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Quantitative Review Finds No Evidence of Cognitive Effects in Healthy Populations From Single-session Transcranial Direct Current Stimulation (tDCS)

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A B S T R A C T

Background: Over the last 15-years, transcranial direct current stimulation (tDCS), a relatively novel form of neuromodulation, has seen a surge of popularity in both clinical and academic settings. Despite numerous claims suggesting that a single session of tDCS can modulate cognition in healthy adult populations (especially working memory and language production), the paradigms utilized and results reported in the literature are extremely variable. To address this, we conduct the largest quantitative review of the cognitive data to date.
Methods: Single-session tDCS data in healthy adults (18–50) from *every* cognitive outcome measure reported by at least two different research groups in the literature was collected. Outcome measures were divided into 4 broad categories: executive function, language, memory, and miscellaneous. To account for the paradigmatic variability in the literature, we undertook a three-tier analysis system; each with less-stringent inclusion criteria than the prior. Standard mean difference values with 95% CIs were generated for included studies and pooled for each analysis.
Results: Of the 59 analyses conducted, tDCS was found to not have a significant effect on any – regardless of inclusion laxity. This includes no effect on any working memory outcome or language production task.
Conclusion: Our quantitative review does not support the idea that tDCS generates a reliable effect on cognition in healthy adults. Reasons for and limitations of this finding are discussed. This work raises important questions regarding the efficacy of tDCS, state-dependency effects, and future directions for this tool in cognitive research.

Introduction

Since its modern resurgence at the turn of the century, transcranial direct current stimulation (tDCS) – a noninvasive neuromodulatory device – has been steadily growing in popularity within both the academic and clinical research sectors. Current theory suggests that tDCS, via time-dependent and polarity specific modulation of neuronal firing patterns, can markedly and predictably enhance a number of higher-order cognitions and behaviors. However, a recent systematic review of the neurophysiologic literature undertaken by this group [1] questions the reliability and significance of tDCS effects on all but one neurophysiologic measure tested. Here, we undertake a quantitative review of the cognition literature to determine if tDCS shows a reliable effect on any cognitive tasks.

A brief review of proposed tDCS mechanisms of action

tDCS is most commonly delivered via 2 electrodes – 1 anode and 1 cathode – affixed to the scalp overlying cortical regions relevant to the outcome measure of interest [2]. It is believed that passing a weak electric current (typically 0.5–2.0 mA) between these two electrodes modulates neuronal firing patterns in the cortical regions underlying the electrodes via two mechanisms of actions. The first occurs *during* stimulation and involves ionic concentration shifts within the extracellular fluid which serve to modulate neuronal resting membrane potentials thereby hypo- and hyperpolarizing neurons underlying the anode and cathode, respectively [3]. The second occurs *following* long duration (>7 min) stimulation and involves long-term potentiation and depression-like mechanisms at the synaptic level thereby effecting hyper- and hypo-communicative activity in neurons underlying the anode and cathode, respectively [3]. To account for these different mechanisms, in this paper we divide studies according to whether

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the outcome measures were obtained during stimulation (online protocols) or following stimulation (offline protocols).

Quantitative-review structure

The poolable cognitive tasks in the literature can be grouped into 4 broad categories: executive functions, language, memory, and miscellaneous. Accordingly, the methods and results sections will be structured around these domains. To be included in this review, the effects of tDCS on a given task must have been explored by at least two different research groups using a comparable tDCS protocol. A full list of studies that assessed the relevant aspects of cognitive function but did not meet these inclusion criteria can be found in Supplemental Material (Fig. S1; Table S3). Each poolable outcome measure that satisfied our inclusion criteria is introduced briefly below.

Executive functions

Executive functions (EFs) are often regarded as a coordinated set of cognitive processes which allow an individual to override more instinctual or automatic responses in order to achieve a specified goal [4]. The following three EF measures met inclusion criteria for this review.

Set-shifting

Individuals must determine which target/s amongst a series of targets are "correct" based on an unspecified rule-set via arbitrarily guessing (e.g. – red fruit amongst a series of food-based images). Occasionally, and without warning or explication, the rule-set will change (e.g. – round vegetables amongst a series of food-based images). Improved performance on this task is reflected by a reduction in the time taken to notice this change, abandon the prior rule-set, and learn the new rule-set [5].

Stop signal task

Individuals are repeatedly presented with a target (e.g. – a visual circle) and asked to respond as quickly as possible each time it appears. Occasionally, however, the target will be paired with a secondary stimulus (e.g. – an auditory beep); in this instance, the individual should *not* respond to the target. This task is a measure of automatic response inhibition [6].

Stroop task

Individuals are presented with stimuli which contain multiple, uniquely processed dimensions (e.g. – the word 'red' written in a green colored font), of which the individual must respond to only one. The speed which with a person can accurately respond is a measure of selective attention and goal maintenance [7].

Language

Linguistic-based cognitive tasks utilize language production speed and accuracy to explore the psychological and neurobiological factors that enable humans to produce and comprehend speech [8]. The following three language measures met inclusion criteria for this review.

Picture-to-word novel-language learning

Individuals are presented with paired images and pseudo-words or words from an unfamiliar language and must learn the pairing of the two. The accuracy with which one can respond to correctly- or incorrectly-joined pairs is thought to be a measure of linguistic learning [9].

Picture naming

Individuals are presented with a series of images (either simple line drawings or photos) and asked to name them as quickly as possible. The time taken to accurately name each object is a measure of lexical access, or 'word-finding ability' [10].

Verbal fluency

Individuals are presented with a phonemic category (e.g. – the letter 'p') or a semantic category (e.g. – animals) and asked to name as many words as possible from said category within a specified time limit. The number of words produced is a measure of semantic access [11].

Memory

Memory-based cognitive tasks utilize memorization and recall speed/accuracy to explore the structures and processes involved in the effective storage and retrieval of information [12]. The following five memory measures met inclusion criteria for this review.

Digit-span recall

Individuals are sequentially presented with verbal strings of numbers which sequentially increase in length and are asked to verbally report the numbers following each presentation. The length of the final number string an individual is able to accurately report back is a measure of digit-span recall WM [13].

Verbal episodic memory

Individuals are presented with a list of words several times and asked to memorize it (encoding). Following a delay period (consolidation), during which time the individual is distracted with non-relevant tasks, the individual is presented with 'target' words and asked whether or not each was present in the prior memorized list. The accuracy with which an individual responds to the targets is a measure of verbal episodic recognition memory. An identical procedure, though replacing words with visual images, is utilized as a measure of visual episodic recognition memory [14].

Visual WM

Individuals are sequentially presented with a string of visual images. Following each string, a single target is visually presented and the individual must respond whether or not said target was in the prior string. The speed and accuracy with which an individual responds to the target is a measure of visual WM [15].

N-back WM

Individuals are presented with a sequential string of stimuli (e.g. – letters or numbers) and asked to generate a response if a stimulus is identical to the one presented '*N*' items prior. The accuracy and speed with which an individual responds to targets is a measure of WM according to the modality of the stimuli utilized [16].

Miscellaneous

An additional four measures met inclusion criteria for this review but could not be grouped into any single cognitive domain.

Mental arithmetic

Individuals are asked to complete simple arithmetic math problems in their head. The speed and accuracy with which an individual can complete these problems is a measure of computational efficiency [17].

Picture viewing/rating

Individuals are asked to view and rate a series of images of differing valences (typically negative and neutral). The average

Table 1
Studies and values for executive function task primary analyses.

Study	N	Active	Ref	Density (mA/cm^2)	Task	SMD (95% CI)	Z value	P value
Set shifting tasks – anode/offline: **ERRORS**								
[25]	30	lDLPFC	rORBIT	0.0286	Cog	0.20 (−0.21, 0.61)	0.978	0.328
	30	lDLPFC	rORBIT	0.0286	Motor	−0.30 (−0.81, 0.21)	−1.150	0.250
[26]	46	lDLPFC	rORBIT	0.0286	Cog	0.08 (−0.42, 0.59)	0.325	0.745
				Fixed effect model		**0.03 (−0.27, 0.32)**	**0.207**	**0.836**
Stop signal task – anode/offline: **NO STOP REACTION TIME**								
[27]	11	rIFG	lORBIT	0.04	–	−0.10 (−0.93, 0.74)	−0.225	0.822
[28]	10a/12s	rIFG	lORBIT	0.0429	–	−0.91 (−1.79, −0.03)	−2.023	0.043
				Fixed effect model		**−0.48 (−1.09, 0.13)**	**−1.555**	**0.12**
Stop signal task – anode/offline: **STOP SIGNAL REACTION TIME (IFG)**								
[27]	11a/22s	rIFG	lORBIT	0.04	–	−0.21 (−0.93, 0.52)	−0.554	0.580
[28]	10a/12s	rIFG	lORBIT	0.0429	–	−0.13 (−0.97, 0.71)	−0.300	0.764
				Fixed effect model		**−0.17 (−0.72, 0.38)**	**−0.615**	**0.538**

General notes: Active = Active electrode location; Ref = Reference electrode location; SMD = Standardized mean difference; A = Active; S = Sham; DLPFC = Dorsolateral prefrontal cortex; ORBIT = Orbitofrontal location; IFG = Inferior frontal gyrus.
Set shifting: Two studies from [25] were omitted due to targeting M1 (no comparable work elsewhere).
Stop signal: All sham participants were pooled for [27].

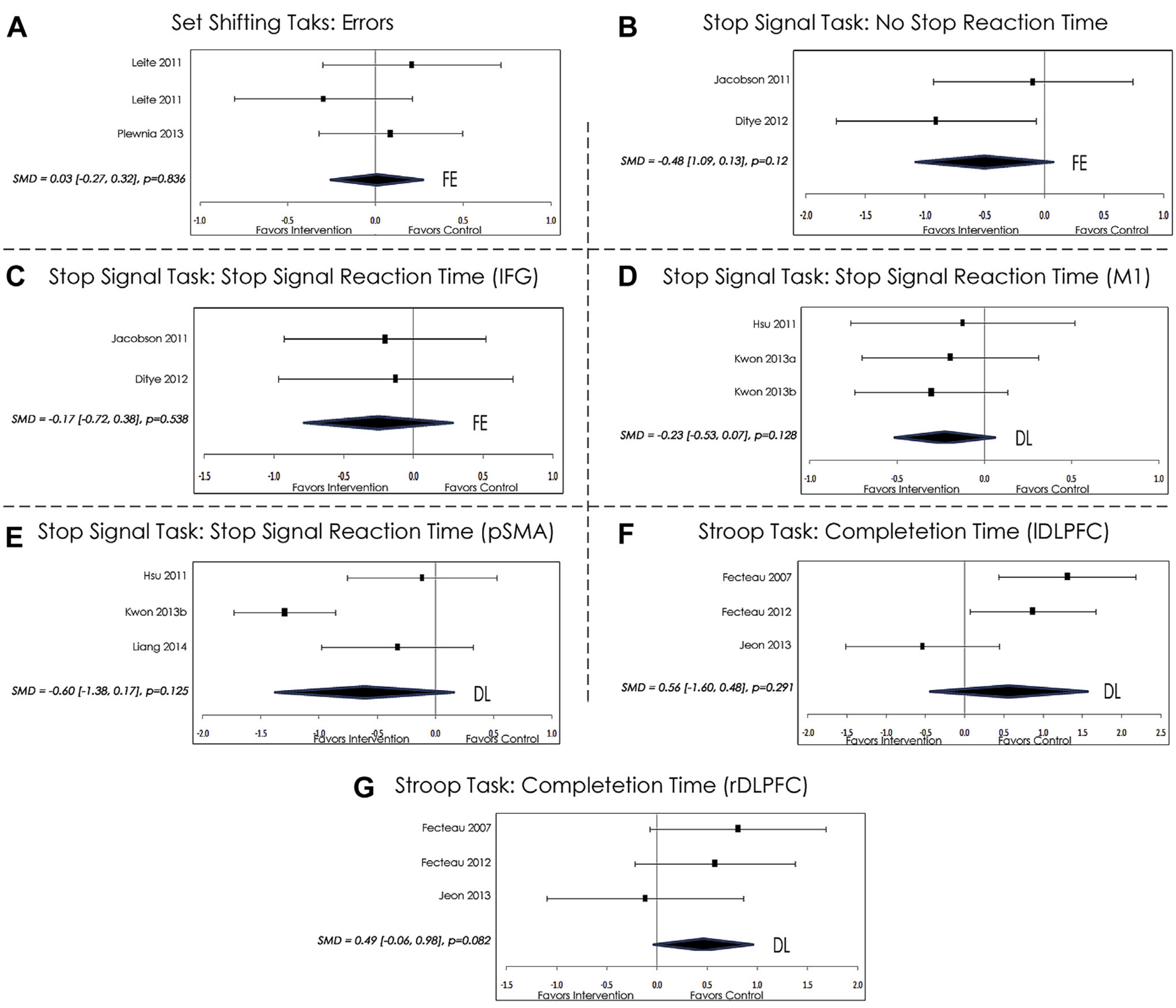

Figure 1. Forest plots for both primary and secondary executive function analyses (SMD = Standard mean difference; FE = Fixed effect model for primary analyses; DL = DerSimonian-Laird mixed-effect model for secondary analyses; Parentheses represent 95% CI).

Table 2
Studies and values for executive function task secondary analyses.

