assessing the research quality of this nascent field.
Results: We identified nine studies, with five reporting a significant impact of tDCS on rumination. We also outlined a few tDCS parameters (e.g., stimulation duration, electrode size) and research methods' features (e.g., within- versus between-research designs) characterizing those positive-finding studies. However, these studies were characterized by substantial heterogeneity (e.g., methodological flaws, lack of open science practices), precluding any definite statement about the best way to target rumination via tDCS. Moreover, several strong methodological limitations were also present across those studies.
Discussion: Although our systematic review identifies the strengths and weaknesses of the available research about the impact of tDCS on rumination, it calls for strong efforts to improve this nascent field's current methodological caveats. We discuss how open science practices can help to usher this field forward.

Contents

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1. Introduction

Transcranial direct current stimulation (tDCS) is a non-invasive brain neuromodulation technique that has become a hot topic in contemporary clinical neuroscience as it can, through the modulation of brain cortical excitability, modulate cognitive and motor domains [1,2]. It consists of the application of a weak, direct electric current through two electrodes, an anode and a cathode. These two electrodes are positioned over one's scalp to reach the neuronal tissue and induce polarization-shifts (i.e., the current flows from the anode to the cathode) on the resting membrane potential without triggering action potentials per se [3,4]. In this way, although individual responses to stimulation are not uniformly excitatory or inhibitory [5], anodal tDCS is generally considered excitatory while cathodal tDCS is generally considered inhibitory [6].

One of the strengths of tDCS is that it allows research blinding [4]. Indeed, many studies included a sham stimulation wherein the electrodes' position is identical to the active tDCS condition but with the current ramping down after a few seconds (e.g., 5 s [7]). This procedure has become commonly used in tDCS research and is known to be a way to provide the initial sensation of stimulation without the subsequent effects on cortical excitability ([4,11], but see [8–11]). Lastly, many studies have also relied on tDCS devices allowing full double-blind study design, highlighting the promise of this procedure in terms of research quality [4].

Because of its non-invasive nature, highly controlled sham condition, and relatively low cost compared to other neuromodulation techniques such as the transcranial magnetic stimulation (TMS), tDCS quickly arose as a promising therapeutic tool. Indeed, several systematic reviews and meta-analyses of randomized controlled trials indicated the safety and therapeutic efficacy of tDCS for a wide range of mental disorders [12], including, among others, depression and mood disorders [13–15], anxiety disorders [16,17], psychotic disorders [18], pain-related disorders [19], substance use disorders [20], and eating disorders [21]. Hence, this literature has prompted an exceptionally positive prospect vis-à-vis tDCS as a therapeutic tool.

However, although the impact of tDCS has not been confined to symptoms of mental disorders [22,23], uncertainty still abounds regarding the psychological mechanisms that may mediate the effects of tDCS on such a broad range of mental disorders. The only psychological mechanism that has been extensively studied so far in the understanding of the impact of tDCS across mental disorders is working memory (WM) [24,25]. Comprehensive research on other mechanisms that may mediate the impact of tDCS on symptom reduction remains rather scarce.

Rumination is perhaps the prime example of such a mechanism [26,27]. Rumination is classically defined as a perseverative, passive, self-focused thinking about the content, causes, and consequences of one's self, feelings, personal concerns, and upsetting experiences, without taking any problem-solving action [28]. It is involved in the onset and maintenance of depression and anxiety disorders [29,30]. Moreover, high rumination rates predict slower treatment response, lower rates of recovery, and higher rates of relapse in mood and anxiety disorders [31,32]. Finally, recent research has pointed to rumination as a viable and plausible target for transdiagnostic clinical interventions [27,33]. Altogether, rumination thus appears as a plausible transdiagnostic feature of psychological disorders [30,34,35].

At the brain level, one common hypothesis shared across several prominent cognitive models of psychopathology is that rumination reflects impairments in top-down executive control, and that this failure results from a decreased activation of the prefrontal cortex, particularly of its dorsolateral part (dlPFC) [36–39]. Clinical and laboratory research have accordingly aligned with this perspective. First, research has extensively demonstrated the existence of strong associations between rumination and reduced top-down executive control, particularly in terms of difficulty to inhibit prepotent responses and shifting from one task to another (for recent meta-analyses, see [40,41]). Moreover, there is mounting evidence indicating that improvement in executive control may mitigate rumination [42–44]. Second, beyond behavioral research, neuroimaging research has also lent strong credence to the hypothesis that dlPFC is critically involved in the onset of rumination, at both the structural (i.e., cortical thickness) [45] and functional levels [46,47].

