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Review article

# Transcranial direct current stimulation (tDCS) modulation of picture naming and word reading: A meta-analysis of single session tDCS applied to healthy participants

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## ABSTRACT

Recent reviews quantifying the effects of single sessions of transcranial direct current stimulation (or tDCS) in healthy volunteers find only minor effects on cognition despite the popularity of this technique. Here, we wanted to quantify the effects of tDCS on language production tasks that measure word reading and picture naming. We reviewed 14 papers measuring tDCS effects across a total of 96 conditions to a) quantify effects of conventional stimulation on language regions (i.e., left hemisphere anodal tDCS administered to temporal/frontal areas) under normal conditions or under conditions of cognitive (semantic) interference; b) identify parameters which may moderate the size of the tDCS effect within conventional stimulation protocols (e.g., online vs offline, high vs. low current densities, and short vs. long durations), as well as within types of stimulation on typically explored by previous reviews (i.e., right hemisphere anodal tDCS or left/right hemisphere cathodal tDCS). In all analyses there was no significant effect of tDCS, but we did find a small but significant effect of time and duration of stimulation with stronger effects for offline stimulation and for shorter durations (< 15 min). We also found some indication of publication bias towards reporting positive effects. We encourage further experimentation in order resolve the disparity between the current popularity of tDCS and its poor efficacy in healthy participants.

## 1. Introduction

Transcranial direct current stimulation (or tDCS) is a popular technique used to modulate cortical excitability via a weak electric current applied on the scalp. The technique is used widely across studies aiming to enhance cognitive functions, with its popularity rising sharply in recent years. According to PubMed, only a few dozen papers were published in the early 2000s, but several thousand have been published in the past ten years, many of which report positive gains on a variety of cognitive tasks. However, a growing number of researchers are calling for the re-evaluation of tDCS in healthy samples because of weak and inconsistent effects (see Underwood, 2016; Walsh, 2013; Horvath et al., 2015a) and broader concerns about the reproducibility of results in neuroscience (see Open Collaboration, 2015; see also Cumming, 2013; Ioannidis, 2005). Here, we carried out several metaanalyses to assess whether single sessions of tDCS can reliably modify performance on language tasks in healthy participants, an area which has received less attention by previous reviews.

Horvath et al. (2015a) were the first to conduct a quantitative review which indicated little – if any – evidence of significant *cognitive*  effects with single sessions of tDCS in healthy participants. Null effects were reported across polarities (anodal or cathodal), cognitive domains (executive functions, language, visual and verbal memory, and miscellaneous higher-cognitive functions), and stimulated areas in the left and right hemisphere (e.g., frontal, temporal, motor and parietal regions). In a second quantitative review of neurophysiological effects (Horvath et al., 2015b), tDCS was only effective in modifying motor evoked potentials (MEPs or muscular 'twitches'). However, these reviews have been criticised for their restrictive inclusion criteria (see Price and Hamilton, 2015). For the cognitive review, to reduce the effects of idiosyncratic stimulation protocols, the authors excluded outcome measures that were not reported by two or more separate labs, which narrowed the number of eligible studies. Unfortunately, this meant many analyses - particularly those including language experiments - pooled just two or three studies to fit the varying degrees of stringency for each analysis (e.g., by outcome measure, by polarity, by stimulation timing). Nonetheless, across all 59 analyses, of which 12 pooled more than 5 studies, no significant results in favour of tDCS were found.

In a meta-analysis, Jacobson et al. (2012) attempted to verify the

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assumption that anodal (or excitatory) tDCS versus cathodal (or inhibitory) tDCS leads to respective improvement versus impairment in performance - an assumption that underpins nearly all cognitive studies using tDCS. The authors found that 81% and 47% of cognitive studies (n = 34) showed, respectively, the expected anodal related improvement and cathodal related impairment across a variety of tasks, including attention, working memory and language. However, this review pooled data from healthy and patient samples. Moreover, the authors were interested in the reliability of outcomes with anodal and cathodal tDCS, rather than an effect of tDCS per se. Therefore, they excluded null results, results that contradicted the anodal-enhancement versus cathodal-impairment assumption, and reported only the largest effects when multiple effects were reported by a study. This meant that of the 4 included studies measuring effects of tDCS on language production with healthy volunteers, 3 reported positive effects of tDCS. This, however, masked the fact that 26 negative effects were excluded.

Other meta-analyses with healthy participants focusing largely on working memory/short-term memory tasks (WM/STM) reported equally weak and/or inconsistent effects. Hill et al. (2016) found small but positive effects on both accuracy and reaction times across *n*-back, span and Sternberg tasks, while other studies found positive effects only in reaction times (Brunoni and Vanderhasselt, 2014; Dedoncker et al., 2016). Importantly, a comprehensive review by Mancuso et al. (2016) found positive results were limited to studies using training paradigms – e.g., where performance on a WM task (e.g., *n*-back) was assessed after practicing the same task or a different WM task (e.g., *Sternberg*) under stimulation.

We know of only one published review that has focused on an effect of tDCS on language tasks in healthy participants. Price et al. (2015) reviewed studies involving verbal fluency (n = 6) and word learning (n = 6)2). Anodal tDCS improved accuracy scores significantly when pooling: a) all studies together; b) four studies where tDCS was applied prior to the task (i.e., offline stimulation) or c) three studies measuring offline tDCS with verbal fluency. However, effects were small to moderate in size (roughly  $\sim$  0.5), and significant outcomes appeared to rely on the exceptionally large effect sizes from one study measuring fluency (~ 1.2, Cattaneo et al., 2011) and one measuring word learning (~ 0.8, Flöel et al., 2008). Furthermore, what is worse, one of these studies has proven difficult to replicate (i.e., Cattaneo et al., 2011; see Penolazzi et al., 2013; Vannorsdall et al., 2016; but also Cattaneo et al., 2016 for response). Horvath (2015) also pointed out that the offline effect for fluency tasks would become non-significant if some data from studies excluded by the authors were instead included and if some mistakes in effect sizes estimates were corrected.

Our review will examine effects of tDCS in picture naming and word reading. Several reasons have informed our choice.

- Reading and naming are widely considered to be good indicators of language competence. Moreover, although these tasks require different levels of processing (semantic, phonological/orthographic, articulatory) there is strong consensus that all these processes are based on relatively limited, frontal and temporal regions in the left hemisphere, which gives us confidence for what stimulation sites to focus on (see Indefrey, 2011; Indefrey and Levelt, 2004; Price, 2000).
- These tasks tap resources such as semantic memory, executive functions, and working memory which are used beyond language tasks making naming and reading good proxies for the general effectiveness of tDCS for other cognitive functions (Badre and D'Esposito, 2009; Binder et al., 2009).
- 3. Studies using naming and reading have reported significant effects of tDCS, but consistent effects have been limited to individuals with language impairments following a stroke. For example, tDCS has been found to facilitate speech and language therapy for word finding difficulties in aphasic patients (see Cappon et al., 2016; de Aguiar et al., 2015; Monti et al., 2013; Crinion, 2016; Elsner et al.,

2015; Sandars et al., 2016; Shah-Basak et al., 2015). The same facilitation may also occur with single application in healthy participants, but this remains to be established.

4. Finally, language production, and picture naming in particular, may be a good task to assess the interplay between the neurophysiological effects of tDCS and levels of cortical excitability.