Study	N	Active	Ref	Density (mA/cm^2)	Task	SMD (95% CI)	Z value	P value
Stop signal task – anode/offline: **STOP SIGNAL REACTION TIME (M1)**								
[32]	14a/28s	rM1	lCHK	0.0938	–	−0.13 (−0.77, 0.52)	−0.381	0.704
[30]	30	rM1	lORBIT	0.0286	–	−0.20 (−0.70, 0.31)	−0.753	0.451
[33]	40	rM1	lORBIT	0.0286	–	−0.30 (−0.75, 0.14)	−1.353	0.176
				DL model		**−0.23 (−0.53, 0.07)**	**−1.521**	**0.128**
Stop signal task – anode/offline: **STOP SIGNAL REACTION TIME (pSMA)**								
[32]	14a/28s	rpSMA	lCHK	0.0938	–	−0.11 (−0.76, 0.53)	−0.347	0.728
[33]	40	rpSMA	lORBIT	0.0286	–	−1.30 (−1.78, −0.81)	−5.267	<0.001
[34]	18	rpSMA	lCHK	0.0938	–	−0.33 (−0.98, 0.33)	−0.973	0.331
				DL Model		**−0.60 (−1.38, 0.17)**	**−1.532**	**0.125**
Stroop task – anode/offline: **COMPLETION TIME (lDLPFC)**								
[35]	10	lDLPFC	rDLPFC	0.0571	–	1.31 (0.34, 2.27)	2.650	0.008
[36]	12	lDLPFC	rDLPFC	0.0571	–	0.87 (0.03, 1.70)	1.032	0.042
[37]	8	lDLPFC	rORBIT	0.0286	–	−0.54 (−1.54, 0.46)	−1.059	0.290
				DL model		**0.56 (−1.60, 0.48)**	**1.056**	**0.291**
Stroop task – anode/offline: **COMPLETION TIME (rDLPFC)**								
[35]	10	rDLPFC	lDLPFC	0.0571	–	0.81 (−0.11, 1.72)	1.734	0.083
[36]	12	rDLPFC	lDLPFC	0.0571	–	0.58 (−0.24, 1.40)	1.387	0.165
[37]	8	rDLPFC	lORBIT	0.0286	–	−0.12 (−1.10, 0.86)	−0.236	0.831
				DL model		**0.49 (−0.06, 0.98)**	**1.737**	**0.082**

General notes: Active = Active electrode location; Ref = Reference electrode location; SMD = Standardized mean difference; A = Active; S = Sham; DLPFC = Dorsolateral prefrontal cortex; ORBIT = Orbitofrontal location; IFG = Inferior frontal gyrus; CHK = Cheek; pSMA = Pre-supplementary motor area.
Stop signal: All sham participants were pooled for [32]. [30] presented conflicting data regarding the number of participants: we used the *N* presented in the results section (*n* = 30).
Stroop task: [38] and [39] were omitted due to utilizing a 6-day and 5-day multiple-day stimulation protocol, respectively (no day 1 data); though, each reported no effect of stimulation on the Stroop task.

rating generated within each valence is a measure of emotional processing [18].

Gambling based risk taking

Individuals participate in a ‘gambling-type’ scenario whereby different actions carry varying, yet clearly understood, consequences (e.g. – choose between two boxes, the first of which has a 90% probability of containing $1 whilst the second has a 10% chance of containing $10). The number of low-probability/high-reward choices an individual selects is a measure of risk-taking propensity [19,20].

Rumination

Individuals are asked to report about the frequency and intensity of mentally generated self-referential thoughts (typically following a pre-arranged negative valence-type scenario, such as receiving a negative grade on an exam) [21].

Methods

Study selection

Papers included in this quantitative review were obtained from a PubMed database search (June 12th, 2014). The search term “transcranial direct current stimulation” generated 1156 papers. The abstract of each of paper was then read to determine which outcome measures were included and what type of population was utilized. This initial review narrowed the study pool to 417 (see Supplemental Material: Fig. S1 for complete study selection flow chart).

Following this, each article was read and the tasks/outcome measures utilized were noted and organized to identify all outcome measures utilized by at least two different research groups. We chose to exclude measures that have only been replicated by a

Table 3
Studies and values for language-based task primary analyses.

Study	N	Active	Ref	Density (mA/cm^2)	Task	SMD (95% CI)	Z value	P value
Novel language learning task (Pictures to words) – anode/offline: **ACCURACY**								
[40]	19	WNKE	rORBIT	0.0286	–	0.18 (−0.46, 0.82)	0.553	0.580
[41]	10	WNKE	rORBIT	0.0286	–	0.28 (−0.60, 1.16)	0.624	0.533
				Fixed effect model		**0.21 (−0.30, 0.73)**	**0.814**	**0.416**
Picture naming task – anode/offline: **RT**								
[42]	12	lDLPFC	rSHLD	0.0571	–	−0.09 (−0.89, 0.71)	−0.217	0.829
[43]	20	lDLPFC	rSHLD	0.0429	–	0.04 (−0.58, 0.66)	0.135	0.893
				Fixed effect model		**−0.01 (−0.50, 0.48)**	**−0.026**	**0.979**
Verbal fluency task – anode/offline: **NUMBER OF WORDS GENERATD**								
[44]	12	lDLPFC	rORBIT	0.0613	PHN	0.23 (−0.57, 1.4)	0.568	0.570
[45]	10	lDLPFC (+Broca)	rORBIT	0.0571	SMT	1.00 (0.07, 1.93)	2.110	0.035
	10	lDLPFC (+Broca)	rORBIT	0.0571	PHN	0.63 (−0.27, 1.53)	1.381	0.167
[46]	18	lDLPFC	rORBIT	0.0571	SMT	−0.23 (−0.89, 0.42)	−0.700	0.484
	18	lDLPFC (+Broca)	rORBIT	0.0571	SMT	0.43 (−0.29, 1.09)	1.283	0.199
	18	lDLPFC (+Broca)	rORBIT	0.0571	SMT	−0.27 (−0.93, 0.39)	−0.809	0.418
				Fixed effect model		**0.20 (−0.11, 0.50)**	**1.259**	**0.208**

General notes: Active = Active electrode location; Ref = Reference electrode location; SMD = Standardized mean difference; A = Active; S = Sham; WNKE = Wernicke’s area; RT = Reaction time; DLPFC = Dorsolateral prefrontal cortex; ORBIT = Orbitofrontal location; PHN = Phonemic; SMT = Semantic.
Picture naming: [37] was omitted from analysis as no quantitative RT data was reported.
Verbal fluency: [47] was omitted from analysis as the young cohort only undertook sham stimulation. [48] did not supply quantitative data for the phonemic fluency task, though they verbally reported no effect of stimulation.

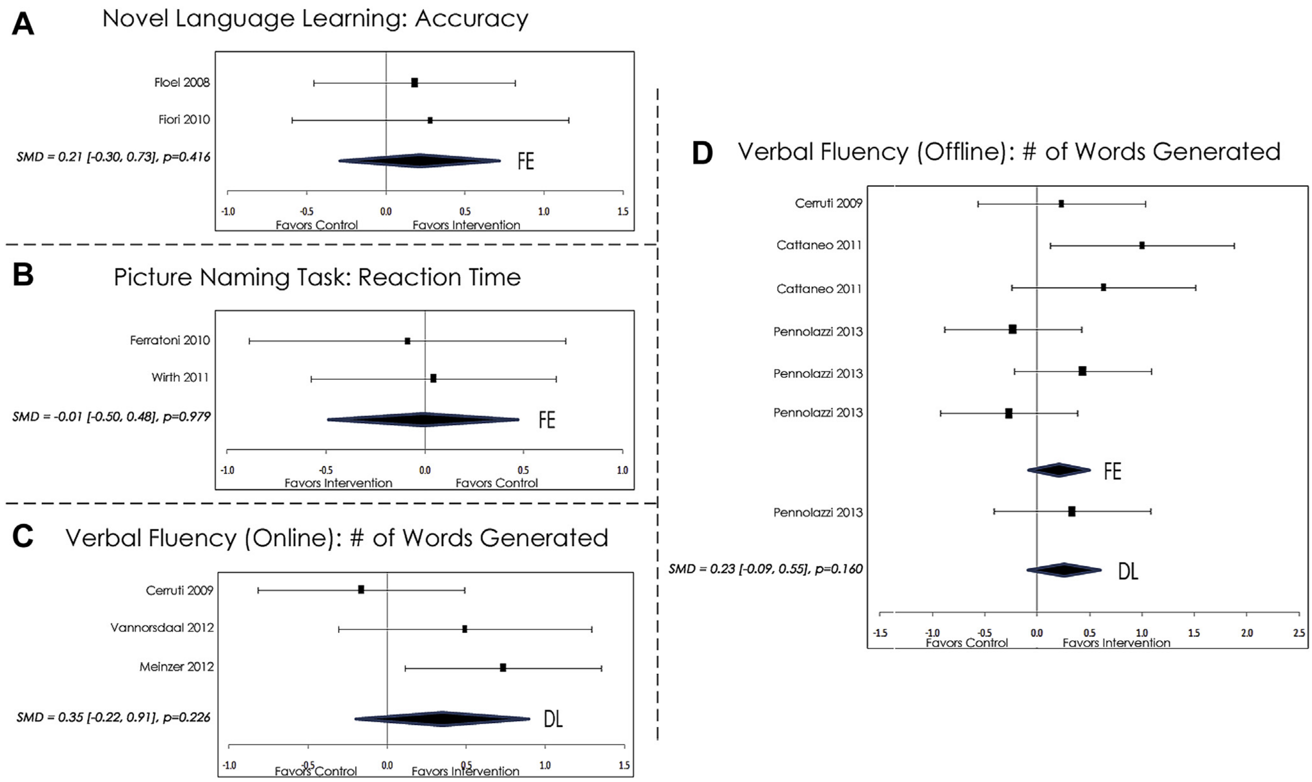

Figure 2. Forest plots for both primary and secondary language analyses (SMD = Standard mean difference; FE = Fixed effect model for primary analyses; DL = DerSimonian-Laird mixed-effect model for secondary analyses; Parentheses represent 95% CI).

single research group to ensure all data included in and conclusions generated by this review accurately reflect the effects of tDCS itself, rather than any unique device, protocol, or condition utilized in a single lab. Examples of non-experimentally based systematic errors reliably influencing the results generated by a single research group can be found in all the sciences, from physics (see: Ref. [22]), to biology (see: Ref. [23]), to medicine (see: Ref. [24]). Due to this inclusion criterion, a number of cognitive outcome measures extant in the literature were omitted due to only being reported by a single research group (see Supplemental Material: Table S2). We want to emphasize that this *does not* suggest said research is in any way faulty or incorrect; rather, that inter-group replication is necessary in order to eliminate any potential non-tDCS influential outcome factors.

Next, the stimulation-to-task relationship was determined for each study. As the mechanism of tDCS is thought to differ *during* and *following* stimulation (see above), included papers were divided into those which utilized an 'online' protocol and those which utilized an 'offline' protocol. Following this, we further divided studies according to the location chosen for the active stimulating tDCS electrode and whether or not anodal or cathodal stimulation was utilized. Finally, all studies not including a sham condition were omitted.

Analysis

Our initial intention was to pool only studies which utilized identical stimulation current densities and electrode montages. However, a look at the results section reveals there is very little direct replication in the literature. Accordingly, we decided to dichotomize current density values (low = 0.0286 mA/cm^2; high > 0.0286 mA/cm^2) and assessed the respected effects independently.

Next, continuous mean and variation data was extracted from each included study. If continuous numerical data was not included, values were extracted from included images (achieved by exporting images to an image editing program, overlaying a standardized grid, and counting relevant values by hand). For each included study, active stimulation values were compared to sham (control) values and a standard mean difference (SMD) with 95% confidence interval (95% CI) effect size was determined. These values were grouped and analyzed using two different meta-analytic software tools to ensure accuracy (Comprehensive Meta-Analysis – v2.0, Biostat, Englewood, NJ, USA; MetaEasy – v1.0.4, Statanalysis, Manchester, UK). No differences were found in obtained values from either program; included images were exported from MetaEasy v1.0.4. Due to the wide paradigmatic variation and unknown effect of multiple-day stimulation protocols (e.g. – 10 consecutive days of anodal stimulation during a learning task), we only analyzed day 1 data from any study utilizing a multiple-day protocol.

Due to parametric variations within papers, we undertook two levels of analyses to balance the tradeoff between the maximum homogeneity achieved by including a smaller number of studies and our desire to also look for any more generalized effects seen across a broader sample of studies. Our primary analysis was limited to studies utilizing the same cognitive task with identical tDCS current densities and reference electrode locations. For this analysis, a fixed-effect (FE) model was utilized since, as the tDCS parameters and task were the same between studies, one would expect fairly homogenous results.