Recently, clinical promises have arisen from neuromodulation research. Several studies have indeed indicated that one can, as compared to sham stimulation, reduce rumination via a transient increase of the neural activity within the left dlPFC via anodal tDCS in both healthy and clinical samples [48,49]. Given the transdiagnostic nature and clinical relevance of rumination, these tDCS studies have prompted an especially enthusiastic appraisal vis-à-vis the prospects of tDCS as a new intervention ripe for targeting rumination [48,49].

However, other studies failed to report such an effect [e.g., 50]. As such, uncertainty remains regarding the ability of tDCS to yield a reliable and robust impact on rumination. Moreover, prior research revealed that both tDCS-related parameters (e.g., montage, stimulation intensity) and inter/intraindividual factors (e.g., age, physiological state) may modulate tDCS effects [51,52]. In this way, one cannot exclude that study-to-study variations in stimulation parameters, montage, sample characteristics, and research protocols modulate tDCS' impact on rumination and may explain these mixed findings.

Therefore, the main goal of this project was to conduct a systematic review of the sham-controlled studies conducted among healthy and clinical samples, investigating the impact of tDCS on rumination. Following previous tDCS-related systematic reviews [24], we included studies relying on a between-subject or within-subject design. As recent systematic reviews on tDCS highlighted the study-to-study variations in terms of stimulation parameters [53–55], we also aimed at examining the potential impact of these parameters in light of the results of this systematic review. Finally, we also aimed at evaluating the methodological quality of this nascent field of research.

2. Methods

We conducted a systematic review according to the PRISMA recommendations ([56,57]; for the PRISMA checklist, see the supplementary material available on the Open Science Framework (https://osf.io/suaf4/). The data extraction and synthesis plan of this systematic review were preregistered on PROSPERO (https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=118540 — Identifier: CRD42018118540).

2.1. Literature search

YH conducted a systematic literature search through November 2019 via PubMed, PsycInfo, and Scopus, using the following search

terms: "tDCS" or "transcranial direct current stimulation" or "brain stimulation" or "neuro modulation" or "direct stimulation" or "transcranial electric stimulation" or "electric stimulation" or "non-invasive brain stimulation" combined with "rumination" or "repetitive negative thinking" or "post event processing" or "post-event processing" or "negative thinking" or "repetitive thinking" or "worry" or "repetitive thought" or "brooding" or "intrusive thoughts" or "ruminative" or "worrying" or "self-reflection". YH and AH reviewed and piloted this search string before conducting the literature search. It comprises various terms that may be used in the literature to refer to tDCS and terms conceptually analog to rumination. We updated the reference list on the 17th of February 2020 using the same search string on PubMed. For each database, the exact formatted codes for the search string are available on the Open Science Framework's account of this project (https://osf.io/gu3na/)

2.2. Selection criteria

We included studies that met the following PICOS criteria [58]: (a) Participants: adult participants, male or female, either healthy volunteers or clinical patients; (b) Intervention: tDCS; (c) Comparison: sham stimulation; (d) Outcomes: at least one state or trait measure of rumination (and analog terms such as worrying) as a dependent variable; (e) Study design: single or double-blind controlled study; (f) Publication type: published in a peer-reviewed journal, written in English. We excluded single case studies as well as studies devoid of sham-stimulation control condition. YH and BO screened the abstracts and titles independently. The inter-rater agreement between them was high (Kappa value: 0.81), and the discrepancies were resolved through discussion. YH then screened the full texts.

2.3. Data extraction

Two authors (YH and OD) extracted the data according to a predefined list of relevant information, which was built upon previous systematic reviews and tDCS research [e.g., 25,54,59,60]. With a kappa value of 0.86, the inter-rater agreement between them was high. The discrepancies were resolved through a discussion with a third author (AH). The main extracted variables were as follows: (a) sample size, (b) type of population (healthy vs clinical samples), (c) handedness (i.e., whether the researchers only recruited right-handed participants), (d) mean age, (e) percentage of women in the sample, (f) blinding, (g) study design (within-subjects or between-subjects), (h) compensation (whether participants received a financial compensation or course credits in exchange for their participation), (i) groups, (j) anode placement, (k) cathode placement, (l) whether the electrodes placement was cephalic (i.e., the two electrodes are placed over the scalp) or not), (m) stimulation intensity, (n) electrode size, (o) stimulation duration, (p) ramping parameters (e.g., 30-s ramp-up and 30-s ramp-down), (q) sham parameters (i.e., whether the current was briefly ramped-up and -down prior and after to absence of stimulation, and, if so its duration and intensity), (r) the interval between sessions (if within-subject design or multi-sessions), (s) the presence of a stressor, (t) the name of the state measure of rumination (if included), (v) the name of the trait measure of rumination (if included). Table 1 depicts the extracted data.