The poor reliability of tDCS may be explained by differences in stimulation parameters across studies (for further discussion, see Antal et al., 2015; Horvath et al., 2016; Nitsche et al., 2015), but also by differences in baseline levels of cortical activity (see Miniussi et al., 2013). This is in part demonstrated by the generally positive effects of tDCS in brain-damaged patients, such as patients with aphasia, which contrasts with the unreliable effects in healthy samples. Following brain damage, levels of cortical excitability may become excessively low or dysfunctional compared to the optimal levels seen in healthy brains, and tDCS may help to change activation towards more optimal levels (for a similar argument, see de Aguiar et al., 2015; Miniussi et al., 2013). Furthermore, several studies with healthy participants have shown that higher baseline levels of cortical excitability can abolish the beneficial effect of anodal tDCS on task performance (see Hsu et al., 2014; Tseng et al., 2012; Berryhill et al., 2014).

Picture naming may be a good task to examine the effects of tDCS in conditions with high levels cortical excitability because this may be approximated in conditions of high semantic interference. Picture naming necessitates cortical excitation - for word retrieval - but also inhibition - for fending off competition from alternatives (for similar argument, see Miniussi et al., 2013). Moreover, the relative need of activation and selection can be manipulated by repeated presentation of semantically related pictures, which raises the general level of activation in the lexical system while, at the same time, increasing the demand on selection. Different paradigms have been used to increase semantic interference effects, such as asking participants to name a picture when a semantically related word is present (as in picture-word interference; Mahon et al., 2007), repeatedly name sets of semantically related pictures versus unrelated pictures (as in cyclic blocked naming; for review, see Belke and Stielow, 2013), or name sets of semantically related pictures intermixed with filler items (as in continuous naming; Howard et al., 2006; Belke, 2013). In this last paradigm, for example, performance deteriorates progressively with each position of a picture in the sequence, showing the negative effects of semantic interference. Several studies have examined whether tDCS modulates these semantic interference effects (see Henseler et al., 2014; Meinzer et al., 2016; Pisoni et al., 2012; Westwood et al., 2017; Wirth et al., 2011). It has been suggested that while the excitatory effects of anodal tDCS may be generally facilitatory when applied to left frontal regions because selection abilities are boosted, when applied to temporal stimulation it may further boost activation of semantically related competitors, thereby increasing interference effects (see Pisoni et al., 2012; see also Canini et al., 2016). Finding whether tDCS modulates semantic interference will indicate whether tDCS interacts with task-induced cortical activation as well as provide evidence on the nature of interference effects.

Our review will attempt to answer the following questions:

- 1) Is there a general effect of anodal tDCS targeting key language areas in the left hemisphere? Most studies investigating language production effects apply anodal tDCS to the left frontal or temporal regions, a protocol which is assumed to give the best chances to elicit a positive effect (see Jacobson et al., 2012, for example). Therefore, we will refer to this stimulation protocol as 'conventional' and examine its effect in our *Primary Analysis*.
- 2) Is the size of the tDCS effect influenced by certain parameters? Our **Moderator Analysis**, therefore, assessed the impact of tDCS parameters including *Timing* (i.e., if tDCS was applied before or during task performance), *Current Density* (e.g., high vs low; .28 vs. ≥

0.057 cm/mA<sup>2</sup>), and *Duration* (e.g., short vs long; < 15 vs.  $\geq$  20 min) within conventional stimulation protocols.

- 3) Is there an effect of tDCS in protocols which are not typical of the field? Our **Secondary Analysis** considered the effectiveness of cathodal tDCS applied to either hemisphere and anodal tDCS applied to the right hemisphere.
- 4) Is there an effect of tDCS in conditions of increased task difficulty? Finally, the effects of anodal tDCS may be particularly evident in conditions where naming is made more difficult by the presence of competitors (possibly with the consequence of higher cortical excitation). Our *Semantic Interference Analysis*, therefore, considered the effect of anodal tDCS in tasks that induce semantic interference effects, where greater effort is needed for selection and control.

#### 2. Method

### 2.1. Data sampling

#### 2.1.1. Eligibility criteria

Papers were included if they: a) tested healthy adult volunteers (between 18- and 60-years of age); b) included a sham control condition; c) were published in English; d) provided details of method/protocol; e) measured picture naming or word reading reaction times and/ or accuracy (given in percentage errors; or other types of accuracy scores); and f) used conventional tDCS protocols (i.e., current administered continuously via a two electrode configuration). Since the effects of tDCS are known to accumulate with repeated applications (Alonzo et al., 2012; Meinzer et al., 2014), we did not include studies that applied tDCS more than once to the same cortical site with the same stimulation polarity (e.g., anodal tDCS applied over multiple days or within an hour following the first application), unless we could extract data from just the first application. Our eligibility criteria were similar to previous reviews (e.g., Mancuso et al., 2016; Price et al., 2015), but likewise broader than those used by reviews targeting studies across more diverse cognitive domains (Horvath et al., 2015a; Jacobson et al., 2012).

#### 2.1.2. Literature search

We searched Science Direct, Web of Knowledge and PubMed databases (from 1999 to early August 2016) using as search keywords: 'tDCS' or 'transcranial direct current stimulation' in combination with 'language', 'verbal', 'linguistic', 'word production', 'naming', 'reading', and 'cognition'. We searched for further articles using the Web of Knowledge citation tracking tool, which displays articles referenced within a given article and articles that cite the article of interest. The initial search returned 3254 articles of which 2635 were removed right away as non-relevant. The text of the remaining 619 papers was read, including papers testing neurologically impaired individuals in case healthy controls were tested. This excluded 598 studies because naming or reading abilities were not measured in healthy participants, leaving 22 articles. Of these, 3 studies targeting reading were further removed because: a) recruited children and adolescents (Costanzo et al., 2016), b) did not include a sham group (Thomson et al., 2015), and c) applied tDCS repeatedly but did not report data from the first application (Heth and Lavidor, 2015). Five studies targeting picture naming were also removed because: a) recruited participants were older than 60-years of age (Ross et al., 2011; Rosso et al., 2013; Holland et al., 2011, 2016), and b) collapsed data across two conditions in which tDCS targeted separate cortical regions (Manenti et al., 2013). This left us with a final sample of 14 papers, some of which reported multiple tDCS conditions (total n = 96; within-participants, n = 86, between-participants, n =10; see Appendix A and B for details on included studies).

#### 2.1.3. Data extraction

We extracted means and standard deviations for reaction times and accuracy rates (percentage errors or other accuracy scores) for all tDCS and sham conditions reported. A java program called Plot Digitizer (Joseph, 2011) was used to convert plotted values into a numerical form if numerical values were not reported by a study (for applications of this method, see Hill et al., 2016; Vaseghi et al., 2015). If no data was reported or could not be extracted, the authors were contacted.

## 2.2. Data analysis

#### 2.2.1. Direction of the tDCS effect

As with other reviews, we quantified an effect of tDCS based on the difference in performance between tDCS and sham conditions using a standardized measure of effect size: a difference between tDCS and sham conditions divided by a measure of variability to standardize the effect (see later for details). In line with the majority of tDCS studies measuring effects on cognition, our general hypothesis was that anodal tDCS of the left hemisphere would enhance whilst cathodal tDCS of the left hemisphere would impair performance. When determining the direction of the effect, we reported effects as positive if consistent with these predictions, and negative otherwise.