For our secondary analysis, all studies which utilized the same outcome measure were pooled and analyzed, regardless of current density and/or reference electrode location. This analysis included both the studies utilized in the first analysis and any additional study that used different current density and/or electrode montage. For this larger analysis, a DerSimonian-Laird (DL) mixed-effects

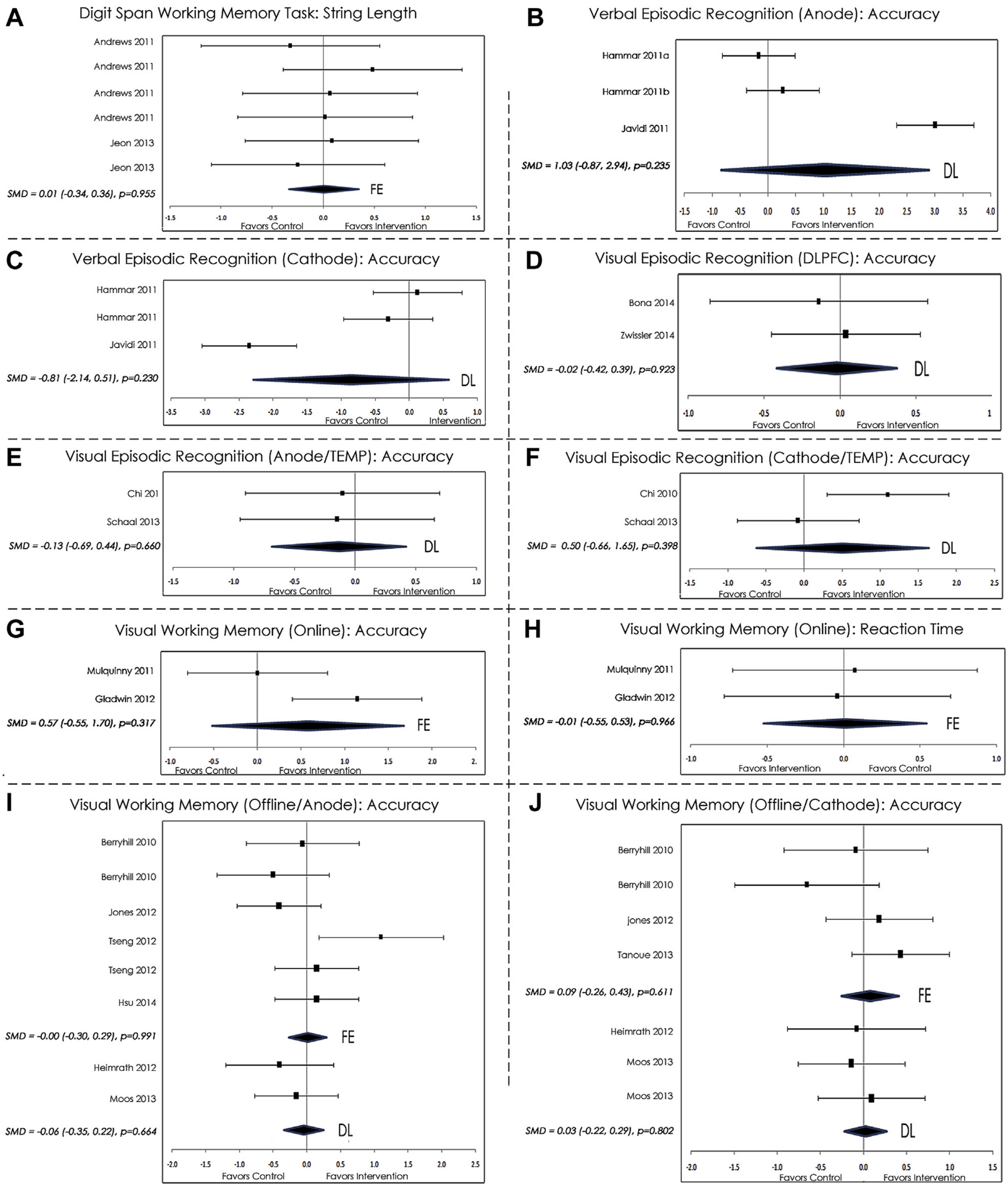

Figure 3. Forest plots for both primary and secondary memory task analyses (n-back excluded) (SMD = Standard mean difference; FE = Fixed effect model for primary analyses; DL = DerSimonian-Laird mixed-effect model for secondary analyses; Parentheses represent 95% CI).

model was selected since, as current density and reference electrode location parameters were variable, one would expect more heterogenous results. As these parameters were chosen prior to analysis, homogeneity I^2 values will not be reported below.

Several studies in the literature have explored outcome measures included in the analysis below whilst targeting a neural region not replicated by a second group. Unfortunately, as these studies did not meet our inclusion criteria, we were unable to pool or meaningfully analyze them. For a list of these studies which have explored one of the outcome measures included in this paper but which targeted a different, non-replicated neural region, please see Supplementary Material (Table S2)

Table 4
Studies and values for executive function task secondary analyses.

Study	N	Active	Ref	Density (mA/cm^2)	Task	SMD (95% CI)	Z value	P value
Verbal fluency task – anode/online: **NUMBER OF WORDS GENERATD**								
[44]	18	lDLPFC	rORBIT	0.0613	PHN	−0.17 (−0.82, 0.49)	−0.494	0.621
[48]	12	lDLPFC	Cz	0.0370	SMT	0.49 (−0.32, 1.30)	1.185	0.236
[51]	20	lDLPFC (+Broca)	rORBIT	0.0286	SMT	0.73 (0.09, 1.38)	2.247	0.025
				DL model		**0.35 (−0.22, 0.91)**	**1.210**	**0.226**
Verbal fluency task – anode/offline: **NUMBER OF WORDS GENERATD**								
[44]	12	lDLPFC	rORBIT	0.0613	PHN	0.23 (−0.57, 1.4)	0.568	0.570
[45]	10	lDLPFC (+Broca)	rORBIT	0.0571	SMT	1.00 (0.07, 1.93)	2.110	0.035
	10	lDLPFC (+Broca)	rORBIT	0.0571	PHN	0.63 (−0.27, 1.53)	1.381	0.167
[46]	18	lDLPFC	rORBIT	0.0571	SMT	−0.23 (−0.89, 0.42)	−0.700	0.484
	18	lDLPFC (+Broca)	rORBIT	0.0571	SMT	0.43 (−0.29, 1.09)	1.283	0.199
	18	lDLPFC (+Broca)	rORBIT	0.0571	SMT	−0.27 (−0.93, 0.39)	−0.809	0.418
[46]	18	lDLPFC (+Broca)	rDLPFC	0.0571	SMT	0.29 (−0.37, 0.95)	0.869	0.385
				DL model		**0.23 (−0.09, 0.55)**	**1.406**	**0.160**

General notes: Active = Active electrode location; Ref = Reference electrode location; SMD = Standardized mean difference; A = Active; S = Sham; WNKE = Wernicke's area; RT = Reaction time; DLPFC = Dorsolateral prefrontal cortex; ORBIT = Orbitofrontal location; PHN = Phonemic; SMT = Semantic.
Verbal fluency: [47] was omitted from analysis as the young cohort only undertook sham stimulation. [48] did not supply quantitative data for the phonemic fluency task, though they verbally reported no effect of stimulation. 1 study from [48] was omitted as it did not include numerical data (though they did verbally report no effect of stimulation on the total number of words generated).

Results

Executive functions: primary analysis

Set shifting

The directly-replicated anode/offline studies revealed a non-significant SMD effect size for the number of errors generated during task completion (Table 1; Fig. 1a). Only 1 study explored cathodal/offline stimulation [25]and only 1 study explored online tDCS on this task [29]; accordingly, no analysis was undertaken for these measures.

Stop signal task

The directly-replicated anode/offline studies revealed a non-significant SMD effect size for inhibitory reaction time to stop-signal stimuli (Table 1; Fig. 1c). In addition [27], and [28] further reported values for reaction time (RT) to non-stop-signal stimuli; analysis of this measure revealed a non-significant SMD effect size (Table 1; Fig. 1b). Only 1 study explored the effect of anodal/online stimulation [30] and only 1 explored the effect of cathodal/offline stimulation on this task [31]; accordingly, no analysis was undertaken for these measures.

Executive functions: secondary analysis

Stop signal task

Six non-directly comparable studies explored this task; 3 targeted M1 and 3 targeted pSMA. Analysis of the different locations revealed no significant SMD effect sizes for inhibitory reaction time to stop-signal stimuli (Table 2; Fig. 1d,e).

Stroop task

The non-directly comparable studies revealed no significant SMD effect sizes for task completion time (Table 2; Fig. 1f,g). 2 studies explored the effects of cathodal/offline stimulation [35,36]. As each came from the same research group, no analysis was undertaken. No studies have explored the effect of online stimulation on this measure.

Language: primary analysis

Novel language learning task

The directly-replicated anode/offline studies revealed a non-significant SMD effect size for task accuracy (Table 3; Fig. 3a). Interestingly, although [41] noted an effect of stimulation on RT [40], noted no effect of stimulation on RT: as this later group did not include any numeric data for this measure (only a verbal report), no analysis could be undertaken for this measure. No studies have explored the effect of online or cathodal stimulation on this task.

Picture naming task

Three studies explored the effect of tDCS on this outcome measure by targeting the temporal lobes (2 from [49], 1 from [50]). Unfortunately [49], only reported numerical data for accuracy (verbally noted no effect of stimulation on RT) whilst [50] only reported numerical data for RT (verbally noted no effect of stimulation on accuracy). Accordingly, no analysis was undertaken for these papers. In addition, 4 studies from 3 papers have explored the effect of tDCS on this outcome measure by targeting the left DLPFC [37,42,43]. Unfortunately [42], and [43] both reported only numerical data for RT (though [42] verbally noted no effect of stimulation on accuracy) whilst [37] only reported numerical data for Accuracy. Accordingly, an analysis could only be undertaken exploring RT. Analysis of this measure revealed a non-significant SMD effect size (Table 3; Fig. 3b). Although 4 studies from 3 papers have explored the effect of anodal/online stimulation on this task, each targeted a different neural region; accordingly, no analysis could be undertaken. Finally, although 4 studies from 3 papers have explored the effect of cathodal stimulation on this task, each targeted a different neural region; accordingly, no analysis was undertaken.

Verbal fluency

The directly-replicated anode/offline studies revealed a non-significant SMD effect size for word generation (Table 3; Fig. 3d). Three comparable studies have explored the effect of anode/online stimulation on this task; however, as the current density and reference electrode location differed between each, we will explore this in the secondary analysis (below). No study has explored the effect of cathodal stimulation on this measure.

Language: secondary analysis

Verbal fluency

The non-directly comparable anode/online and anode/offline studies revealed no significant SMD effect size for word generation (Table 4; Fig. 2c,d). No study explored the effect of cathodal stimulation on this measure.

Table 5
Studies and values for memory task primary analyses (N-Back excluded).

Study	*N*	Active	Ref	Density (mA/cm^2)	Task	SMD (95% CI)	Z value	*P* value
Digit span working memory task (forward & backward) – anode/offline: **SPAN**								
[52]	10	lDLPFC	rORBIT	0.0286	Forward	−3.22 (−1.21, 0.56)	−0.716	0.474
	10	lDLPFC	rORBIT	0.0286	Backward	0.483 (−0.41, 1.37)	1.065	0.287
	11a/10s	lDLPFC	rORBIT	0.0286	Forward	0.065 (−0.79, 0.92)	0.148	0.882
	11a/10s	lDLPFC	rORBIT	0.0286	Backward	0.018 (−0.84, 0.87)	0.040	0.968
[37]	8a/16s	lDLPFC	rORBIT	0.0286	Forward	0.084 (−0.77, 0.93)	0.194	0.846
	8a/16s	lDLPFC	rORBIT	0.0286	Backward	−0.25 (−1.10, 0.60)	−0.574	0.566
				Fixed effect model		**0.01 (−0.34, 0.36)**	**0.056**	**0.955**
Visual working memory – anode/online: **ACCURACY**								
[53]	12	lDLPFC	rORBIT	0.0286	STRNBRG	0.000 (−1.62, 0.86)	0.000	1.000
[54]	14	lDLPFC	rORBIT	0.0286	STRNBRG	1.14 (0.34, 1.94)	2.803	0.005
				Fixed effect model		**0.57 (−0.55, 1.70)**	**1.000**	**0.317**
Visual working memory – anode/online: **RT**								
[53]	12	lDLPFC	rORBIT	0.0286	STRNBRG	−0.07 (−0.87, 0.73)	−0.177	0.859
[54]	14	lDLPFC	rORBIT	0.0286	STRNBRG	0.04 (−0.70, 0.78)	0.107	0.915
				Fixed effect model		**−0.01 (−0.55, 0.53)**	**−0.042**	**0.966**
Visual working memory – anode/offline: **ACCURACY**								
[55]	11	rPPC	lCHK	0.0429		−0.07 (−0.90, 0.77)	−0.153	0.878
	11	rPPC	lCHK	0.0429		−0.50 (−1.35, 0.35)	−1.160	0.246
[56]	20	rPPC	lCHK	0.0429		−0.42 (−1.04, 0.21)	−1.298	0.194
[57]	9	rPPC	lCHK	0.0938		1.06 (0.07, 2.04)	2.099	0.036
	20	rPPC	lCHK	0.0938		0.14 (−0.48, 0.76)	0.451	0.652
[58]	20	rPPC	lCHK	0.0938		0.14 (−0.48, 0.76)	0.451	0.652
				Fixed effect model		**−0.00 (−0.30, 0.29)**	**−0.012**	**0.991**
Visual working memory – cathode/offline: **ACCURACY**								
[55]	11	rPPC	lCHK	0.0429		−0.09 (−0.93, 0.75)	−0.211	0.833
	11	rPPC	lCHK	0.0429		−0.66 (−1.52, 0.20)	−1.504	0.133
[56]	20	rPPC	lCHK	0.0429		0.18 (−0.44, 0.80)	0.569	0.569
[59]	24	rPPC	lCHK	0.0429		0.43 (−0.14, 1.00)	1.468	0.142
				Fixed effect model		**0.09 (−0.26, 0.43)**	**0.509**	**0.611**
Two-back working memory task – anode/offline: **RT**								
[53]	12	lDLPFC	rORBIT	0.02857	2-Back	−0.45 (−1.26, 0.36)	−1.095	0.274
[60]	18	lDLPFC	rORBIT	0.02857	2-Back	−0.29 (−0.95, 0.37)	−0.868	0.385
				Fixed effect model		**−0.39 (−0.90, 0.12)**	**−1.364**	**0.173**
[61]	10	lDLPFC	rORBIT	0.05714	2-Back	−0.33 (−1.22, 0.55)	−0.741	0.459
[60]	18	lDLPFC	rORBIT	0.05714	2-Back	−0.02 (−0.68, 0.63)	−0.073	0.942
				Fixed effect model		**−0.13 (−0.66, 0.40)**	**−0.499**	**0.617**
Three-back working memory task – anode/online: **ACCURACY**								
[62]	15	lDLPFC	rORBIT	0.02857	3-Back	0.31 (−0.41, 1.03)	0.855	0.393
[63]	12	lDLPFC	rORBIT	0.02857	3-Back	0.05 (−0.71, 0.81)	0.125	0.901
				Fixed effect model		**0.19 (−0.33, 0.71)**	**0.706**	**0.480**
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.36 (−0.37, 1.08)	0.966	0.334
[63]	12	lDLPFC	rORBIT	0.05714	3-Back	−0.05 (−0.81, 0.71)	−0.128	0.898
				Fixed effect model		**0.16 (−0.36, 0.69)**	**0.612**	**0.541**
Three-back working memory task – anode/online: **RT**								
[62]	15	lDLPFC	rORBIT	0.02857	3-Back	0.00 (−0.71, 0.72)	0.011	0.991
[63]	12	lDLPFC	rORBIT	0.02857	3-Back	−0.30 (−1.11, 0.50)	−0.736	0.462
				Fixed effect model		**−0.13 (−0.67, 0.40)**	**−0.481**	**0.631**
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.01 (−0.70, 0.73)	0.032	0.974
[63]	12	lDLPFC	rORBIT	0.05714	3-Back	−0.32 (−1.13, 0.48)	−0.781	0.435
				Fixed effect model		**−0.14 (−0.67, 0.40)**	**−0.495**	**0.621**