2.4. Quality assessment

We assessed the studies' quality using the "RoB2" tool of the Cochrane Collaboration [61]. This tool aims at determining the possible sources of bias in randomized trials: (a) randomization process, (b) deviations from intended interventions, (c) missing outcome data, (d) measurement of the outcome, (e) selection of the reported results. This tool comprises a series of signaling questions within each domain that aim to elicit information about the study's features relevant to the risk of bias. A decision algorithm then generates a judgment about the risk of bias from each domain, based on the signaling questions, and also creates an overall risk of bias. Two authors (YH and OD) independently evaluated the risk of bias for each study. The inter-rater agreement was high, with a *kappa* value of 0.61. The few discrepancies were resolved through a discussion with a third author (AH).

3. Results

3.1. Study selection

Fig. 1 depicts the PRISMA flowchart diagram, summarizing the flow of information from identification to studies' inclusion [56,57]. Our search strategy identified 109 publications, of which 40 were duplicates. To consider the latest publications, a final search on PubMed identified seven additional records on the 17th of February 2020. We removed duplicates and then screened the abstracts from the remaining 76 publications. We excluded 63 papers from this step, as they were review articles, qualitative studies, case studies, dissertation abstracts, study protocols, and non-English articles. We further screened the remaining 13 articles, and we excluded four articles for the following reasons: (a) Rumination was not a dependent variable ($n = 1$); (b) The study did not include a sham tDCS group ($n = 3$). After applying these exclusions, we found that nine studies satisfied the inclusion criteria (see Fig. 1).

4. Quality assessment

As shown in Fig. 2, the overall risk of bias was high, with four studies exhibiting a high risk of bias, and the five remaining ones showing some concerns. When looking at the criterion individually (see Fig. 2), two characteristics stood out: only one study exhibited a low risk of bias regarding the random sequence generation, and none of the studies was free of potent, selective reporting. On the other hand, most studies exhibited a low risk of bias in terms of deviations from the intended intervention, processing of missing outcome data, or outcomes measurement. Altogether, these results suggest that random sequence generation and selective reporting were the two most problematic quality criteria. Note that only one study was pre-registered, but discrepancies were identified between the pre-registered protocol and the published research.

4.1. Summary of the main studies' findings

As depicted in Table 2, five out of the nine studies reported that tDCS significantly alleviated rumination. In two studies, anodal tDCS on the left dlPFC significantly reduced state rumination, as compared to sham stimulation [48,49]. In one study [62], this effect was found only through the mediation of the enhancement of WM operations. In another study [63], a bihemispheric tDCS-montage (anode on the right dlPFC and the cathode on the left dlPFC) increased state rumination, as compared to the opposite tDCS-montage (i.e., the anode on the left dlFPC and the cathode on the right dlPFC) and sham stimulation. Finally, one study [64] indicated that a 10-session cathodal stimulation program (over the right dlPFC) reduced trait worry compared to sham stimulation, among patients with a general anxiety disorder. The four other studies did not report any direct effect of tDCS on state or trait ruminations.

4.2. Characteristics of included studies

4.2.1. Sample characteristics

Tables 1 and 2 summarize the main characteristics of the nine studies. The sample size varied from 18 to 118 participants. Three studies recruited only women, and most of the studies had more women than men (average = 81.39% of women; min = 46%; max = 100%). Note that only De Raedt et al. [49] provided a justification for this restriction

Table 1
Sample characteristics, design of the studies, online task characteristics, and rumination measures characteristics.

Study	Sample characteristics					Protocol characteristics				Online task	Stressor	Rumination measure		Location
	N	Type	Handed-ness	Mean Age	% Women	Blinding	Design	Compe-nsation	Conditions (*n*)			State	Trait	
Baeken et al. (2017)	40	H	R	22.55	100	S	W-S	F	(a) tDCS; (b) sham tDCS	None	No. 5 min resting period.	MRSI		BE
Clarke et al. (2020)	95	H	–	22.13	78.9	S	B-S	–	(a) tDCS + mindfulness (*25*); (b) tDCS + mindwandering (*25*); (c) sham tDCS + mindfulness (*23*); (d) sham tDCS + mindwandering (*22*)	Minfulness bodyscan	Participants were asked to actively worry for 5 min	Frequency of negative intrusive thoughts during a mindful breathing task		AU
De Raedt et al. (2017)	32	H	R	22.6	100	S	W-S	F	(a) tDCS; (b) sham tDCS	None	Listening to audio of criticizing comments	MRSI		BE
De Putter et al. (2015)	66	H	–	23.09	80.3	D	B-S	F	(a) tDCS + WM training (*22*[b]); (b) tDCS control training (*22*); (c) sham tDCS (*22*)	WM training and Control training	No. 10 min resting period.	MRSI	RRS	BE
Kelley et al. (2013)	90	H	R	–	66.6	D	B-S	C	(a) bipolar tDCS, anode on left dlPFC (*29*); (b) bipolar tDCS, anode on right dlPFC (*28*); (c) sham tDCS (*33*)	None	Negative feedback on essay (after 10 min of tDCS)[a]	10 item state rumination measure + thought listing procedure		USA
Movahed et al. (2018)	18	*GAD*	–	28.7	46	S	B-S	–	(a) tDCS (*6*); (b) sham tDCS (*6*); (c) pharmacotherapy (*6*)	None			PSWQ	IR
Vanderhasselt et al. (2013)	32	H	R	22.28	62.5	S	W-S	–	(a) tDCS; (b) sham tDCS	IST	No. 8 min resting period.	MRSI	RRS	BR
Vanderhasselt et al. (2015)	33	*MDD*	R	44.03	72.7	D	B-S	–	(a) tDCS (*19*); (b) sham tDCS (*14*)	PASAT training			RRS	BR
Voss et al. (2018)	118	H	R	23.32	100	D	B-S	F & C	(a) tDCS, anode on left dlPFC (*40*); (b) tDCS, cathode on left dlPFC (*38*); (c) sham tDCS (*40*)	modified CVLT	Film with violent content followed by 10 min resting period	Modified PTQ	Modified PTQ	DE