Note that our Primary analysis still included studies which looked at semantic interference in picture naming. Here, however, we did not consider effects of tDCS on interference, but on picture naming in general (i.e., across conditions; effects on interference have been looked at separately in our Semantic Interference analysis). Some studies predicted a paradoxical inhibitory effect for anodal tDCS when applied to the temporal lobes - an area involved in lexical activation - in conditions of high interference. The rationale being that, in conditions with semantic distractors, anodal tDCS would boost the activation of competing alternatives as well as the target, thus making selection more difficult (see Henseler et al., 2014; Pisoni et al., 2012). This prediction, however, has been confirmed only by one study (Pisoni et al., 2012), with other studies reporting opposite outcomes (Meinzer et al., 2016) or no effect at all (Henseler et al., 2014; Westwood et al., 2017). Thus, when we included studies measuring interference in our Primary analyses, we coded effects in line with our general prediction that anodal tDCS should improve whilst cathodal tDCS should impair performance. In our Semantic Interference analysis we looked separately at the effects for temporal and frontal tDCS. Anticipating our results, we did not detect differences by site of stimulation, thus supporting our choice of coding.

Our Secondary analysis wanted to investigate other less commonly used tDCS protocols. Here, we included studies that applied anodal tDCS to the right hemisphere (see Jeon and Han, 2012; Ross et al., 2010; Younger et al., 2016). Given the inhibitory relationship between left and right hemispheres (Chiarello and Maxfield, 1996; Thiel et al., 2006a, 2006b; Vines et al., 2008), we expected that, compared to sham, right-hemisphere anodal tDCS would inhibit (and thus impair) language capacities located in the left hemisphere (for a similar prediction, see Hamilton et al., 2011, Hartwigsen et al., 2010). Thus, we coded as positive results consistent with this outcome; negative otherwise. Other included studies applied tDCS of either polarity to the cerebellum (see Boehringer et al., 2013; Pope and Miall, 2012). Because cerebellar nuclei are thought to inhibit frontal regions, some authors argue that the excitatory effects of anodal tDCS would impair performance on frontally mediated tasks, and vice versa for cathodal tDCS (for a similar prediction, see review by van Dun et al., 2016; and a study included in our review, Pope and Miall, 2012).<sup>1</sup> Thus, we coded as positive results consistent with the paradoxical anodal impair versus cathodal improve outcome for studies targeting the cerebellum.

 $<sup>^1</sup>$  Note, we note that one included study by Boehringer et al. (2013) predicted a cathodal-inhibition effect. However, because the effect was zero overall the sign for this effect has no impact on the analysis.

#### 2.2.2. Effects from within- and between-participant studies

Most studies assessing effects of tDCS on cognition used a withinstudy design, where the same participants were administered sham and real tDCS. Despite this, most previous reviews calculated effect sizes as being drawn from a between-participants design (see Horvarth et al., 2015; Jacobson et al., 2012; Price et al., 2015; but also see Mancuso et al., 2016). This method, however, overestimates variance (which is reduced in a within-participants design) and, therefore, reduces the chances of finding significant results. Our review included both withinparticipant and between-participant studies. To increase precision, we used different methods to estimate effects for within- and betweenparticipant designs (see Lakens, 2013; Borenstein et al., 2009).

For <u>between-participant studies</u>, we measured effect sizes using Cohen's d with Hedges'g correction. Thus:

Cohen's d = 
$$\frac{M_{tDCS} - M_{sham}}{SD_{pooled}}$$

where  $M_{tDCS}$  is the mean from the tDCS condition,  $M_{sham}$  is the mean from the sham condition, and  $SD_{pooled}$  is the pooled standard deviation, calculated as follows:

$$SD_{pooled} = \sqrt{\frac{(n_{tDCS} - 1)SD_{tDCS} + (n_{sham} - 1)SD_{sham}}{(n_{tDCS} + n_{sham}) - 2}}$$

(where values for  $n_{tDCS}$  and  $n_{sham}$  are the sample sizes for the tDCS and sham conditions and  $SD_{tDCS}$  and  $SD_{sham}$  are the standard deviations).

Cohen's d, was multiplied by the coefficient J to give Hedges' g, which corrects for the upward bias in Cohen's d for samples less than 20 (Hedges and Olkin, 1985). We calculated J as:

$$J = 1 - \frac{3}{4df - 1}$$

(where *df* is the degrees of freedom used to calculate estimate  $SD_{pooled}$ , which for two independent samples is: *df* for  $SD_{pooled} = n_{tDCS} + n_{sham}$ -2; where  $n_{tDCS}$  is the number of participants in the tDCS condition, and  $n_{sham}$ , the number of participants in the sham condition; see Borenstein et al., 2009). Hedges' *g* can be interpreted in the same way as Cohen's *d* – i.e., effect sizes of 0.2, 0.5, and 0.8 roughly equate to small, medium and large effect sizes, respectively.

For <u>within-participant studies</u>, effect sizes were estimated as the difference between conditions multiplied by a measure of association of scores in the two conditions and then divided by the standard deviation of the difference scores. Thus

$$Hedges'g = J \times \left( \frac{(M_{tDCS} - M_{sham}x(\sqrt{2(1 - Corr)}))}{SD_{diff}} \right)$$
$$SD_{diff} = \sqrt{SD_{tDCS}^2 + SD_{sham}^2 - 2xCorrxSD_{tDCS}xSD_{sham}}$$

where *Corr* is the correlation between scores in tDCS and sham conditions. Since correlations were not reported by studies, we set a conservative correlation of 0.6 based on data from several of our own studies (see Westwood et al., 2017). The review by Mancuso et al. (2016) used a similar mid-range value. All effects were calculated using Comprehensive Meta-Analysis Software V3.0.

#### 2.2.3. Multiple dependent effects

In a meta-analysis, effect size estimates should be drawn from different participant samples. Violating this assumption of independence leads to an underestimation of variance and an overestimation of statistical significance (i.e., a Type 1 Error or False Positive; see Lipsey and Wilson, 2001). Previous studies have not always preserved this assumption (see Horvath et al., 2015a; Dedoncker et al., 2016). Those reviews that preserved it selected only one effect per study, thus reducing power (see Jacobson et al., 2012; Price et al., 2015). We used composite effects for conditions carried out by the same participants where we expected similar effects of tDCS (e.g., naming/reading of different types of stimuli, such as nouns vs verbs or people vs places; online vs offline stimulation at different time intervals). We report separate effect sizes for conditions where different effects of tDCS were clearly expected (e.g., anodal vs. cathodal tDCS) and when participants carried out two tasks (e.g., reading and naming). The effect of different parameters was assessed in the *Moderator* analyses.