General notes: Active = Active electrode location; Ref = Reference electrode location; SMD = Standardized mean difference; A = Active; S = Sham; DLPFC = Dorsolateral prefrontal cortex; ORBIT = Orbitofrontal location; DELT = Deltoid muscle; ATL = Anterior temporal lobe; SMG = Supramarginal gyrus; STRNBRG = Sternberg working memory task; PPC = Posterior parietal cortex; CHK = Cheek; IPS = Inferior parietal sulcus; RT = Reaction time.
Digit span: Two sham groups were pooled in Jeon 2013.
Visual working memory: Values collapsed across hemifields and array sizes. Values for the second study from Tseng 2012 and Hsu 2014 are collapsed across all participants (data appear to be identical for these studies). Bolognini 2010 was omitted from analysis as they did not report any data for accuracy. Tanoue 2013 utilized a cueing paradigm – only the data from the cue-less trials was utilized.
N-back tasks: Data for [64] and [63] were collapsed across two online blocks. [60] was omitted from both accuracy and RT analysis due to no discernable quantitative data being made available. A description in the text noted no effect of either low- or high-density stimulation on accuracy or RT. [52] was omitted from analysis due to not reporting quantitative data. [65] was omitted due to utilizing a 10-day stimulation protocol (no day 1 data). 1 study from [60] was omitted due to not reporting quantitative data (though they verbally reported no effect of stimulation on accuracy or RT data during a 3-back task, and no effect on accuracy during a 2-back task).

Memory: primary analysis

Digit span working memory

The directly-replicated anode/offline studies revealed a non-significant SMD effect size for span length (Table 5; Fig. 3a). No studies explored the effects of online or cathodal stimulation on this task.

Visual working memory

The directly-replicated anode/online studies revealed a non-significant SMD effect size for task accuracy or RT (Table 5; Fig. 3g,h). Similarly, anode/offline studies revealed a non-significant SMD effect size for task accuracy (Table 5; Fig. 3i). With regards to cathode/offline stimulation, analysis of the directly-replicated cathode/offline studies revealed a non-significant SMD effect size

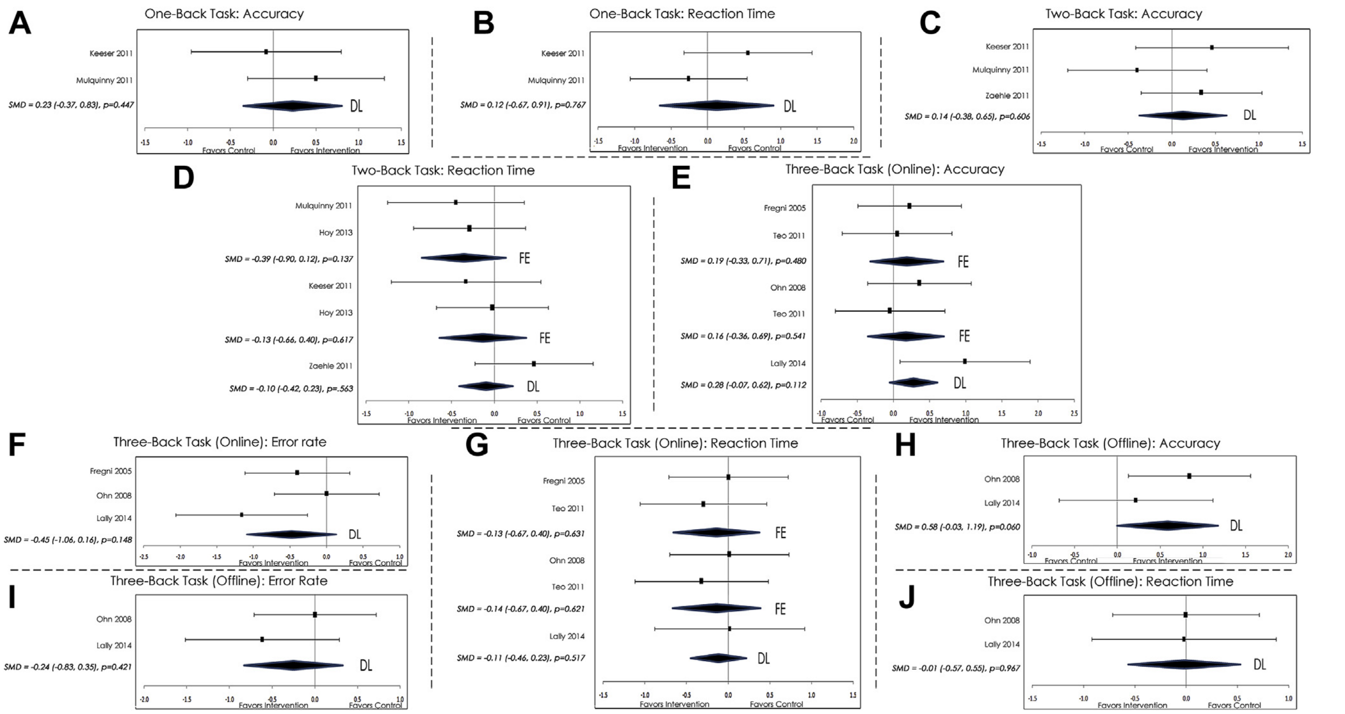

Figure 4. Forest plots for both primary and secondary n-back task analyses (SMD = Standard mean difference; FE = Fixed effect model for primary analyses; DL = DerSimonian-Laird mixed-effect model for secondary analyses; Parentheses represent 95% CI).

on task accuracy (Table 5; Fig. 3j). No studies explored the effect of cathodal/online stimulation on this task. Finally, 2 studies have explored the effect of anode/offline and cathode/offline stimulation on this task whilst targeting the cerebellum [66,67]. Unfortunately [66], only reported quantitative data for RT (verbally reported no effect on accuracy) whilst [67] only reported quantitative data for accuracy (verbally noted no effect on accuracy); accordingly, no analysis was undertaken.

N-back working memory

As task difficulty increases with *N*, we decided to divide and analyze the remaining studies according to *N* (so that the effects of stimulation during a 1-back task do not skew effects during a 3-back task). Analyses of the directly-replicated studies revealed no significant SMD effect size for any measure (Table 5; Fig. 4a,e,g).

Memory: secondary analysis

Verbal episodic memory

The non-directly comparable anode and cathode studies during encoding revealed no significant SMD effect size for task accuracy (Table 6; Fig. 3b,c). With regards to anode during *recognition* [69], only reported numerical data for accuracy (verbally reported no effect on RT) whilst [82] only reported numerical data for RT (verbally reported no effect on accuracy); accordingly, no analysis was undertaken.

Visual episodic memory

The non-directly comparable anodal studies at each electrode location revealed no significant SMD effect size for task accuracy (Table 7; Fig. 3d,e). Similarly, the non-directly comparable cathodal studies revealed a non-significant SMD effect size for task accuracy (Table 6; Fig. 3f).

Visual working memory

The non-directly comparable anode/offline studies revealed a non-significant SMD effect size for task accuracy (Table 6; Fig. 3i). The non-directly comparable cathode/offline studies also revealed a non-significant SMD effect size on task accuracy (Table 6; Fig. 3j). No studies explored the effect of cathodal/online stimulation on this task.

N-back working memory

Again, as task difficulty increases with *N*, studies were divided according to *N* (so that the effects of stimulation during a 1-back task did not skew effects during a 3-back task). For a full breakdown, see Table 6 and Fig. 4. Analyses of the non-directly comparable studies revealed no significant SMD effect size for task accuracy, reaction time, or false alarm rate at any level.

Memory: additional pooled analyses

As many of the aforementioned memory studies utilize tasks which explore a similar memory system (e.g. – working memory), we ran 8 additional analyses combining all studies exploring the same memory system (regardless of specific task utilized). First, we pooled all anodal/online n-back working memory tasks, regardless of the '*n*' value. Analysis revealed no significant SMD effect size for accuracy SMD ([95% CI] = 0.19 [−0.13, 0.51], $z = 1.187$, $P = 0.235$: Fig. 5a) or RT (SMD [95% CI] = −0.14 [−0.46, 0.18], $z = -0.851$, $P = 0.395$: Fig. 5b). Next, we pooled all anodal/offline n-back working memory tasks, regardless of the '*n*' value. Again, analysis revealed no significant SMD effect size for accuracy (SMD [95% CI] = 0.29 [−0.02, 0.60], $z = 1.845$, $P = 0.065$: Fig. 5e) or RT (SMD [95% CI] = −0.16 [−0.42, 0.09], $z = -1.266$, $P = 0.206$: Fig. 5f). Next, we pooled all anodal/online tasks exploring working memory (with a similar neural target). Again, analysis revealed no significant SMD effect size for accuracy (SMD [95% CI] = 0.29 [−0.04, 0.61], $z = 1.699$, $P = 0.089$: Fig. 5c) or RT (SMD [95% CI] = −0.10 [−0.37, 0.17],

Table 6
Studies and values for memory task secondary analyses (N-Back excluded).