Note. The dash means that data were not reported. GAD = General Anxiety Disorder; H = Healthy; R = right-handed; S = Single blinding; D = double blinding; W-S = within-subjects; B-S = between-subjects; F = financial; C = course credits; WM = working memory; MRSI = Momentary Ruminative Self-Focus Inventory; PTQ = Perseverative Thinking Questionnaire; RRS = Ruminative Response Scale; PSWQ = Penn State Worry Questionnaire; PASAT = Paced Auditory Serial Addition Task; CVLT = California Verbal Learning Test.

[a] Participants read this negative feedback during the last 5 min of tDCS stimulation.

[b] Not reported, but participants were randomly assigned to one of the 3 groups. Thus, considering groups of equal size, we assumed 22 participants per group.

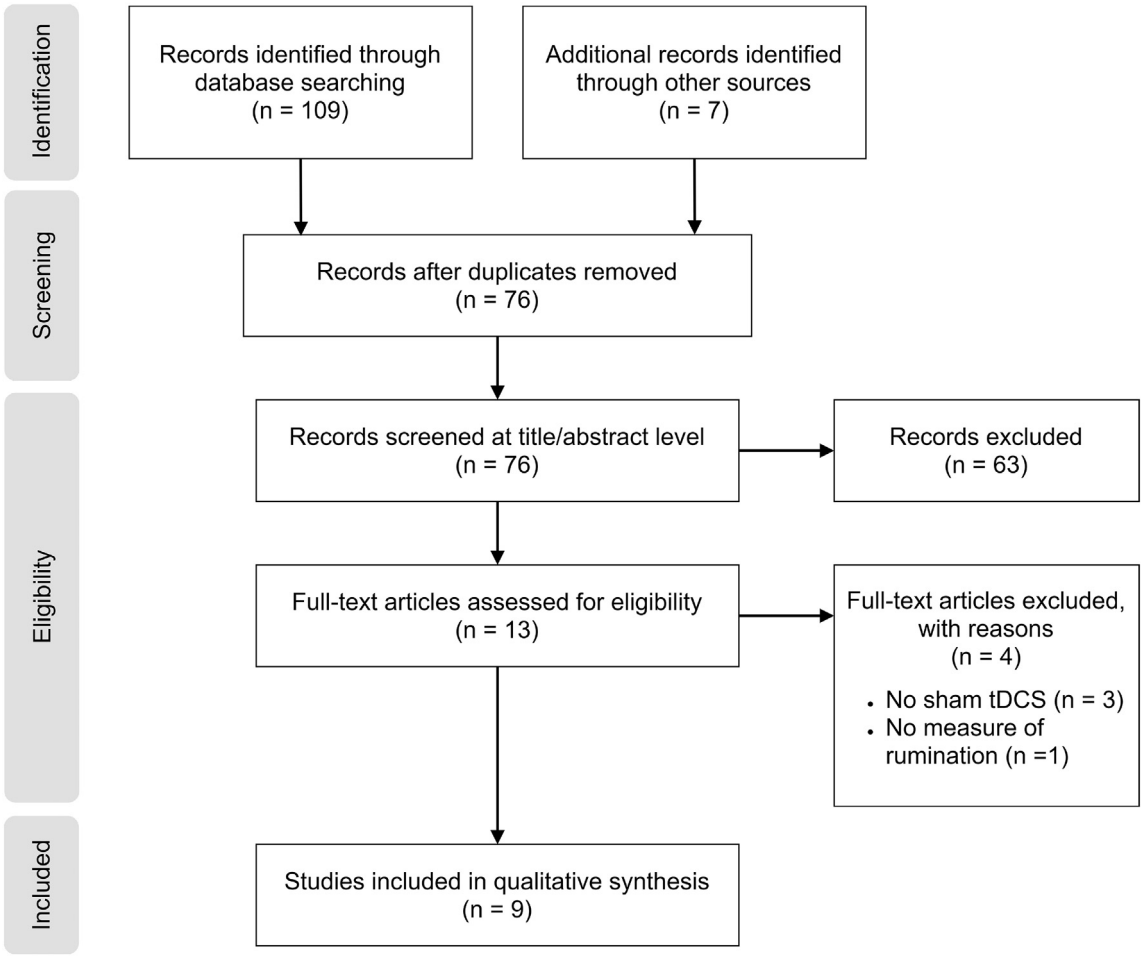

Fig. 1. PRISMA flow diagram.