Composite effect sizes can be calculated using mean performance and variance. However, this does not consider the inter-correlation between conditions, and therefore overestimates the error term (Borenstein et al., 2009). We calculated the variance based on a formula devised by Borenstein et al. (2009; M. Borenstein, June 10, 2017 by personal communication), which accounts for inter-correlation. For example, to calculate the mean effect size and composite variance for *two dependent effect sizes*:

$$Mean = \frac{1}{2}(Y_1 + Y_2);$$
  
Composite Variance =  $\left(\frac{1}{2}\right)^2 (V_1 + V_2 + 2r\sqrt{V_1}\sqrt{V_2})$ 

where  $V_1$  and  $V_2$  are the variances for the condition means  $Y_1$  and  $Y_2$ , and r is the correlation coefficient – i.e., an estimate of the extent to which variances co-vary. Since r is generally not reported we assumed a plausible correlation of 0.6, based in part on our own data (Westwood et al., 2017) but also advice by Borenstein et al. (2009). Assuming a correlation of 0 means that each outcome contributes new, unrelated information to the summary effect size, thus the composite variance of two unrelated samples is half of the mean variance. This may underestimate true variance and lead to a Type I Error (False Positive). Assuming instead a correlation of 1.0 means outcomes in one sample duplicate those in the other, thus the composite variance is just the mean variance of the two samples. This may over estimate variance and lead to a Type II Error (False Negative; see Appendix B for breakdown of composite effects).<sup>2</sup>

#### 2.2.4. Heterogeneity

Heterogeneity refers to variation in effect sizes across studies. Such variation may arise from random sampling error, or from true differences between studies due, for instance, to variation in stimulation parameters, language domain, or target site (i.e., *true heterogeneity*). True heterogeneity is assumed if effect estimates differ more than would be expected from sampling error alone. True heterogeneity can question the reliability of the summary effect. The conventional test for heterogeneity is the *Cochran's Q statistic*. A significant *Q* indicates that studies differ in their estimates of effects, but it is more difficult to conclude that studies are alike from a non-significant *Q* because *Q* suffers from low power with small sample sizes. To counter this, we increased the *p* value to 0.10 to exclude heterogeneity (Higgins et al., 2003). We also quantified heterogeneity as a percentage using the  $I^2$  index.

$$I^2 index = 100x \frac{Q - (k - 1)}{Q}$$

An  $I^2$  index of 0% means variation in effect sizes is all due to sampling error, whilst an index of 100% means all variation is due to true heterogeneity. Using a rule of thumb,  $I^2$  indexes = 75%, 50%, and 25% reflect respectively high, medium and low true heterogeneity (Lipsey and Wilson, 2001).

#### 2.2.5. Fixed effect vs. random effects

A fixed effect model assumes there is a *true* effect that is the same across all studies and that variation in the size of this effect results from

 $<sup>^{2}</sup>$  Comprehensive Meta-Analysis V3.0 cannot alter the correlation value – fixing it at either 1 or 0 – so the mean and corrected variance was first calculated in Microsoft Excel and then these values were imputed into CMA. Formulae for calculating the effect size presented in *Effects from within- and between-participant studies* still apply here.

sampling error alone. This assumes no heterogeneity. More weight is assigned to larger studies and less weight to smaller studies as a result. A random effects model assumes the variation across studies is *also* due to differences in the chosen experimental methodology, such as stimulation montage, current intensity, stimulation duration, participant design, and outcome measure (Brunoni and Vanderhasselt, 2014; Dedoncker et al., 2016; Hill et al., 2016; Price et al., 2015). This is a more conservative assumption. We have therefore used a random effects model in our meta-analyses. With this model, every study contributes to the effect size estimate, and small studies are not given a smaller weight.

#### 2.2.6. Outliers

We planned to exclude effect size estimates from each analysis which were 3 standard deviations above or below the summary effect size to avoid extreme values biasing the outcome. In all analyses, no study met this criterion, so no study was excluded.

#### 2.2.7. Publication bias

Publication bias refers to the tendency to publish studies with significant results and leave in the file-drawer studies with null results. The presence of bias would question the validity of a significant effect in our review. We therefore used funnel plots to identify publication bias. These are scatter plots where effect sizes are plotted against a measure of a study's precision, such as the number of participants or, in our case, standard error. Effects from smaller (or less precise) studies should spread more around the mean effect size, while effects from larger (or more precise) studies should cluster more around the mean. In the absence of bias, the distribution will be due to sampling error alone and be symmetrical around the true effect (reflected by the mean), with the distribution of scores being smaller for larger/more precise studies and increasingly greater for smaller/less precise studies. This will give the plots a characteristic inverted funnel shape. In the case of publication bias, instead, the distribution will be asymmetrical. Studies with fewer participants are more likely to obtain positive or negative results by chance, but, in the presence of bias, positive results will be published while negative results will be missing. We used the trim-and-fill procedure, which corrects for bias by trimming outliers and imputing effects to generate a (simulated) symmetrical distribution, thereby providing an unbiased summary effect size estimate (Lipsey and Wilson, 2001). We established the significance of bias using a method proposed by Egger et al. (1997).<sup>3</sup> When we look at publication bias, we use Cohen's d effect size estimates because Hedges' g already slightly corrects for bias.

#### 3. Results

#### 3.1. Primary analyses

Our focus here was to assess the efficacy of what are arguably conventional protocols for targeting language areas. These include anodal tDCS applied to the left frontal or temporal regions (see Tables B.1 and B.2 for a listing of conditions and how they were aggregated). Figs. 1 and 2 show forest plots and summary statistics of effects on speed and accuracy scores. Effects are reported as positive if consistent with the general hypothesis that left anodal tDCS improves performance; negative otherwise. Figures report summary effects separately for reading and naming tasks and cumulating across tasks, where composite effect size estimates were used to preserve the assumption of independence in cases where participants carried out both tasks. Funnel plots following trim-and-fill correction for bias are found in Fig. 3. Summary statistics are also provided reporting effect estimates before and after trim-and-fill along with the Egger's test for significance of publication bias.

There are no significant effects of tDCS on either reaction times or accuracy with the overall effects being close to 0. This is true when results are pooled across tasks and when they are considered separately. In spite of no significant results overall (even before correcting for publication bias), there is still some evidence of bias. Across both analyses the trim-and-fill procedure weakened the summary effect size. Although this effect was not significant with reaction times, it approached significance with accuracy scores.

#### 3.2. Moderator analyses

Moderator analyses were carried out to identify parameters which may modulate the effectiveness of tDCS. We limited these analyses to studies which used conventional stimulation, which are more numerous. We carried out General Linear Model univariate linear regressions with size of tDCS effect (in Hedges' g) as the dependent variable and either Timing (Online vs. Offline), Current Density (0.28 vs.  $\geq$  0.057 cm/mA<sup>2</sup>), or Stimulation Duration (< 15 vs.  $\geq$  20 min), as the independent variables, all of which were dummy coded as categorical variables. Results are shown in Table 1. We found that Timing and Duration significantly moderated the tDCS effect size. Specifically, greater - yet still small - effects were observed for shorter (< 15 min) versus longer ( $\geq 20$  mins) stimulation durations in terms of reaction times ( $M \pm SE$ ; .29 ± .08 vs. - 0.047 ± .08) and for offline tDCS versus online tDCS in terms of accuracy ( $M \pm SE$ ; .29 ± .11 vs. -0.07  $\pm$  .08). It is difficult to know how much weight we should put on these significant results given the null results we report in the previous and subsequent analyses and that the effects are not observed across both reaction times and accuracy scores. Moreover, the impact of Timing is confounded with Duration as shorter durations were overrepresented in studies using offline stimulation, and vice versa. In reaction times, shorter durations make up 6 of the 10 effects for offline stimulation, whilst longer durations make up 6 of the 9 effects for online stimulation (see Table B.1); in accuracy scores, shorter durations make up 1 of the 3 effects for offline stimulation, whilst longer durations make up 3 of the 6 effects for online stimulation (see Table B.2).