Study	*N*	Active	Ref	Density (mA/cm^2)	Task	SMD (95% CI)	Z value	*P* value
Verbal episodic memory task: recognition (stim during encoding) – anode: **ACCURACY**								
[68]	18	lDLPFC	rORBIT	0.0286	Errorless Learning	−0.17 (−0.82, 0.49)	−0.502	0.616
	18	lDLPFC	rORBIT	0.0286	Errorful Learning	0.268 (−0.39, 0.92)	0.800	0.424
[69]	16	lDLPFC	rORBIT	0.0816	–	3.00 (1.99, 4.01)	5.821	<0.001
				DL model		**1.03 (−0.87, 2.94)**	**1.188**	**0.235**
Verbal episodic memory task: recognition (stim during encoding) – cathode: **ACCURACY**								
[68]	18	lDLPFC	rORBIT	0.0286	Errorless Learning	0.120 (−0.53, 0.77)	0.360	0.719
	18	lDLPFC	rORBIT	0.0286	Errorful Learning	−0.31 (−0.97, 0.35)	−0.932	0.351
[69]	16	lDLPFC	rORBIT	0.0816	–	−2.35 (−3.25, −1.45)	−5.117	<0.001
				DL model		**−0.81 (−2.14, 0.51)**	**−1.201**	**0.230**
Visual episodic memory task: recognition (stim during encoding) – anode: **ACCURACY (DLPFC)**								
[70]	15	lDLPFC	rORBIT	0.0286	Cued Learning	0.037 (−0.45, 0.53)	0.146	0.884
[71]	24a/48s	lDLPFC	rDELT	0.0571	–	−0.14 (−0.86, 0.58)	−0.385	0.700
				DL model		**−0.02 (−0.42, 0.39)**	**−0.096**	**0.923**
Visual episodic memory task: recognition (stim during encoding) – anode: **ACCURACY (TEMP)**								
[72]	12	lATL	rATL	0.0571	–	−0.11 (−0.91, 0.70)	−0.257	0.797
[73]	12	lSMG	rORBIT	0.08	–	−0.15 (−0.95, 0.65)	−0.365	0.715
				DL model		**−0.13 (−0.69, 0.44)**	**−0.440**	**0.660**
Visual episodic memory task: recognition (stim during encoding) – cathode: **ACCURACY (TEMP)**								
[72]	12	lATL	rATL	0.0571	–	1.10 (0.24, 1.96)	2.509	0.012
[73]	12	lSMG	rORBIT	0.08	–	−0.08 (−0.88, 0.72)	−0.198	0.843
				DL model		**0.50 (−0.66, 1.65)**	**0.845**	**0.398**
Visual working memory – anode/offline: **ACCURACY**								
[55]	11	rPPC	lCHK	0.0429		−0.07 (−0.90, 0.77)	−0.153	0.878
	11	rPPC	lCHK	0.0429		−0.50 (−1.35, 0.35)	−1.160	0.246
[56]	20	rPPC	lCHK	0.0429		−0.42 (−1.04, 0.21)	−1.298	0.194
[57]	9	rPPC	lCHK	0.0938		1.06 (0.07, 2.04)	2.099	0.036
	20	rPPC	lCHK	0.0938		0.14 (−0.48, 0.76)	0.451	0.652
[58]	20	rPPC	lCHK	0.0938		0.14 (−0.48, 0.76)	0.451	0.652
[74]	12	rPPC	lPPC	0.0286		−0.42 (−1.22, 0.39)	−1.005	0.315
[75]	20	rIPS	lORBIT	0.0286		−0.16 (−0.78, 0.46)	−0.495	0.620
				DL model		**−0.06 (−0.35, 0.22)**	**−0.435**	**0.664**
Visual working memory – cathode/offline: **ACCURACY**								
[55]	11	rPPC	lCHK	0.0429		−0.09 (−0.93, 0.75)	−0.211	0.833
	11	rPPC	lCHK	0.0429		−0.66 (−1.52, 0.20)	−1.504	0.133
[56]	20	rPPC	lCHK	0.0429		0.18 (−0.44, 0.80)	0.569	0.569
[59]	24	rPPC	lCHK	0.0429		0.43 (−0.14, 1.00)	1.468	0.142
[74]	12	rPPC	lPPC	0.0286		−0.08 (−0.88, 0.72)	−0.200	0.842
[75]	20	rIPS	lORBIT	0.0286		−0.14 (−0.76, 0.48)	−0.448	0.654
	20	rIPS	lORBIT	0.0571		0.09 (−0.53, 0.71)	0.293	0.769
				DL model		**0.03 (−0.22, 0.29)**	**0.251**	**0.802**
One-back working memory task – anode/offline: **ACCURACY**								
[61]	10	lDLPFC	rORBIT	0.05714	1-Back	−0.08 (−0.96, 0.80)	−0.184	0.854
[53]	12	lDLPFC	rORBIT	0.02857	1-Back	0.50 (−0.31, 1.31)	1.206	0.228
				DL model		**0.23 (−0.37, 0.83)**	**0.760**	**0.447**
One-back working memory task – anode/offline: **RT**								
[61]	10	lDLPFC	rORBIT	0.05714	1-Back	0.55 (−0.34, 1.44)	1.208	0.227
[53]	12	lDLPFC	rORBIT	0.02857	1-Back	−0.26 (−1.07, 0.54)	−0.638	0.524
				DL model		**0.12 (−0.67, 0.91)**	**0.296**	**0.767**
Two-back working memory task – anode/offline: **ACCURACY**								
[61]	10	lDLPFC	rORBIT	0.05714	2-Back	0.46 (−0.43, 1.35)	1.019	0.308
[53]	12	lDLPFC	rORBIT	0.02857	2-Back	−0.40 (−1.21, 0.41)	−0.970	0.332
[76]	16	lDLPFC	rMAST	0.02857	2-Back	0.39 (−0.36, 1.04)	0.949	0.343
				DL model		**0.14 (−0.38, 0.65)**	**0.515**	**0.606**
Two-back working memory task – anode/offline: **RT**								
[53]	12	lDLPFC	rORBIT	0.02857	2-Back	−0.45 (−1.26, 0.36)	−1.095	0.274
[60]	18	lDLPFC	rORBIT	0.02857	2-Back	−0.29 (−0.95, 0.37)	−0.868	0.385
[61]	10	lDLPFC	rORBIT	0.05714	2-Back	−0.33 (−1.22, 0.55)	−0.741	0.459
[60]	18	lDLPFC	rORBIT	0.05714	2-Back	−0.02 (−0.68, 0.63)	−0.073	0.942
[76]	16	lDLPFC	rMAST	0.02857	2-Back	0.46 (−0.24, 1.17)	1.293	0.196
				DL model		**−0.10 (−0.42, 0.23)**	**−0.579**	**0.563**
Three-back working memory task – anode/online: **ACCURACY**								
[62]	15	lDLPFC	rORBIT	0.02857	3-Back	0.31 (−0.41, 1.03)	0.855	0.393
[63]	12	lDLPFC	rORBIT	0.02857	3-Back	0.05 (−0.71, 0.81)	0.125	0.901
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.36 (−0.37, 1.08)	0.966	0.334
[63]	12	lDLPFC	rORBIT	0.05714	3-Back	−0.05 (−0.81, 0.71)	−0.128	0.898
[77]	9a	lDLPFC	rCHK	0.02857	3-Back	0.97 (0.01, 1.92)	1.988	0.047
	10							
				DL model		**0.28 (−0.07, 0.62)**	**1.589**	**0.112**
Three-back working memory task – anode/online: **FA**								
[62]	15	lDLPFC	rORBIT	0.02857	3-Back	−0.40 (−1.13, 0.32)	−1.095	0.273
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.00 (−0.72, 0.72)	0.000	1.000
[77]	9a	lDLPFC	rCHK	0.02857	3-Back	−1.16 (−2.14, −0.19)	−2.339	0.019
	10							

Table 6 (*continued*)

Study	N	Active	Ref	Density (mA/cm^2)	Task	SMD (95% CI)	Z value	P value
				DL model		**−0.45 (−1.06, 0.16)**	**−1.446**	**0.148**
Three-back working memory task – anode/online: **RT**								
[62]	15	lDLPFC	rORBIT	0.02857	3-Back	0.00 (−0.71, 0.72)	0.011	0.991
[63]	12	lDLPFC	rORBIT	0.02857	3-Back	−0.30 (−1.11, 0.50)	−0.736	0.462
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.01 (−0.70, 0.73)	0.032	0.974
[63]	12	lDLPFC	rORBIT	0.05714	3-Back	−0.32 (−1.13, 0.48)	−0.781	0.435
[77]	9a 10	lDLPFC	rCHK	0.02857	3-Back	0.02 (−0.88, 0.92)	0.037	0.971
				DL model		**−0.11 (−0.46, 0.23)**	**−0.648**	**0.517**
Three-back working memory task – anode/offline: **ACCURACY**								
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.84 (0.10, 1.59)	2.214	0.027
[77]	9a 10	lDLPFC	rCHK	0.02857	3-Back	0.22 (−0.69, 1.12)	0.466	0.641
				DL model		**0.58 (−0.03, 1.19)**	**1.879**	**0.060**
Three-back working memory task – anode/offline: **FA**								
[64]	15	lDLPFC	rORBIT	0.04	3-Back	0.00 (−0.72, 0.72)	0.000	1.000
[77]	9a 10	lDLPFC	rCHK	0.02857	3-Back	−0.62 (−1.54, 0.31)	−1.312	0.190
				DL model		**−0.24 (−0.83, 0.35)**	**−0.804**	**0.421**
Three-back working memory task – anode/offline: **RT**								
[64]	15	lDLPFC	rORBIT	0.04	3-Back	−0.01 (−0.72, 0.71)	−0.015	0.988
[77]	9a 10	lDLPFC	rCHK	0.02857	3-Back	−0.02 (−0.92, 0.88)	−0.047	0.962
				DL model		**−0.01 (−0.57, 0.55)**	**−0.041**	**0.967**

General notes: Active = Active electrode location; Ref = Reference electrode location; SMD = Standardized mean difference; A = Active; S = Sham; DLPFC = Dorsolateral prefrontal cortex; ORBIT = Orbitofrontal location; DELT = Deltoid muscle; ATL = Anterior temporal lobe; SMG = Supramarginal gyrus; STRNBRG = Sternberg working memory task; PPC = Posterior parietal cortex; CHK = Cheek; IPS = Inferior parietal sulcus; RT = Reaction time; MAST = Mastoid; FA = False alarms.
Verbal episodic memory: [68] presented only values pooled between online and offline measures. Two studies from [69] were omitted: one for targeting M1, one for generating stimulation during recognition (no comparable work elsewhere). [78] was omitted due to using very-short duration (1.6 s) stimulation during recognition only (no comparable work elsewhere). [79] was omitted due to utilizing a 5-day stimulation protocol (no day 1 data).
Visual episodic memory: Two studies from [54] were omitted as they utilized an interference paradigm in the Sternberg task (no comparable work elsewhere). [80] was omitted due to using a 10-day stimulation paradigm (no day 1 data). Values were collapsed across array sizes.
Visual working memory: Values collapsed across hemifields and array sizes. Values for the second study from [57] and [58] are collapsed across all participants (data appear to be identical for these studies). [81] was omitted from analysis as they did not report any data for accuracy. [59] utilized a cueing paradigm – only the data from the cue-less trials was utilized.
Two-back: [60] was omitted from the accuracy analysis due to no discernable quantitative data being made available. A description in the text noted no effect of either low- or high-density stimulation on accuracy.
Three-back: Only data from day one of [77] was used for analysis. Data for [64] and [63] were collapsed across two online blocks. [60] was omitted from both accuracy and RT analysis due to no discernable quantitative data being made available. A description in the text noted no effect of either low- or high-density stimulation on accuracy or RT.

$z = -0.715$, $P = 0.474$: Fig. 5d). Next, we pooled all anodal/offline tasks exploring working memory (with a similar neural target). Again, analysis revealed no significant SMD effect size for accuracy (SMD [95% CI] = 0.17 [−0.06, 0.4], $z = 1.438$, $P = 0.151$: Fig. 5g). Finally, we pooled all anodal during encoding episodic memory tasks. Again, analysis revealed no significant SMD effect size for accuracy (SMD [95% CI] = 0.53 [−0.33, 1.38], $z = 1.211$, $P = 0.226$: Fig. 5h). Complete analyses can be found in Supplemental Material: Table S1.

Miscellaneous: primary analysis

Due to a lack of directly replicable studies, no primary analysis could be undertaken on these measures.

Miscellaneous: secondary analysis

Mental arithmetic

The non-directly comparable anode/offline studies revealed a non-significant SMD effect size for task accuracy and RT (Table 7; Fig. 6a,b). Only 1 study explored the effect of online stimulation on this task [93]; accordingly, no analysis was undertaken. No studies explored the effect of cathodal stimulation on this task.

Picture viewing/rating

The non-directly comparable anode/online studies revealed no significant SMD effect size for either negative or neutral valence image ratings (Table 7; Fig. 6c,e,f,h). Similarly, the non-directly comparable cathode/online studies revealed no significant SMD effect size for either negative or neutral valence image ratings (Table 7; Fig. 6d,g). Only 1 study explored the effect of offline stimulation on this task [94]; accordingly, no analysis was undertaken.

Risk taking

The remaining non-comparable anode/online studies revealed no significant SMD effect size for task performance (Table 7; Fig. 6i). Analysis of the non-comparable cathode/online studies revealed a non-significant SMD effect size for task performance (Table 7; Fig. 6j). Only 1 study explored the effect of offline stimulation on this task [95]; accordingly, no analysis was undertaken for this measure.

Rumination task

The non-comparable anode/offline studies revealed a non-significant SMD effect size for rumination intensity (Table 7; Fig. 6k). Only 1 study explored the effect of cathodal stimulation on this task [91]; accordingly, no analysis was undertaken. No studies explored the effect of online stimulation on this task.

Discussion

In this paper, we pooled and analyzed every cognitive outcome measure in the literature explored by at least two different research groups utilizing healthy adult populations, the same stimulation-to-task relationship, the same active electrode location, and

Table 7
Studies and values for miscellaneous task secondary analyses.