to women; the other studies did not. Participants' mean age across studies was 26.08 years old ($SD = 7.56$). And whereas six studies recruited right-handed participants, the others did not report participants' handedness.

Only two studies had a clinical sample qualifying either for generalized anxiety disorder [64] or major depressive disorder [65]; others relied exclusively on healthy volunteers.

4.3. Study design

Three studies relied on a within-subjects design; each study including a between-session interval of at least 48 h. Moreover, the two studies relying on a clinical sample included multiple sessions of active tDCS [64,65]. Details are available in Table 2. In terms of the blinding, only four studies had a double blinding procedure. Finally, five studies

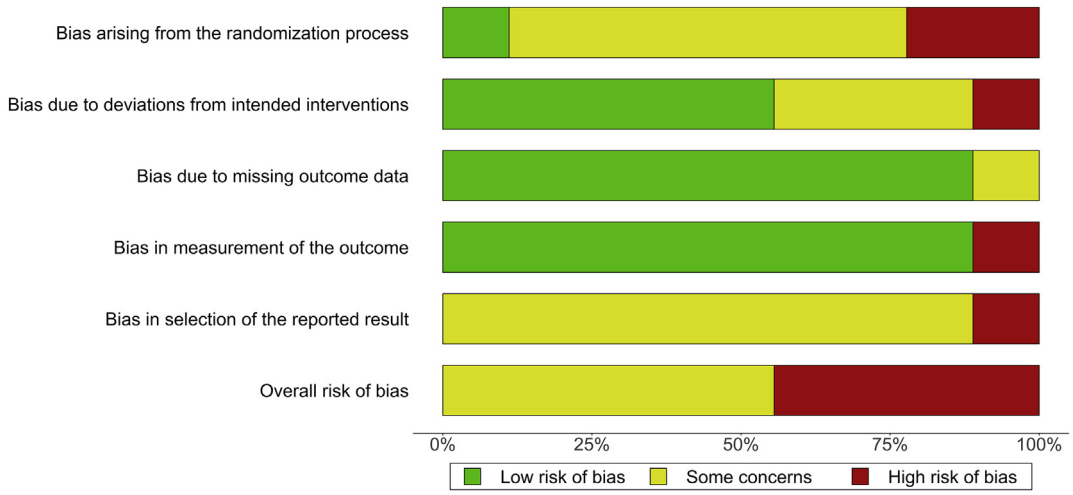

Fig. 2. Risk of bias assessment.

Table 2
TDCS parameters and summary of results.