#### 3.3. Semantic interference analysis

For studies using picture-word interference (Henseler et al., 2014) and cyclic blocked naming (Meinzer et al., 2014; Pisoni et al., 2012) we calculated semantic interference as the difference in reaction times between semantically related and unrelated distractor conditions. For studies using continuous picture naming, we calculated semantic interference as the difference in reaction times between items in positions 1 and 2 and items in positions 4 and 5 in a sequence of semantically related pictures (for same method, see Westwood et al., 2017). All studies used anodal tDCS and measured reaction times. Only two studies (Henseler et al., 2014; Westwood et al., 2017) also measured semantic interference in terms of percentage errors, so we focused on reaction times. Because of different predictions in the case of temporal and frontal stimulation (for discussion, see Westwood et al., 2017), we also carried out separate analyses for these two conditions. Fig. 4 shows summary effects separately for temporal and frontal stimulation and cumulating across stimulation sites, where composite scores were used to preserve the assumption of independence in cases where temporal and frontal stimulation were administered to the same participant sample (see Table B.3 for a listing of conditions and how they were aggregated). We found no effect of tDCS either overall or when considering each stimulation site separately.

<sup>&</sup>lt;sup>3</sup> This calculates bias using the effect size estimate and the inverse of standard error (or 'precision'). A linear regression is performed on the standard normal deviate (i.e., effect size over the inverse of standard error), with the inverse of standard error serving as a predictor variable. Bias is calculated in terms of the extent to which the intercept deviates from zero (Egger et al., 1997). A significant outcome indicates bias.

	Study	Hedges' g	Lower	Upper			1		1	1	1	1	
	Fertonani et al. (2010), Exp 1	0.28	-0.25	0.82					-			_	
	Fertonani et al. (2010), Exp 2	0.62	0.04	1.20									
	Fertonani et al. (2014)	0.50	0.05	0.95									
	Henseler et al. (2014)	-0.08	-0.40	0.24						-	.		
	Meinzer et al. (2016)	0.03	-0.36	0.42							<u> </u>		
20	Pisoni et al. (2012), Exp 1	-0.50	-1.06	0.07			+		•				
Ē	Pisoni et al. (2012), Exp 2	0.33	-0.22	0.87					-		-	_	
Z	Sparing et al. (2008)	0.20	-0.28	0.69									
	Westwood et al. (2016), Exp 1A	0.02	-0.43	0.46						-			
	Westwood et al. (2016), Exp 1B	0.01	-0.41	0.43						-			
	Westwood et al. (2016), Exp 1C	-0.14	-0.58	0.31				-			-		
	Westwood et al. (2016), Exp 2	-0.33	-0.80	0.13					-				
	Wirth et al. (2011)	-0.04	-0.46	0.38						-	-		
	Average	0.05	-0.10	0.20									
	Heterogeneity	Q = 17, df =	12, p = .13	$I^2 = 31\%$									
20	Jeon and Han (2012)	0.37	-0.56	1.31				-					
all	Westwood et al. (2016), Exp 1A	0.15	-0.29	0.60					-				
éa	Westwood et al. (2016), Exp 1B	0.05	-0.37	0.47									
-	Westwood et al. (2016), Exp 1C	-0.04	-0.48	0.41							-		
	Average	0.08	-0.17	0.32							-		
	Heterogeneity	Q = .8, df = 3	3, p = .86	$I^2 = 0\%$									
	Overall Average	0.07	-0.08	0.21									
		<i>Q</i> = 18, df =	13, p = .17	$I^2 = 27\%$		- 0	1	-		1	1		~
					-1.	50	-1.00	-0	.50	0.00	0.50	1.0	υ
							Fa	vours Sha	m		Favours	Anodal	

Fig. 1. Forest plots for the size of tDCS effects on reaction times in naming, reading and overall. Error bars reflect 95% confidence intervals. Effects size given in Hedges' g.



Fig. 2. Forest plot for the size of the tDCS effect on accuracy. Error bars reflect 95% confidence intervals. Effects size given in Hedges' g.

#### 3.4. Secondary analysis

Here we explored studies that used less common combinations of stimulation polarity and locus of stimulation. These included cathodal tDCS of either hemisphere or right hemisphere with anodal tDCS. We assumed that right-hemisphere anodal tDCS would impair language capacities given the widely held assumption that right hemisphere excitation leads to left hemisphere inhibition (Chiarello and Maxfield, 1996; Thiel et al., 2006a, 2006b). We assumed that left-hemisphere cathodal tDCS would impair performance given its inhibitory effect on cortical excitability (see Hamilton et al., 2011; Hartwigsen et al., 2010; Woods et al., 2016), but we expect that cathodal tDCS would be paradoxically facilitatory in the case of cerebellum stimulation because cerebellar nuclei are hypothesized to exert inhibitory effects on the frontal lobes (see van Dun et al., 2016). Results are reported in Fig. 5 (see Table B.4 for a listing of conditions and how they were aggregated). Again, we found no significant effect of tDCS for any combination of polarity and stimulation site, except for right anodal tDCS for reaction times. This effect was not expected, and should be treated with caution given the small sample size (N = 3) and that all three included studies originally reported a null effect of anodal tDCS (Jeon and Han, 2012; Sparing et al., 2008). We also estimated a significant effect in Pope and Miall (2012), contrary to the authors, who reported a null effect. This discrepancy is due to the measure we chose to estimate the tDCS effect. Pope and Miall (2012) measured reading across six trials, which were composed of five repetitions of the same stimuli followed by a sixth trial with new stimuli. The authors included all trials in their tDCS analysis, which could have diluted the effect of anodal tDCS, due to repetitions. To avoid effects of repetition, we, instead, only used performance on the sixth trial (but we could have equally chosen the first trial).

#### 4. General discussion

We carried out a number of meta-analyses to quantify the effects of tDCS on language tasks whilst accounting for factors that could

#### **PRIMARY ANALYSIS: Left Hemisphere Anodal tDCS**



Summary Statistics: Publication Bias

95% CI

Lower

.10 .20 **B**0

 $\frac{1.7}{2.1}$ 

After Trim-and-Fill

.02

-.11

Upper

.28

Fig. 3. Funnel plots for effect of anodal tDCS using conventional parameters. Effects size given in Cohen's d. Summary statistics given in table below which shows before and after trim-and-fill effect sizes and Egger's test of publication bias.

### Table 1

RTs

Acc

.07

-.01

Before Trim-and-Fill

Lower

-.08

-.17

95% CI

Upper

14

Results of linear regressions for effect size estimates separately for reaction times (left) and accuracy scores (right). Significant results are highlighted in bold.