Study	*N*	Active	Ref	Density (mA/cm^2)	Task	SMD (95% CI)	*Z* value	*P* value
Mental arithmetic ability – anode/offline: **ACCURACY**								
[83]	10	rPAR	lORBIT	0.0571	MULT	0.18 (−0.70, 1.06)	0.3989	0.691
[84]	16	rPAR	lORBIT	0.0286	SUB	−0.23 (−0.93, 0.47)	−0.647	0.518
				DL model		**−0.07 (−0.62, 0.47)**	**−0.261**	**0.794**
Mental arithmetic ability – anode/offline: **TIME TO SOLVE**								
[83]	10	rPAR	lORBIT	0.0571	MULT	−0.18 (−1.06, 0.70)	−0.398	0.691
[84]	16	rPAR	lORBIT	0.0286	SUB	−0.33 (−1.03, 0.37)	−0.925	0.355
				DL model		**−0.27 (−0.82, 0.28)**	**−0.971**	**0.331**
Negative valence picture viewing – anode/online: **NEGATIVITY RATING (lDLPFC)**								
[85]	23	lDLPFC	rORBIT	0.0571	–	−0.26 (−0.84, 0.32)	−0.884	0.377
[86]	16a/32s	lDLPFC	rM1	0.0286	–	−0.37 (−0.97, 0.24)	−1.192	0.233
[87]	20	lDLPFC	rDLPFC	0.0429	–	0.14 (−0.48, 0.76)	0.438	0.661
				DL model		**−0.17 (−0.52, 0.18)**	**−0.968**	**0.333**
Negative valence picture viewing – cathode/online: **NEGATIVITY RATING (lDLPFC)**								
[86]	16a/32s	lDLPFC	rM1	0.0286	–	−0.25 (−0.86, 0.35)	−0.826	0.409
[87]	20	lDLPFC	rDLPFC	0.0429	–	0.33 (−0.30, 0.95)	1.029	0.304
				DL model		**0.03 (−0.54, 0.60)**	**0.106**	**0.915**
Negative valence picture viewing – anode/online: **NEGATIVITY RATING (rDLPFC)**								
[87]	20	rDLPFC	lDLPFC	0.0429	–	0.33 (−0.30, 0.95)	1.029	0.304
[88]	23a/25s	rDLPFC	lORBIT	0.0429	–	−0.70 (−1.28, −0.12)	−2.347	0.019
				DL model		**−0.19 (−1.20, 0.81)**	**−0.374**	**0.709**
Neutral valence picture viewing – anode/online: **NEGATIVITY RATING (lDLPFC)**								
[86]	16a/32s	lDLPFC	rM1	0.0286	–	−0.12 (−0.72, 0.48)	−0.389	0.697
[87]	20	lDLPFC	rDLPFC	0.0429	–	0.15 (−0.47, 0.77)	0.476	0.634
				DL model		**0.01 (−0.42, 0.45)**	**0.054**	**0.957**
Neutral valence picture viewing – cathode/online: **NEGATIVITY RATING (lDLPFC)**								
[86]	16a/32s	lDLPFC	rM1	0.0286	–	0.42 (−0.19, 1.02)	1.336	0.181
[87]	20	lDLPFC	rDLPFC	0.0429	–	0.33 (−0.30, 0.95)	1.026	0.305
				DL model		**0.37 (−0.06, 0.81)**	**1.673**	**0.094**
Neutral valence picture viewing – anode/online: **NEGATIVITY RATING (rDLPFC)**								
[87]	20	rDLPFC	lDLPFC	0.0429	–	0.33 (−0.30, 0.95)	1.026	0.305
[88]	23a/25s	rDLPFC	lORBIT	0.0429	–	−0.05 (−0.62, 0.52)	−0.175	0.861
				DL model		**0.12 (−0.30, 0.54)**	**0.560**	**0.575**
Gambling-based risk taking – anode/online: **RISK PROPENSITY**								
[35]	10	lDLPFC	rDLPFC	0.0571	MB	−2.95 (−4.22, −1.69)	−4.568	<0.001
[89]	12	lDLPFC	rDLPFC	0.0571	GT	0.58 (−0.24, 1.39)	1.385	0.166
[90]	16	lDLPFC	rDLPFC	?	GT	0.14 (−0.55, 0.84)	0.404	0.687
				DL model		**−0.67 (−2.39, 1.06)**	**−0.754**	**0.451**
Gambling-based risk taking – cathode/online: **RISK PROPENSITY**								
[35]	10	lDLPFC	rDLPFC	0.0571	MB	−3.38 (−4.74, −2.01)	−4.848	<0.001
[89]	12	lDLPFC	rDLPFC	0.0571	GT	−1.92 (−2.89, −0.96)	−3.895	<0.001
[90]	16	lDLPFC	rDLPFC	?	GT	0.00 (−0.69, 0.69)	0.000	1.000
				DL model		**−1.70 (−3.61, 0.22)**	**−1.738**	**0.082**
Rumination task – anode/offline: **SELF-RUMINATION INTENSITY**								
[91]	29a/33s	lDLPFC	rDLPFC	0.0571	–	0.07 (−0.43, 0.57)	0.282	0.778
[92]	32	lDLPFC	rORBIT	0.0571	–	−0.09 (−0.58, 0.40)	−0.364	0.716
				DL model		**−0.01 (−0.36, 0.34)**	**−0.063**	**0.950**

General notes: Active = Active electrode location; Ref = Reference electrode location; SMD = Standardized Mean Difference; A = Active; S = Sham; PAR = Parietal cortex; MULT = Multiplication task; SUB = Subtraction task; RT = Reaction time; DLPFC = Dorsolateral prefrontal cortex; MB = Monetary balloon analogue risk task; GT = Gambling Task.
Mental math: The value reported by [83] combined both RT and Accuracy – accordingly, the same value was used for both the accuracy and RT analyses. As the value represents an improvement following stimulation, it is represented as positive (higher score) in the accuracy analysis and negative (faster response) in the RT analysis.
Picture viewing: All sham participants were pooled for [86]. Two studies from [85] were omitted from analysis due to targeting M1 and V1, respectively (no comparable work elsewhere). Only the 'maintain' condition from [88]was analyzed.
Risk taking: Due to the unknown current density of [90], we analyzed using a DL model. Two studies from [35] were omitted for not including a sham condition.

comparing to a sham (control) condition. Of the 59 analyses undertaken, tDCS was not found to generate a significant effect on any. Taken together, the evidence does not support the assertion that a single-session of tDCS has a reliable effect on cognitive tasks in healthy adult populations.

A common criticism leveled at quantitative reviews concerns biased study selection: more specifically, through more- or less-stringent inclusion criteria, it is possible to skew analyses toward a positive result (for discussion, see: Ref. [96]). To address this issue, in this paper we undertook a two-tier analysis system. First we combined only those studies which demonstrated a direct replication of tDCS parametric values. The analysis was then expanded to combine all papers that targeted the same neural region and utilized the same task (regardless of current density and/or reference electrode location). Finally, in the case of memory, the analysis was further expanded to combine all papers that targeted the same neural region and utilized tasks thought to measure the same cognitive skill (e.g. – working memory). None of these analysis generated significant results. This suggests that the null results found in this paper are not likely the result of any specific sampling criteria (see Limitations section below).

One potential explanation for our findings rests in state-dependency: a concept which suggests that the effect an external stimulus exerts on the brain (and, by extension, cognition) is highly influenced by the state of the brain at the time of stimulus onset [97]. For instance, there is a large body of literature that demonstrates that the outcomes of single-, paired-, and repetitive-pulse TMS can be modulated according to the initial

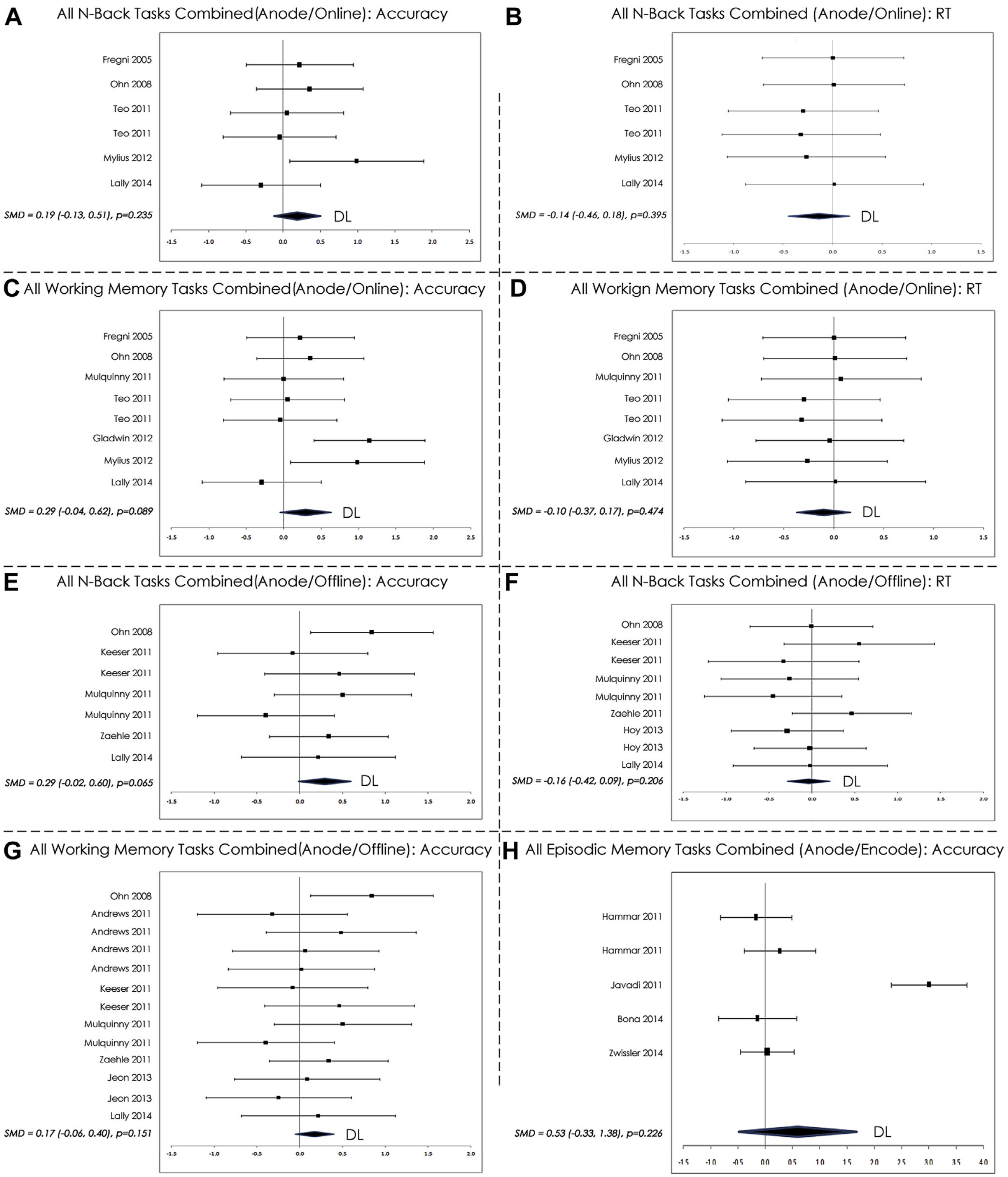

Figure 5. Forest plots for each pooled-task memory analysis (SMD = Standard mean difference; FE = Fixed effect model for primary analyses; DL = DerSimonian-Laird mixed-effect model for secondary analyses; Parentheses represent 95% CI).

cortical activation state of the targeted neural region (for review: Ref. [98]). Similarly, several studies have demonstrated that the effect of single-session tDCS on MEP amplitude can be negated following behavioral or cognitive priming [99,100] or reversed following neural priming using TMS [101]. Accordingly, it is likely that differential state-dependent effects between different studies included in this analysis influenced the null results obtained.

Luckily, state-dependent effects can be elucidated, controlled for, and possibly even leveraged to enhance the effects of tDCS; unfortunately, there is not enough comprehensive reporting in the literature to undertake such a synthesis at this point. It would be

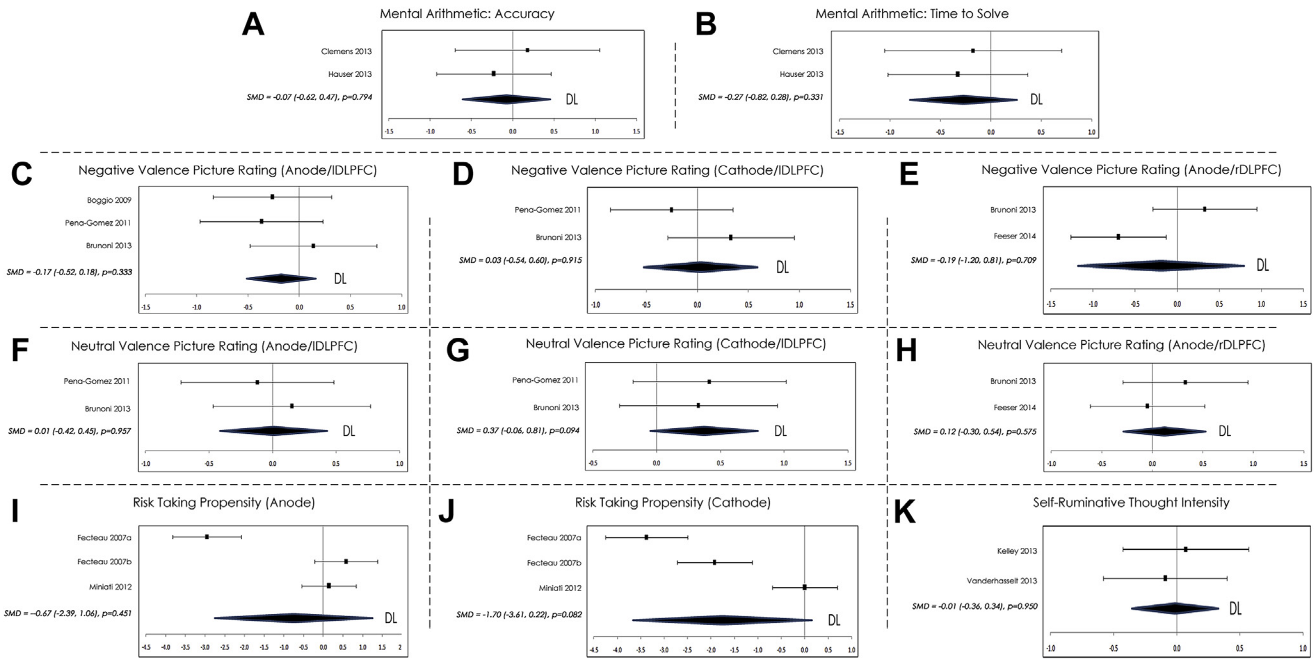

Figure 6. Forest plots for both secondary miscellaneous task analyses (SMD = Standard mean difference; FE = Fixed effect model for primary analyses; DL = DerSimonian-Laird mixed-effect model for secondary analyses; Parentheses represent 95% CI).

beneficial if future research included information concerning the time-of-day, day-of-week, duration, etc. of unique stimulation sessions and the satiation-levels, energy-levels, amount of sleep, etc. of individual participants. The inclusion of this information will not only allow for correlative and regression analyses to contextualize individual findings, but will also allow for more robust and meaningful quantitative pooling in the future.