Study	tDCS Parameters								Sham parameters	Electrode placement determination	*N* of active tDCS sessions	BSI	Summary of results
	Montage Type	Anode location	Cathode location	Current Density (mA/cm^2)	Intensity (mA)	Electrode Size (cm^2) and Shape	Duration (min)	Ramp-up; ramp-down (s)					
Baeken et al. (2017)	Cephalic	Left dlFPC	Contralateral supraorbital area	0.06	1.5	25 rectangular	20	30; 30	Ramping the current up and down	Neuronavigation	1	>48 h	Anodal tDCS on the left DLPFC reduced state rumination compared to sham
Clarke et al. (2020)	Extra-cephalic	Left dlFPC	Left superior trapezius muscle	0.0667	2	30	20	30; 30	1 min of 1 mA stimulation between ramp-up and ramp-down	10–20 system	1		*No effect of anodal tDCS on intrusive thoughts*
De Raedt et al. (2017)	Cephalic	Left dlFPC	Contralateral supraorbital area	0.0429	1.5	35	20	30; 30	Ramping the current up and down	Neuronavigation	1	>48 h	Anodal tDCS on the left dlPFC reduced rumination compared to sham
De Putter et al. (2015)	Cephalic	Left dlFPC	Contralateral supraorbital area	0.08	2	25	25	30; 30	Ramping the current up and down	10–20 system	1		*No effect of anodal tDCS on rumination*
Kelley et al. (2013)	Bihemis-pheric	(a) Left dlPFC (b) Right dlPFC	(a) Right dlPFC (b) Left dlPFC	0.0571	2	35 rectangular	15	5; 5	30 s of 1 mA stimulation between ramp-up and ramp-down	10–20 system	1		Bihemispheric tDCS stimulation, with the anode on the right dlPFC and the cathode on the left dlPFC increased state rumination, compared to the opposite montage and to sham.
Movahed et al. (2018)	Extra-cephalic	Contra-lateral deltoid muscle	Right dlPFC	–	2	–	20	–	–	–	10 sessions over 4 weeks		Cathodal tDCS on the right DLPFC decreased worry at post-test and 2 months follow-up.
Vanderhasselt et al. (2013)	Cephalic	Left dlFPC	Contralateral supraorbital area	0.0571	2	35	20	30; 30	Ramping the current up and down	10–20 system	1	>48 h	The influence of anodal tDCS on left DLPFC on rumination was mediated by the enhancement of WM operations for angry faces (but no direct effect of tDCS on rumination was found)
Vanderhasselt et al. (2015)	Bihemis-pheric	Left dlFPC	Right dlPFC	0.08	2	25 rectangular	30	30; 15	Ramping the current up and down	10–20 system	10 sessions over 2 weeks/10 working days		*WM training reduced brooding among depressive patients but neuromodulation of the DLPFC did not have any supplementary effect on the reduction of rumination*
Voss et al. (2018)	Extra-cephalic	(a) Left dlPFC (b) Contra-lateral deltoid muscle	(a) Contra-lateral deltoid muscle (b) Left dlPFC	0.0286	1	35	20	5; 5	30 s of 1 mA stimulation between ramp-up and ramp-down	10–20 system	2		*No effect of tDCS on rumination was found nor was there any interaction with the WM task*

Note. The dash means that data were not reported. BSI = between session interval: dlPFC = dorsolateral prefrontal cortex; WM = working memory.

included a participant's compensation—either financial compensation or course credits.

4.3.1. Assessment of rumination

As shown in Table 1, two in nine studies did not assess state rumination (i.e., to which extent one is ruminating now), and focused only on trait rumination (i.e., one's general tendency to ruminate). Note that these two studies were conducted in clinical samples. Five studies assessed trait rumination, with most of them ($n = 3$) relying on the Ruminative Response Scale [RRS; 66].

Among the seven studies assessing state rumination, there were variations in the way state rumination was captured. On the one hand, as individuals naturally tend to ruminate when confronted with stressors, four studies included a laboratory stressor to elicit rumination (for details about the stressors, see Table 1). As shown in Table 1, except for Kelley and al. [63], the stressor and the measurement of post-stressor state rumination were administered offline (post-tDCS stimulation) among these studies. On the other hand, three studies did not include any formal laboratory stressors to induce rumination but relied on a rest period to do so. This rest period was placed between the end of the stimulation and the assessment of state rumination. As depicted in Table 1, rest periods lasted either, 5, 8, or 10 min. Moreover, most studies ($n = 4$) assessed state rumination via the Momentary Ruminative Self-Focus Inventory [MRSI; 67].

4.3.2. Tasks administered during tDCS (online task)

As depicted in Table 1, five studies had a task administered simultaneously to the stimulation (i.e., online tasks). In four studies, it was computerized cognitive tasks tapping onto working memory. In one study, it was a mindfulness body scan procedure [50].

4.3.3. tDCS parameters and electrodes' placements

The distinct stimulation parameters are summarized in Table 2. The most commonly used parameters were as follows: a stimulation intensity of 2 mA ($n = 6$), a stimulation duration of 20 min ($n = 5$), an electrodes' size of 35 cm^2 ($n = 4$), and a ramping-up and ramping-down of the direct current intensity of 30 s each ($n = 5$). Interestingly, only three studies explicitly reported the shape of the electrodes (see Table 2). However, there were large study-to-study variations in terms of electrodes' placements (see Table 2). Although eight in nine studies had the anode located over the left dlPFC, cathode placement was not consistent across studies. Six studies had a cephalic montage with either the cathode placed over the contralateral supraorbital area ($n = 4$) or a bihemispheric ("lateralized") montage over the dlPFC ($n = 2$). Studies using bihemispheric montages are based on the assumption that by stimulating simultaneous homotopic regions (with an anode and a cathode), the interhemispheric balance will shift towards the anode, thus potentially favoring the cognitive processing performed on that hemisphere [5]. Moreover, one study had a montage wherein the cathode was placed over the right dlPFC and the anode over the contralateral deltoid muscle [64]. Note that 8 studies of the 9 provided information about the exact procedure used for the electrode placement. Among those, the electrodes' placement was determined either via neuronavigation tools ($n = 2$ studies) or in accordance with the international 10–20 system of electrode placement along with manual measurement to align with this system ($n = 6$).