	RTs				Accurac	у		
Moderator	Beta	t	р	R <sup>2</sup>	Beta	t	р	$R^2$
Offline vs. Online	- 0.4	- 1.7	0.12	0.14	- 0.72	- 2.7	<u>0.03</u>	0.5
$\begin{array}{c} 0.28 \text{ vs.} \geq \\ 0.057 \text{ cm/} \\ \text{mA}^2 \end{array}$	- 0.1	- 0.43	0.67	0.01	- 0.55	- 1.7	0.13	0.3
< 15 vs. ≥ 20 mins	- 0.58	- 2.9	<u>0.01</u>	0.33	0.22	0.6	0.57	0.05

moderate the outcome. We found no significant effect of tDCS when applied using conventional, best-evidence parameters – i.e., anodal lefthemisphere tDCS applied to frontal and temporal regions. This was true across tasks (naming and reading) and outcome measures (reaction times and accuracy). We also found no significant effect of tDCS in modulating effects of semantic interference disregarding site of stimulation (frontal or temporal), and no effects of tDCS with less used stimulation parameters – i.e., cathodal tDCSof either hemisphere or anodal tDCS of the right hemisphere. In our moderator analyses, we did find that tDCS administered offline and for a shorter duration (< 15 min) produced greater effects. These effects, however, should be interpreted with caution. Effects were small (~.3 Hedges' g), confounded with one another, and contrary to predictions that greater effects should occur with longer durations (see Hill et al., 2016; see Fertonani and

Egger's test

13

.06

Upper

5 1

95% CI

Lower

-1.33

-.89



Fig. 4. Forest plots for the size of the effect of tDCS when considering studies measuring semantic interference effects on picture naming. Error bars reflect 95% confidence intervals. Effects size given in Hedges' g.

Miniussi, 2016; Woods et al., 2016). We believe, therefore, that more weight should be given to the large number of null findings we report, which are, overall, consistent with mounting scepticism about whether tDCS can reliably modulate cognition in healthy participants, at least

with single applications (see Horvath et al., 2015a; Mancuso et al., 2016).

Given our negative results, one may ask the question: why are there so many reports of significant results across the wider tDCS literature,

Measure Protocol	Study	Hedges' g	Lower	Upper
Reaction Times				
Left Cathodal tDC	5 Fertonani et al. (2010), Exp 1	0.18	-0.35	0.72
	Fertonani et al. (2010), Exp 2	-0.28	-0.82	0.26
	Sparing et al. (2008)	-0.17	-0.65	0.31
	Average	-0.09	-0.39	0.21
	Heterogeneity	Q = 2, df = 2	2, p = .47	$I^2 = 0\%$
Right Anodal tDC	5 Jeon and Han (2012)	-0.02	-0.95	0.90
	Pope and Miall (2012)*	-0.68	-1.28	-0.09
	Sparing et al. (2008)	-0.29	-0.78	0.20
	Average	-0.39	-0.74	-0.04
	Heterogeneity	Q = 1.7, df =	= 2, <i>p</i> = .4	$I^2 = 0\%$
Right Cathodal tDC	Boehringer et al. (2012)	0.00	-0.31	0.31
	Pope and Miall (2012)*	1.37	0.72	2.01
	Average	0.03	-0.24	0.30
	Heterogeneity	Q = 14, df = 1	L, p < .001	<i>I</i> <sup>2</sup> = 93%
Accuracy				
Left Anodal tDC	S Younger et al. (2016)	0.60	-0.18	1.39
 Right Anodal tDC	S leon and Han (2012)	-0.02	-0.95	0.90
	Ross et al. (2012)	0.00	-0.48	0.48

Younger et al. (2016)

Average

Heterogeneity

Fig. 5. Summary of effect sizes of tDCS when considering studies using atypical stimulation parameters. Lower and Upper reflect 95% confidence intervals.

0.06

0.01

-0.71

-0.40

Q = .32, df = 2, p = .85  $l^2 = 0\%$ 

0.82

0.34

but also specifically across language studies? A number of factors may contribute. First of all, although we did not find any significant effect of tDCS, we still found some evidence of publication bias in our primary analysis where there is more consensus that stimulation parameters may be effective and therefore a stronger expectation of significant results. A similar bias has been found in another meta-analysis quantifying effects of tDCS on working memory tasks (see Mancuso et al., 2016). Publication bias may produce the false impression of solid effects of tDCS, even in the case of single session application in healthy participants. Secondly, reports of significant effects using conventional parameters cluster in studies where a number of conditions are run with the same participants. Since whatever effect is responsible for the better performance with real tDCS versus sham is likely to affect all conditions (whether this is really due to tDCS or to chance factors), this will unduly inflate the significance of tDCS. This problem is well demonstrated by inspection of effects for individual conditions presented in Table B.1. We see that 6 out of 40 (or 15%) of conditions showed a significant result, but when conditions using the same participants are collapsed this drops to 2 out of 25 (or 8%). This is consistent with results being significant by chance (see also, Medina and Cason, 2017).

Finally, individual reports of positive effects of tDCS may not reflect a true effect. tDCS studies generally recruit between 20 and 30 participants, and according to one estimate the typical power achieved across cognitive studies is roughly 14%, and maybe less (see Medina and Cason, 2017). Low power naturally reduces the probability of finding a significant effect if one in fact truly exists, but it also gives undue weight to some large effects which could be significant by chance (Button et al., 2013; Minarik et al., 2016). A meta-analysis is of course an ideal tool to assess effects in fields where individual studies are underpowered. Even if we assume a small effect size of 0.25, our smaller cumulated sample (n = 160; primary analysis for accuracy) gave us good power (with a probability = 0.79) to find a significant effect if one was present, assuming a within-participants design (typical of tDCS studies measuring effects on language).

We acknowledge that the negative outcomes of our meta-analyses may be due to variability in the parameters used by different studies as well as by individual variability in the response to tDCS. It is commonly assumed that anodal and cathodal tDCS respectively up- and downregulate cortical excitability, and that increasing stimulation duration/ density will increase the effect (see Hill et al., 2016; Kim et al., 2014; Teo et al., 2011). However, a non-linear system like the brain is unlikely to have a linear response to an externally applied electric current. First, effects may reverse with higher intensities of stimulation because of a homeostatic response (for effects on motor excitability see Batsikadze et al., 2013; Fertonani and Miniussi, 2016). Additionally, the effect of the current may interact with the present level of cortical excitability which may, in turn, depend on task demands (Fertonani and Miniussi, 2016; Miniussi et al., 2013), and/or individual differences in base-line levels of excitation or cognitive ability (see, Hsu et al., 2014; Tseng et al., 2012; Berryhill et al., 2014; Bikson and Rahman, 2013; Krause et al., 2013). We considered semantic interference - a proxy for heightened cortical excitation relative to normal cortical activity - but still found no evidence of significant tDCS modulation (see also Westwood et al., 2017). Our review, therefore, suggests that we are yet to find the conditions in which the level of cortical excitability is optimal for improving performance, at least in language tasks within a single session of tDCS and in healthy participants.

It is also important to stress that we focused on studies recruiting young healthy participants. In contrast to our null results, positive effects of tDCS in naming tasks have been consistently noted in aphasic patients (for review, see Cappon et al., 2016; Crinion, 2016; Sandars et al., 2016). Positive effects have also been reported in older adults, although less consistently (see Fertonani et al., 2014; Ross et al., 2011). It is possible, therefore, that positive effects are much easier to elicit in populations where levels of cortical excitation are suboptimal due to brain damage or aging. Finally, our investigation was limited to picture naming and word reading tasks. It is possible that single applications of tDCS cannot modify processes and/or representations involved in these tasks since they are so well established through years of practice. Positive results, instead, may be achieved in other tasks where more novel processes are engaged. Learning paradigms, for example, may provide more positive results, even in control participants (Flöel et al., 2008; Fiori et al., 2010; Meinzer et al., 2014), because here, as in the case of aphasic patients with brain-damage, representations are weaker and in a more 'plastic' state. Alternatively, cognitive effects in healthy participants may be reliable only when tDCS is administered repeatedly with cumulative effects (Alonzo et al., 2012; Meinzer et al., 2014).