Beyond methodological reporting, it is worth noting the relative lack of detailed data reporting in the literature. Though many studies explored for this analysis verbally reported a null finding on a particular measure, many did not offer quantitative or visual data amenable to pooling. This lack of data reporting has the undesirable effect of skewing quantitative analyses (such as this one). Accordingly, it would be beneficial if new studies included numerical data for all measures, even those with null results: only by doing so can more meaningful analyses take place in the future.

Limitations

A major limitation of this analysis is the lack of comparable research available in the current tDCS literature. Of the 50 cognitive outcome measures replicated between two different research groups included in this paper, 35 include only 2 or 3 papers. Accordingly, these analyses must be interpreted with caution. It is worth noting, however, that of these 35 outcome measures, 25 include papers report opposing effect sizes. This means > 70% of analyses which include only 2 or 3 papers contain at least 1 paper reporting enhancement and at least 1 paper reporting impairment following tDCS. As noted above, this may be due to varied state-dependency effects between different studies. Until more direct replication of older research is undertaken and more data are made available for pooling, it is difficult to conclude the true effect of this device.

Another limitation of this analysis concerns the population utilized. Although our results suggest tDCS has no reliable effect on cognitions in healthy adults, it remains to be seen whether or not tDCS can influence these measures in juvenile, elderly, or infirm populations. It is certainly possible that tDCS (known to be a relatively 'weak' form of modulation) simply does not work in a manner which can modulate a healthy, optimally performing brain (see: Ref. [102]). This does not preclude it from being able to modulate infirm, developing, or deteriorating brains. Additional analyses exploring the impact of tDCS in these populations are certainly warranted (examples of elderly population tDCS reviews: [103,104]; examples of infirm population tDCS meta-analyses: [105–107]).

This paper only explores cognitive measures undertaken during or following one session of tDCS. As noted in the results section, there are many studies which have utilized a multiple-day stimulation paradigm (e.g. Refs. [39,65,79,108]). It is wholly possible that several sessions of tDCS are required in order for a reliable effect to be seen. In this instance, it has been argued tDCS impacts cognition via repeated exposure and, possibly, overnight consolidation (see: Refs. [109,110]). Unfortunately, there simply are not enough comparable multiple-day stimulation studies conducted by two different research groups to assess if this is the case. As before, in order to determine the effect of repeated sessions of tDCS, more work directly replicating older research is required.

Conclusion

Taken together, we have found no evidence that single-session tDCS has a reliable effect on cognitions in healthy adult populations. When this is combined with our previous work which suggested tDCS does not have a reliable effect on neurophysiologic measures beyond MEP amplitude [1], it becomes difficult avoid questions of device efficacy. It is important to note, however, that these findings may be due to state-dependency effects which, with elucidation, can be controlled for and leveraged. In addition, our findings do not preclude the possibility that tDCS has an effect on different populations (juvenile, elderly, infirm), when utilized multiple-times over several days or weeks, or on behavioral tasks. Nor does this preclude the possibility that tDCS could be effective if utilized in a novel fashion (hi-definition tDCS, spinal tDCS, pulsed current tDCS, etc.). Despite this, as this field moves forward, it will be important future studies include measures which directly replicate prior work, explore potential state-dependent effects within and between studies, and report quantitative data for all explored outcome measures (so that a more clear picture of the state of the field can be derived).

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.brs.2015.01.400.

References

[1] Horvath JC, Forte JD, Carter O. Evidence that transcranial direct current stimulation (tDCS) generates little-to-no reliable neurophysiologic effect beyond MEP amplitude modulation in healthy human subjects: a systematic review. Neuropsychologia 2015;66:213–36.
[2] Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. J Physiol 2000;527(Pt 3):633–9.
[3] Stagg CJ, Nitsche MA. Physiological basis of transcranial direct current stimulation. Neuroscientist 2011;17(1):37–53.
[4] Elliott R. Executive functions and their disorders. Br Med Bull 2003;65:49–59.
[5] Kiesel A, Steinhauser M, Wendt M, et al. Control and interference in task switching—a review. Psychol Bull 2010;136(5):849–74.
[6] Verbruggen F, Logan GD. Response inhibition in the stop-signal paradigm. Trends Cogn Sci 2008;12(11):418–24.
[7] Macleod CM. Half a Century of research on the Stroop effect – an integrative review. Psychol Bull 1991;109(2):163–203.
[8] Evans V, Green M. Cognitive linguistics: an introduction. Edinburgh: Edinburgh University Press; 2006.
[9] Breitenstein C, Knecht S. Development and validation of a language learning model for behavioral and functional-imaging studies. J Neurosci Methods 2002;114(2):173–9.
[10] Johnson CJ, Paivio A, Clark JM. Cognitive components of picture naming. Psychol Bull 1996;120(1):113–39.
[11] Costafreda SG, Fu CH, Lee L, Everitt B, Brammer MJ, David AS. A systematic review and quantitative appraisal of fMRI studies of verbal fluency: role of the left inferior frontal gyrus. Hum Brain Mapp 2006;27(10):799–810.
[12] Anderson JR. Learning and memory. New Jersey: John Wiley & Sons, Inc; 2000.
[13] Conway AR, Kane MJ, Bunting MF, Hambrick DZ, Wilhelm O, Engle RW. Working memory span tasks: a methodological review and user's guide. Psychon Bull Rev 2005;12(5):769–86.
[14] Tulving E. Episodic memory: from mind to brain. Annu Rev Psychol 2002;53:1–25.
[15] Sternberg S. Memory-scanning: mental processes revealed by reaction-time experiments. Am Sci 1969;57(4):421–57.
[16] Kane MJ, Conway AR, Miura TK, Colflesh GJ. Working memory, attention control, and the N-back task: a question of construct validity. J Exp Psychol Learn Mem Cogn 2007;33(3):615–22.
[17] Ashcraft MH. Cognitive arithmetic: a review of data and theory. Cognition 1992;44(1–2):75–106.
[18] Olofsson JK, Nordin S, Sequeira H, Polich J. Affective picture processing: an integrative review of ERP findings. Biol Psychol 2008;77(3):247–65.
[19] Buelow MT, Suhr JA. Construct validity of the Iowa gambling task. Neuropsychol Rev 2009;19(1):102–14.
[20] Lejuez CW, Read JP, Kahler CW, et al. Evaluation of a behavioral measure of risk taking: the Balloon Analogue Risk Task (BART). J Exp Psychol Appl 2002;8(2):75–84.
[21] Smith JM, Alloy LB. A roadmap to rumination: a review of the definition, assessment, and conceptualization of this multifaceted construct. Clin Psychol Rev 2009;29(2):116–28.
[22] Gieryn TF. The ballad of Pons and Fleischmann: experiment and narrative in the (un)making of cold fusion. In: McMullin E, editor. The social dimensions of science. Indiana: University of Notre Dame Press; 1992.
[23] Mobley A, Linder SK, Braeuer R, Ellis LM, Zwelling L. A survey on data reproducibility in cancer research provides insights into our limited ability to translate findings from the laboratory to the clinic. PLoS One 2013;8(5):e63221.
[24] Osherovich L. Doubts about tragretin in AD. SciBX 2013;6(21).
[25] Leite J, Carvalho S, Fregni F, Gonçalves OF. Task-specific effects of tDCS-induced cortical excitability changes on cognitive and motor sequence set shifting performance. PLoS One 2011;6(9):e24140.
[26] Plewnia C, Zwissler B, Längst I, Maurer B, Giel K, Krüger R. Effects of transcranial direct current stimulation (tDCS) on executive functions: influence of COMT Val/Met polymorphism. Cortex 2013;49(7):1801–7.
[27] Jacobson L, Javitt DC, Lavidor M. Activation of inhibition: diminishing impulsive behavior by direct current stimulation over the inferior frontal gyrus. J Cogn Neurosci 2011;23(11):3380–7.
[28] Ditye T, Jacobson L, Walsh V, Lavidor M. Modulating behavioral inhibition by tDCS combined with cognitive training. Exp Brain Res 2012;219(3):363–8.
[29] Leite J, Carvalho S, Fregni F, Boggio PS, Gonçalves ÓF. The effects of cross-hemispheric dorsolateral prefrontal cortex transcranial direct current stimulation (tDCS) on task switching. Brain Stimul 2013;6(4):660–7.
[30] Kwon JW, Nam SH, Lee NK, Son SM, Choi YW, Kim CS. The effect of transcranial direct current stimulation on the motor suppression in stop-signal task. NeuroRehabilitation 2013;32(1):191–6.
[31] Reinhart RM, Woodman GF. Causal control of medial-frontal cortex governs electrophysiological and behavioral indices of performance monitoring and learning. J Neurosci 2014;34(12):4214–27.
[32] Hsu TY, Tseng LY, Yu JX, Kuo WJ. Modulating inhibitory control with direct current stimulation of the superior medial frontal cortex. Neuroimage 2011;56(4):2249–57.
[33] Kwon YH, Kwon JW. Response inhibition induced in the stop-signal task by transcranial direct current stimulation of the pre-supplementary motor area and primary sensoriomotor cortex. J Phys Ther Sci 2013;25(9):1083–6.
[34] Liang WK, Lo MT, Yang AC, et al. Revealing the brain's adaptability and the transcranial direct current stimulation facilitating effect in inhibitory control by multiscale entropy. Neuroimage 2014;90:218–34.
[35] Fecteau S, Pascual-Leone A, Zald DH, et al. Activation of prefrontal cortex by transcranial direct current stimulation reduces appetite for risk during ambiguous decision making. J Neurosci 2007;27(23):6212–8.
[36] Fecteau S, Boggio P, Fregni F, Pascual-Leone A. Modulation of untruthful responses with non-invasive brain stimulation. Front Psychiatry 2013;3:97.
[37] Jeon SY, Han SJ. Improvement of the working memory and naming by transcranial direct current stimulation. Ann Rehabil Med 2012;36(5):585–95.
[38] Kadosh RC, Soskic S, Iuculano T, Kanai R, Walsh V. Modulating neuronal activity produces specific and long-lasting changes in numerical competence. Curr Biol 2010;20(22):2016–20.
[39] Richmond L, Wolk D, Chein J, Olson IR. Transcranial direct current stimulation enhances verbal working memory training performance over time and near-transfer outcomes. J Cogn Neurosci 2014;26(11):2443–54.
[40] Floel A, Rösser N, Michka O, Knecht S, Breitenstein C. Noninvasive brain stimulation improves language learning. J Cogn Neurosci 2008;20(8):1415–22.
[41] Fiori V, Coccia M, Marinelli CV, et al. Transcranial direct current stimulation improves word retrieval in healthy and nonfluent aphasic subjects. J Cogn Neurosci 2011;23(9):2309–23.
[42] Fertonani A, Rosini S, Cotelli M, Rossini PM, Miniussi C. Naming facilitation induced by transcranial direct current stimulation. Behav Brain Res 2010;208(2):311–8.
[43] Wirth M, Rahman RA, Kuenecke J, et al. Effects of transcranial direct current stimulation (tDCS) on behaviour and electrophysiology of language production. Neuropsychologia 2011;49(14):3989–98.
[44] Cerruti C, Schlaug G. Anodal transcranial direct current stimulation of the prefrontal cortex enhances complex verbal associative thought. J Cogn Neurosci 2009;21(10):1980–7.
[45] Cattaneo Z, Pisoni A, Papagno C. Transcranial direct current stimulation over Broca's region improves phonemic and semantic fluency in healthy individuals. Neuroscience 2011;183:64–70.
[46] Penolazzi B, Pastore M, Mondini S. Electrode montage dependent effects of transcranial direct current stimulation on semantic fluency. Behav Brain Res 2013;248:129–35.
[47] Meinzer M, Lindenberg R, Antonenko D, Flaisch T, Flöel A. Anodal transcranial direct current stimulation temporarily reverses age-associated cognitive decline and functional brain activity changes. J Neurosci 2013;33(30):12470–8.
[48] Vannorsdall TD, Schretlen DJ, Andrejczuk M, et al. Altering automatic verbal processes with transcranial direct current stimulation. Front Psychiatry 2012;3:73.
[49] Sparing R, Dafotakis M, Meister IG, Thirugnanasambandam N, Fink GR. Enhancing language performance with non-invasive brain stimulation—a transcranial direct current stimulation study in healthy humans. Neuropsychologia 2008;46(1):261–8.
[50] Ross LA, McCoy D, Wolk DA, Coslett HB, Olson IR. Improved proper name recall by electrical stimulation of the anterior temporal lobes. Neuropsychologia 2010;48(12):3671–4.
[51] Meinzer M, Antonenko D, Lindenberg R, et al. Electrical brain stimulation improves cognitive performance by modulating functional connectivity and task-specific activation. J Neurosci 2012;32(5):1859–66.
[52] Andrews SC, Hoy KE, Enticott PG, Daskalakis ZJ, Fitzgerald PB. Improving working memory: the effect of combining cognitive activity and anodal transcranial direct current stimulation to the left dorsolateral prefrontal cortex. Brain Stimul 2011;4(2):84–9.
[53] Mulquiney PG, Hoy KE, Daskalakis ZJ, Fitzgerald PB. Improving working memory: exploring the effect of transcranial random noise stimulation and transcranial direct current stimulation on the dorsolateral prefrontal cortex. Clin Neurophysiol 2011;122(12):2384–9.
[54] Gladwin TE, den Uyl TE, Wiers RW. Anodal tDCS of dorsolateral prefontal cortex during an implicit association test. Neurosci Lett 2012;517(2):82–6.