Finally, regarding the sham stimulation, three different types of scenarios were identified. In the first scenario, the current was ramped-up, then ramped-down immediately ($n = 5$). In the second one, the current was ramped-up, then maintained during 30 s, and finally ramped-down ($n = 2$). Finally, the current was ramped-up, then turned on for 1 min at 1 mA, and ramped-down ($n = 1$).

5. Discussion

In this systematic review, we aimed at providing a comprehensive examination of the sham-controlled tDCS studies targeting rumination among healthy participants or patients with psychiatric disorders, and to assess the research quality of this nascent field. Through this process, nine studies were identified, with only five reporting a significant impact of tDCS on rumination. However, although we did our best to try to identify the most desirable combination of tDCS parameters and methodological features across these five studies reporting a significant impact of tDCS on rumination, these studies were characterized by substantial heterogeneity; thus, precluding any definite statement about the impact of tDCS on rumination. Hereafter, we discuss the critical issues and questions raised by this systematic review.

This review's central finding is the high heterogeneity between studies (e.g., study protocol, tDCS parameters, rumination measures). Although heterogeneity can somewhat be viewed as a strength, in the present case, it precludes any reliable inferences regarding which combination of parameters works or does not. Therefore, it is essential to converge towards the use of more uniformized protocols, and then examine consistency of the findings across iterations. However, despite the heterogeneity, one can strikingly summarize the most frequent tDCS parameters across studies as follows: a stimulation duration of 20 min, a stimulation intensity of 2 mA, and 35 cm^2 electrodes. The most frequently reported sham parameters were a 30-s ramping-up of the stimulation intensity, immediately followed by ramping down the stimulation intensity for 30 s. Of course, the fact that these parameters stand out as the most common in the present systematic review does not imply that they are the best ones to tap precisely onto rumination. In contrast, it is worth noting that these parameters (current density higher than 0.028 mA/cm^2 and stimulation duration longer than 10 min) have been identified as the most optimal ones in previous systematic reviews and meta-analyses looking at the impact of tDCS on other cognitive processes [25,54]. Moreover, note that the use of $35cm^2$-size electrodes, a current intensity of 2 mA, and a 20-min duration stimulation have been explicitly recommended as the "gold standard" parameters in the application of tDCS to enhance attention, learning, and memory, in both healthy and clinical populations [68].

Beyond the tDCS parameters, a few study's characteristics also stood out among the studies that did achieve to impact on rumination via tDCS: except [64], they mostly relied on a within-subject design, included right-handed participants only, and compensated participants for their participation. And, although they may appear anecdotal, these three features should not come as a surprise as they have been already pointed out in other works: (a) a within-subject design is the most common design in tDCS studies [69]; (b) handedness is critical to control for as tDCS stimulation yields different results in a right-handed population compared to left-handed or mixed-handed people [60]; and (c) ensuring that participants' incentives are high improves the effectiveness of tDCS [59,70]. Lastly, although researchers assessed rumination with various measures, each single session tDCS study comprised a resting period prior to the administration of the state rumination measure. Future iterations of studies investigating the effect of tDCS on rumination could thus rely on the combination of these parameters – or give a rationale to explain different design choices – and see whether these results replicate across different laboratories, countries, and samples. One may also wonder whether we could identify specific sets of parameters (e.g., other electrode placement, other stimulation duration) that may drive the null-findings studies. Yet, the heterogeneity between these studies was considerable, and we were unable to identify any specific pattern of parameters or research design's features that would automatically thwart the impact of tDCS on rumination.

This systematic review has conceptual, methodological, and practical implications. In the brain imaging literature, rumination has been associated with activation within the dlPFC [47] and broader cerebral

networks [71]. Accordingly, recent models [37,72] have given the dlPFC a central role. Thus, the studies' results in this systematic review dovetail with the hypothesis that the dlPFC may play a pivotal role. On the other hand, although rumination involves the dlPFC, it also relies on other regions, such as the inferior parietal lobe [73,74]. Future iterations may also want to examine the potential impact of targeting those regions. At a methodological level, some of the heterogeneity problems mentioned earlier are not specific to the rumination research field but concern the entire tDCS research literature: the tDCS montage, the sample (i.e., sample characteristics or sample size), and open science practices. Different aspects could be improved. For instance, many studies were imprecise about their randomization process, their a priori sample calculation (for a discussion about tDCS studies and the importance of sample size, see [75]), and future studies would need to be more transparent. Additionally, although we did not extract whether researchers checked and reported adverse effects, future studies should do so as adverse effects might render the blinding procedure ineffective [8].