#### 5. Conclusions

Undoubtedly our results are not encouraging regarding the ability of tDCS to modulate cognitive performance in a single session with healthy participants. It is too early, however, to conclude that tDCS is generally ineffective in this population. Future studies should investigate tDCS effects on tasks which involve learning and/or involve repeated application of tDCS. Future studies should also continue to investigate interactions with underlying levels of cortical excitation. Historically, novel interventions pass through a hype cycle - i.e., an initial peak of interest which then wanes with growing scepticism before conditions in which the intervention can operate reliably are established. Hopefully, the same will occur with tDCS. In this endeavour, however, it is very important to have a fair assessment of the limits of this technique and of the conditions in which there is no or limited efficacy. We have already learned from another form of brain stimulation, transcranial magnetic stimulation (TMS), that the torrent of what later turned out to be false positive or unreliable reports generated so much noise that it slowed the uptake of TMS in conditions where effects are indeed reliable, such as in clinical depression (see Walsh, 2013). We hope our review will help in establishing the right scope of application of tDCS.

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# Appendix A. Sample of studies included in the review, with details on stimulation parameters and a summary of findings

Author	N	Exp	Design	Polarity	Timing	mA	Density	Anode (cm2)	Duration	Hemisphere	Site	Reference	Measure
Boehringer et al. (2013)	39	1	Within	C,S	Off	2	0.080	25	25	R	Cerebellum	Right Cheek	RTs
The right cereb involved rea reading spec	ellur Iding eds.	n was g aloue	targeted v 1 a list of 4	vith cathoo 42 colour v	lal stimul words as i	ation fast a	, and parti s possible.	icipants we Comparis	ere tested or ons betweer	n various tasks n pre and post	before and af scores showed	ter stimulatio l no significa	on. One task ant effect on
Fertonani et al. (2010)	12	1	Within	A,C,S	Off	2	0.057	35	8	L	dlPFC	Right Shoulder	RTs
Fertonani et al. (2010)	12	2	Within	A,C,S	Off	2	0.057	35	10	L	dlPFC	Right Shoulder	RTs
In two separate following ar tDCS, which but there wa Fertonani et al. (2014)	exp noda was as no 20	erime l or ca s attril o effec 1	nts, the au thodal tD outed to sh t on accur Within	ithors mea CS to the l nort inter-s racy scores A,S	sured pic eft dlPFC timulation Off, On	ture 1 . <i>Expe</i> n inte 2	naming ac eriment 1: erval. Expe 0.057	curacy and naming ac <i>riment 2:</i> F 35	d reaction ti curacy and Participants 10	mes for two se reaction times were faster aft L	ets of stimuli ( did not show er anodal tDC dlPFC	actions and any signific S but not cat Right Shoulder	objects) ant effect of hodal tDCS, RTs
Old and young	part	icipan	ts were gi	ven anoda	l tDCS on	line a	and offline	e in separa	te condition	s. Picture nam	ing reaction t	imes, but no	t accuracy,
Were signific Henseler et al. (2014)	36	y fast 1	er both fo Within	r online an A,S	On On	2	0.080	er adults a 25	25	L	er adults. IFG, TG	Right Orbit	RTs, Acc
Anodal tDCS wa interference related distr percentage of Jeon and Han	as ap task actor of er 8	oplied . Wor rs (i.e. rors a 1	to the left d distracto , for interf nd reactio Between	inferior fr ors were pr ference, 10 n times. A,S	ontal gyru resented a 0 ms SOA Off	us (LI it diff As; for 1	FG) or mi erent picto facilitatio 0.029	ddle tempo ure stimuli on, 300 ms 35	oral gyrus (N i onset asynd SOAs). The 20	MTG) whilst pa chronies (SOAs re was no effec L,R	articipants per b) to measure ct of tDCS in a dlPFC	formed the p the different ny conditions Contra	icture-word ial effects of s in terms of RTs, Acc
Participants we Boston Nami (colour cond divided by 4 the number second sylla reduced for compared to improved fr Meinzer et al. (2016)	re ac ng T ition test of hi ble h ble h left a o pre om p 24	lminis est (KI ), and perio ints pr int; 0 modal -stimu pre-sti 1	tered anoc BNT). The colour we ds). Partic rovided (e. -points for tDCS com ilation val mulation i Within	dal tDCS to Stroop tasl ords in inco- cipants wer .g., 4-point r no respon .pared to pr ues both ir immediatel A,S	the right a required ongruent re asked to s with no se; 60 is t re-stimula nmediate y and two On	or lef l part colou o nam hints the m ation. ly aft o-wee 1	t dlPFC. S icipants to r ink (inten- ne pictures s; 3-points aximum s Left and r er stimula ek after sti 0.029	ubjects per o name colo erference co s, and hints with mea core overa ight anoda tion and t imulation. 35	cformed a se our names p ondition). Th s were giver ningful hint 11). For the S 1 stimulation wo-weeks la 20	ries of tasks, in rinted in black e KBNT involv whenever new s, 1-point with Stroop task, rea n lead to a sign tter. For the <i>Ki</i> L	cluding the St (word conditional red parallel ver cessary. Perfor first syllable action times in ificantly dimin BNT, the left a TG, LIFG	roop task and on), Xs printe rsions with ( mance was r hint; ½hal the word co hished interfe nodal stimul Right Orbit	the Korean- d in colours 50 items neasured by f a point for <i>ndition</i> were erence effect lation group RTs
The authors app participants stimulation onwards. Pisoni et al.	plied perf redu 12	l anod ormec ced th 1	al tDCS to l the cyclic ne magnitu Within	the left ir c blocked 1 1de of sem A,S	nferior fro naming ta antic inte Off	ontal g isk. T irferei 2	gyrus (LIF he results nce in ear 0.057	G) and posishowed no ly cycles, w 35	sterior midd o overall eff whilst pMTC 20	lle and superic ects of anodal G/STG reduced L	or temporal gy tDCS relative interference	ri (pMTG/ST to sham. Ho from the sec Right	CG) whilst wever, LIFG ond cycle RTs
(2012)												Orbit	
Pisoni et al. (2012)	12	2	Within	A,S	Off	2	0.057	35	20	L	IFG	Right Orbit	RTs

Participants performed the cyclic blocked picture naming tasks immediately after anodal tDCS to the left inferior frontal gyrus (LIFG) or left Wernicke's area (LMTG) in two separate experiments. *Experiment 1 (LMTG tDCS)*: participants were much slower overall, and responses were much more slower for semantically related picture sets compared to sham – i.e., anodal tDCS boosted semantic interference. *Experiment 2 (LIFG*) S.J. Westwood, C. Romani

*tDCS*): though there was no overall facilitatory effect of anodal tDCS there was a significant reduction in the size of semantic interference effect. There was no statistical difference between related and unrelated sets for real stimulation, but there was in sham stimulation.