[55] Berryhill ME, Wencil EB, Coslett HB, Olson IR. A selective working memory impairment after transcranial direct current stimulation to the right parietal lobe. Neurosci Lett 2010;479(3):312–6.
[56] Jones KT, Berryhill ME. Parietal contributions to visual working memory depend on task difficulty. Front Psychiatry 2012;3:81.
[57] Tseng P, Hsu TY, Chang CF, et al. Unleashing potential: transcranial direct current stimulation over the right posterior parietal cortex improves change detection in low-performing individuals. J Neurosci 2012;32(31):10554–61.
[58] Hsu TY, Tseng P, Liang WK, Cheng SK, Juan CH. Transcranial direct current stimulation over right posterior parietal cortex changes prestimulus alpha oscillation in visual short-term memory task. Neuroimage 2014;98:306–13.
[59] Tanoue RT, Jones KT, Peterson DJ, Berryhill ME. Differential frontal involvement in shifts of internal and perceptual attention. Brain Stimul 2013;6(4):675–82.
[60] Hoy KE, Emonson MR, Arnold SL, Thomson RH, Daskalakis ZJ, Fitzgerald PB. Testing the limits: investigating the effect of tDCS dose on working memory enhancement in healthy controls. Neuropsychologia 2013;51(9):1777–84.
[61] Keeser D, Padberg F, Reisinger E, et al. Prefrontal direct current stimulation modulates resting EEG and event-related potentials in healthy subjects: a standardized low resolution tomography (sLORETA) study. Neuroimage 2011;55(2):644–57.
[62] Fregni F, Boggio PS, Nitsche M, et al. Anodal transcranial direct current stimulation of prefrontal cortex enhances working memory. Exp Brain Res 2005;166(1):23–30.
[63] Teo F, Hoy KE, Daskalakis ZJ, Fitzgerald PB. Investigating the role of current strength in tDCS modulation of working memory performance in healthy controls. Front Psychiatry 2011;2:45.
[64] Ohn SH, Park CI, Yoo WK, et al. Time-dependent effect of transcranial direct current stimulation on the enhancement of working memory. Neuroreport 2008;19(1):43–7.
[65] Martin DM, Liu R, Alonzo A, et al. Can transcranial direct current stimulation enhance outcomes from cognitive training? A randomized controlled trial in healthy participants. Int J Neuropsychopharmacol 2013;16(9):1927–36.
[66] Ferrucci R, Marceglia S, Vergari M, et al. Cerebellar transcranial direct current stimulation impairs the practice-dependent proficiency increase in working memory. J Cogn Neurosci 2008;20(9):1687–97.
[67] Macher K, Böhringer A, Villringer A, Pleger B. Cerebellar-parietal connections underpin phonological storage. J Neurosci 2014;34(14):5029–37.
[68] Hammer A, Mohammadi B, Schmicker M, Saliger S, Münte TF. Errorless and errorful learning modulated by transcranial direct current stimulation. BMC Neurosci 2011;12:72.
[69] Javadi AH, Walsh V. Transcranial direct current stimulation (tDCS) of the left dorsolateral prefrontal cortex modulates declarative memory. Brain Stimul 2012;5(3):231–41.
[70] Bona S, Silvanto J. Accuracy and confidence of visual short-term memory do not go hand-in-hand: behavioral and neural dissociations. PLoS One 2014;9(3):e90808.
[71] Zwissler B, Sperber C, Aigeldinger S, Schindler S, Kissler J, Plewnia C. Shaping memory accuracy by left prefrontal transcranial direct current stimulation. J Neurosci 2014;34(11):4022–6.
[72] Chi RP, Fregni F, Snyder AW. Visual memory improved by non-invasive brain stimulation. Brain Res 2010;1353:168–75.
[73] Schaal NK, Krause V, Lange K, Banissy MJ, VJWilliamson. Pitch memory in nonmusicians and musicians: revealing functional differences using transcranial direct current stimulation. Cereb Cortex 2014.
[74] Heimrath K, Sandmann P, Becke A, Müller NG, Zaehle T. Behavioral and electrophysiological effects of transcranial direct current stimulation of the parietal cortex in a visuo-spatial working memory task. Front Psychiatry 2012;3:56.
[75] Moos K, Vossel S, Weidner R, Sparing R, Fink GR. Modulation of top-down control of visual attention by cathodal tDCS over right IPS. J Neurosci 2012;32(46):16360–8.
[76] Zaehle T, Sandmann P, Thorne JD, Jäncke L, Herrmann CS. Transcranial direct current stimulation of the prefrontal cortex modulates working memory performance: combined behavioural and electrophysiological evidence. BMC Neurosci 2011;12:2.
[77] Lally N, Nord CL, Walsh V, Roiser JP. Does excitatory fronto-extracerebral tDCS lead to improved working memory performance? F1000Res 2013;2:219.
[78] Javadi AH, Cheng P, Walsh V. Short duration transcranial direct current stimulation (tDCS) modulates verbal memory. Brain Stimul 2012;5(4):468–74.
[79] Gomes-Osman J, Field-Fote EC. Bihemispheric anodal corticomotor stimulation using transcranial direct current stimulation improves bimanual typing task performance. J Mot Behav 2013;45(4):361–7.
[80] Motohashi N, Yamaguchi M, Fujii T, Kitahara Y. Mood and cognitive function following repeated transcranial direct current stimulation in healthy volunteers: a preliminary report. Neurosci Res 2013;77(1–2):64–9.
[81] Bolognini N, Fregni F, Casati C, Olgiati E, Vallar G. Brain polarization of parietal cortex augments training-induced improvement of visual exploratory and attentional skills. Brain Res 2010;1349:76–89.
[82] Manenti R, Brambilla M, Petesi M, Ferrari C, Cotelli M. Enhancing verbal episodic memory in older and young subjects after non-invasive brain stimulation. Front Aging Neurosci 2013;5:49.
[83] Clemens B, Jung S, Zvyagintsev M, Domahs F, Willmes K. Modulating arithmetic fact retrieval: a single-blind, sham-controlled tDCS study with repeated fMRI measurements. Neuropsychologia 2013;51(7):1279–86.
[84] Hauser TU, Rotzer S, Grabner RH, Mérillat S, Jäncke L. Enhancing performance in numerical magnitude processing and mental arithmetic using transcranial direct current stimulation (tDCS). Front Hum Neurosci 2013;7:244.
[85] Boggio PS, Zaghi S, Fregni F. Modulation of emotions associated with images of human pain using anodal transcranial direct current stimulation (tDCS). Neuropsychologia 2009;47(1):212–7.
[86] Pena-Gomez C, Vidal-Piñeiro D, Clemente IC, Pascual-Leone Á, Bartrés-Faz D. Down-regulation of negative emotional processing by transcranial direct current stimulation: effects of personality characteristics. PLoS One 2011;6(7):e22812.
[87] Brunoni AR, Vanderhasselt MA, Boggio PS, et al. Polarity- and valence-dependent effects of prefrontal transcranial direct current stimulation on heart rate variability and salivary cortisol. Psychoneuroendocrinology 2013;38(1):58–66.
[88] Feeser M, Prehn K, Kazzer P, Mungee A, Bajbouj M. Transcranial direct current stimulation enhances cognitive control during emotion regulation. Brain Stimul 2014;7(1):105–12.
[89] Fecteau S, Knoch D, Fregni F, Sultani N, Boggio P, Pascual-Leone A. Diminishing risk-taking behavior by modulating activity in the prefrontal cortex: a direct current stimulation study. J Neurosci 2007;27(46):12500–5.
[90] Minati L, Campanha C, Critchley HD, Boggio PS. Effects of transcranial direct-current stimulation (tDCS) of the dorsolateral prefrontal cortex (DLPFC) during a mixed-gambling risky decision-making task. Cogn Neurosci 2012;3(2):80–8.
[91] Kelley NJ, Hortensius R, Harmon-Jones E. When anger leads to rumination: induction of relative right frontal cortical activity with transcranial direct current stimulation increases anger-related rumination. Psychol Sci 2013;24(4):475–81.
[92] Vanderhasselt MA, Brunoni AR, Loeys T, Boggio PS, De Raedt R. Nosce te ipsum–Socrates revisited? Controlling momentary ruminative self-referent thoughts by neuromodulation of emotional working memory. Neuropsychologia 2013;51(13):2581–9.
[93] Kasahara K, Tanaka S, Hanakawa T, Senoo A, Honda M. Lateralization of activity in the parietal cortex predicts the effectiveness of bilateral transcranial direct current stimulation on performance of a mental calculation task. Neurosci Lett 2013;545:86–90.
[94] Maeoka H, Matsuo A, Hiyamizu M, Morioka S, Ando H. Influence of transcranial direct current stimulation of the dorsolateral prefrontal cortex on pain related emotions: a study using electroencephalographic power spectrum analysis. Neurosci Lett 2012;512(1):12–6.
[95] Weber MJ, Messing SB, Rao H, Detre JA, Thompson-Schill SL. Prefrontal transcranial direct current stimulation alters activation and connectivity in cortical and subcortical reward systems: a tDCS-fMRI study. Hum Brain Mapp 2014;35(8):3673–86.
[96] Walker E, Hernandez AV, Kattan MW. Meta-analysis: Its strengths and limitations. Cleve Clin J Med 2008;75(6):431–9.
[97] Silvanto J, Muggleton N, Walsh V. State-dependency in brain stimulation studies of perception and cognition. Trends Cogn Sci 2008;12(12):447–54.
[98] Silvanto J, Pascual-Leone A. State-dependency of transcranial magnetic stimulation. Brain Topogr 2008;21(1):1–10.
[99] Quartarone A, Morgante F, Bagnato S, et al. Long lasting effects of transcranial direct current stimulation on motor imagery. Neuroreport 2004;15(8):1287–91.
[100] Antal A, Terney D, Poreisz C, Paulus W. Towards unravelling task-related modulations of neuroplastic changes induced in the human motor cortex. Eur J Neurosci 2007;26(9):2687–91.
[101] Lang N, Siebner HR, Ernst D, et al. Preconditioning with transcranial direct current stimulation sensitizes the motor cortex to rapid-rate transcranial magnetic stimulation and controls the direction of after-effects. Biol Psychiatry 2004;56(9):634–9.
[102] Batsikadze G, Moliadze V, Paulus W, et al. Partially non-linear stimulation intensity-dependent effects of direct current stimulation on motor cortex excitability in humans. J Physiol 2013;591(Pt 7):1987–2000.
[103] Rosenberg O, Shoenfeld N, Kotler M, Dannon PN. Mood disorders in elderly population: neurostimulative treatment possibilities. Recent Pat CNS Drug Discov 2009;4(2):149–59.
[104] Berryhill ME, Jones KT. tDCS selectively improves working memory in older adults with more education. Neurosci Lett 2012;521(2):148–51.
[105] Kalu UG, Sexton CE, Loo CK, Ebmeier KP. Transcranial direct current stimulation in the treatment of major depression: a meta-analysis. Psychol Med 2012;42(9):1791–800.
[106] Lima MC, Fregni F. Motor cortex stimulation for chronic pain: systematic review and meta-analysis of the literature. Neurology 2008;70(24):2329–37.
[107] Butler AJ, Shuster M, O'Hara E, Hurley K, Middlebrooks D, Guilkey K. A meta-analysis of the efficacy of anodal transcranial direct current stimulation for upper limb motor recovery in stroke survivors. J Hand Ther 2013;26(2):162–70. quiz 171.
[108] Schambra HM, Abe M, Luckenbaugh DA, Reis J, Krakauer JW, Cohen LG. Probing for hemispheric specialization for motor skill learning: a transcranial direct current stimulation study. J Neurophysiol 2011;106(2):652–61.
[109] Marshall L, Kirov R, Brade J, Mölle M, Born J. Transcranial electrical currents to probe EEG brain rhythms and memory consolidation during sleep in humans. PLoS One 2011;6(2):e16905.
[110] Reis J, Schambra HM, Cohen LG, et al. Noninvasive cortical stimulation enhances motor skill acquisition over multiple days through an effect on consolidation. Proc Natl Acad Sci U S A 2009;106(5):1590–5.