There was a general lack of open science practices in the reviewed studies. Pre-registrations, sharing anonymized data in publicly accessible repositories (e.g., OSF), sharing code, and computerized tasks would usher the field forward (for a discussion, see [76]). If researchers moved in this direction, it would maximize transparency, research quality, and replicability. In other scientific domains, such open science research practices have already yielded striking impacts. For example, after 2000 (after registration was required in this field), only 8% of the studies investigating the treatment or prevention of cardiovascular disease showed a significant benefit of the intervention, whereas 57% of studies published before 2000 did [77]. Therefore, we believe that open science practices are a critical next step for the field.

The present findings might yield some clinical implications. If the observation that tDCS impacts rumination should turn to be true, it would allow brand new translational interventions for rumination. But to do so, researchers should move to clinical samples and conduct sufficiently powered randomized controlled trials comparing tDCS to treatment as usual, and not only rely on laboratory studies in small-sized healthy samples. Movahed et al. [64] have already set the scene for such a translation, though their sample size was minimal (n by group $= 6$). Future iterations would thus want to determine which stimulation parameters, montage, sample characteristics, and research protocols ultimately magnify the effect of tDCS on rumination compared to treatment as usual. On the other hand, it is not always a guarantee that the group-level findings can generalize to the individual's level required for the case-conceptualization and clinical recommendations of a specific client [78]. Thus, intensive idiographic approaches may help clarify, and best understand the clinical value of tDCS integration in the treatment routine (for examples of such idiographic approaches, see [79–81]). Lastly, only two studies investigated the effect of repeated sessions of tDCS. Therefore, researchers should further conduct studies with repeated sessions of tDCS and follow-up assessments as evidence suggests that longer trials with a higher number of sessions are associated with better outcomes [e.g., 82,83].

Our systematic review also highlights some limitations that require further investigation in future research. First, the impact of completing a task during the stimulation is unclear in the tDCS literature. The same question applies to the stressor: all but one study [63] used an offline stressor. A critical step in future iterations would thus be to clarify the respective impacts of online versus offline stressors as well as of online versus an offline task's completion. Moreover, although it is commonly assumed that anodal stimulation increases cortical excitability and that cathodal stimulation decreases cortical excitability, research has shown that this is not always the case; anodal and cathodal stimulation can have asymmetric effects to the ones expected, especially in the context of tDCS studies focusing on cognitive processes [5,84]. Therefore, investigating how the type of task and stressor (and when they are used) influences the effect of tDCS is especially relevant as tDCS does not induce activity in resting neural networks but modulates cortical excitability, plasticity, and functional connectivity by interacting with concurrent brain activity [4,85].

Second, although there is a high correlation between the trait and state ruminations [67], uncertainty remains regarding the respective tDCS' impact on those two constructs. Future research is thus needed to elucidate this issue: (1) by investigating state and trait rumination in single session tDCS studies; and (2), even more importantly, by conducting longitudinal studies of repeated tDCS sessions in order to address the current gaps in this literature. One may also wonder whether trait rumination moderates tDCS' impact on state rumination. Three of the included studies measured both trait and state rumination, but only one [62] formally tested this hypothesis. They found that trait rumination did moderate the mediation effect (i.e., the higher the trait rumination, the better the improvement on working memory performance induced by tDCS, and the less they ruminated). Thus, future iterations would want to examine whether this moderated mediational effect remains at varying tDCS parameters and samples.

6. Conclusions

In conclusion, the results of the present systematic review are not definitive. Instead, they set the scene up for the field's larger, ongoing effort to modifying transdiagnostic mechanisms like rumination via brain stimulation techniques. However, because this is the first systematic review of the impact of tDCS on rumination, we also discussed the methodological caveats of this research field to help usher the field forward. From these caveats, we have formulated the following methodological guidelines for future iterations[1] by researchers: (a) embrace open science practices (i.e., more transparency regarding the randomization; pre-registration; and data sharing), (b) use larger sample sizes to increase statistical power, (c) favor the use of protocols and parameters from past studies (unless authors have strong reasons to do otherwise) to ease cumulative science, (d) uncover the best tDCS protocol in general and for particular outcomes (e) and, recruit clinical samples. Like other systematic reviews on emerging research fields, ours fulfills a valuable niche wherein identifying strengths and limitations provides critical clues for larger, more definitive future efforts.

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Declaration of competing interest

None.

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[1] To ease the reporting of future tDCS studies on rumination, we also created a checklist that includes all the relevant features discussed in this systematic review. We believe that adopting such a checklist may help usher the reproducibility and research quality of this field forward. The checklist is available on the Open Science Framework (https://osf.io/hzkgt/).

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