Pope and Miall (2012)	22 1	Between	A,C,S	Off	2	0.08	25	20	R	Cerrebellum	Left Deltoid	RTs
After anodal or task was per significant e tDCS compa	cathod formed ffect, w red to	al tDCS to th 6 times (5 t ith enhancen sham (and ar	e right ce imes with nent in ter nodal tDC	rebellum, the same ms of lear S).	partio stimu ning r	cipants re Ili then o ate (i.e., )	epeatedly p n the 6th t change bet	performed 1 ime new st ween the fi	noun and verb r imuli were pres rst and last repe	eading and ver sented). Only v etition for post-	b generation erb generati tDCS scores)	n tasks. Each on showed a for cathodal
Ross et al. (2010)	15 1	Within	A,S	On	1.5	0.043	35	15	L,R	ATL	Contra Cheek	Acc
Participants we overall reduc right ATL w	re give ction in ith a 1	n anodal tDC reaction tim 1% increase	S of the ri es or impr when nam	ight or lef ovement i ning pictu	t ante in acc res of	rior temp uracy, dif faces.	ooral lobes ficult to na	whilst nan me items (	ning pictures of responses > 5 s	faces and plac ) showed a ben	es. Though t efit of anoda	there was no l tDCS to the
Sparing et al. (2008)	15 1	Within	A,C,S	On, Off	2	0.057	35	7	L,R	CP5,CP6	Contra Orbit	RTs
The authors me stimulation a was a signifi data was no	asured session cant re t repor	picture nam s, anodal tDC duction in na ted.	ing speeds S was app aming imp	s and accu plied to le mediately	iracy ft or i follov	rates dur right Wer wing left	ing stimul nicke's are Wernicke	ation, imm a or cathoo anodal con	ediately, 5 and dal tDCS was ap npared to sham.	10 min after st pplied to the lef Accuracy was	imulation. I ft Wernicke's unaffected	n separate s area. There by tDCS, but
et al. (2012)	25 1	Within	A,8	Off	1.5	0.060	25	20	L	pIC	Analogue	Acc
Anodal tDCS wa Woodcock R sight reading	as admi eading g effici	nistered to the Mastery Tes	ne posteri t-Revised- ading list	or tempor Normativ of words	al cor e Upd as fast	tex befor late or W t as possi	e participa RMT; Test ble) partic	nts perforr of Word R ularly in b	ned several asso leading Efficien elow average re	essments of wo cy or TOWRE). aders.	rd reading a Anodal tDO	bilities (e.g., CS improved
Westwood et al. (2017)	18 1	A Within	A,S	On	1	0.111	9	15	L	IFG	Contra Orbit	RTs, Acc
Westwood et al. (2017)	20 1	B Within	A,S	On	1.5	0.060	25	25	L	IFG	Contra Orbit	RTs, Acc
Westwood et al. (2017)	18 1	C Within	A,S	On	1.5	0.060	25	25	L	TG	Right Orbit	RTs, Acc
Westwood et al. (2017)	20 2	Within	A,S	On	1.5	0.060	25	25	L	IFG	Right Orbit	RTs
Across four exp blocked nam errors.	erimen ning) ar	ts participant nd word read	ts were ad ing tasks.	lministere The stud	d ano y faile	dal tDCS ed to find	whilst per any effec	forming pi t of tDCS in	cture naming ( n all experimen	continuous pict ts either in terr	ture naming ns of RTs or	and cyclic percentage
Wirth et al. (2011)	20 1	Within	A,S	Off	1.5	0.043	35	37	L	dlPFC	Right Shoulder	RTs
Anodal tDCS ta performed p RTs, Simple	rgeted ost-stir	the left dlPF( nulation. The	C whilst p re was no formance	articipant overall e remained	s perf ffect c unch	formed the formed the formed the formed the formed by the	e cyclic bl out there w	ocked nam vas a signifi	ing task. A sim	ple picture nan in the semantic	ning task wa interferenc	as then e in terms of
Younger et al. (2016)	32 1	Between	A,S	Off	1.5	0.060	25	20	L,R	IPL	Contra Orbit	Acc

Participants were administered either anodal or sham tDCS to the left or right inferior parietal lobe (IPL) after which they were asked to perform two measures of reading ability: single word reading efficiency and rhyme judgment. Participants who received left IPL tDCS improved in terms of reading efficiency relative to sham, but improved less on rhyme judgment relative to right IPL tDCS.

N = number of participants; On = online; Off = offline; A = anodal; S = sham; C = cathodal; ATL = anterior temporal lobe; dlPFC = dorsolateral prefrontal cortex; TG = temporal gyrus; pTC = posterior temporal cortex; Acc = percentage errors; RTs = reaction times.

Appendix B. Listing of studies included in our meta-analysis with between-participants effect size estimates (as often reported in the literature) and our own composite effect size estimate based on a within-design assumption where appropriate. Note, for *Moderator analyses*, different effects sizes were used for online and offline stimulation since this was a parameter of interest. Effects were aggregated for the *Primary* and *Secondary* analyses to avoid violations of the independence assumption. We indicate significant effects as reported by authors in the paper (with *Y* or *N*) and as we report based on our composite effect size estimates (underlined)

See: Tables B.1–B.4

## Table B.1

Studies used in Primary and Moderator analyses with reaction times as the dependent variable.

Author	Exp	Timing	Loci	Condition	N	Shar	n	tDCS	;	Sig.	Hedges' g	95%CI		М	Variance	Hedges' g	95%CI	
						М	SD	М	SD			Lower	Upper	(Sham – tDCS)			Lower	Upper
Fertonani et al. (2010)	1	Off	LdlPFC	Objects	12	739	81	731	99	Ν	0.08	- 0.66	0.83	22	463	0.28	- 0.25	0.82
		Off	LdlPFC	Actions	12	907	104	871	78	Ν	0.36	- 0.41	1.14					
	2	Off	LdlPFC	Objects	12	617	51	590	47	Y	0.51	- 0.29	1.31	38	262	0.62	0.04	1.20
		Off	LdlPFC	Actions	12	789	100	741	58	Y	0.55	- 0.26	1.35					
Fertonani et al. (2014)	1	Off	LdlPFC	Objects	20	757	72	710	72	Y	0.63	- 0.03	1.28	28	133	0.52	0.07	0.97
		Off	LdlPFC	Actions	20	585	57	576	56		0.15	- 0.45	0.75					
		On	LdlPFC	Objects	20	757	72	720	69	Y	0.50	- 0.13	1.14	22	129	0.42	- 0.02	0.86
		On	LdlPFC	Actions	20	585	57	578	55		0.12	- 0.48	0.72					
Henseler et al. (2014)	1	On	LIFG	Associated	36	683	66	692	66	Ν	- 0.13	- 0.59	0.32	- 4	62	- 0.08	- 0.40	0.24
		On	LIFG	Unrelated	36	706	66	719	72	N	- 0.18	- 0.64	0.27					
		On	LIFG	Semantic	36	763	72	764	72	N	- 0.01	- 0.47	0.44					
		On	LIFG	Unrelated	36	730	60	734	60	N	- 0.07	- 0.52	0.39					
		On	LMIG	Associated	30	706	66	695 704	12	IN N	- 0.17	- 0.77	0.43					
		On	IMTG	Semantic	36	763	72	762	72	N	0.03	- 0.50	0.03					
		On	LMTG	Unrelated	36	730	60	725	48	N	0.09	- 0.51	0.68					
Jeon and Han (2012)	1	Off	LdlPFC	Stroop; neutral	8	11	3	10	2	N	0.37	- 0.56	1.31	1	2	0.37	- 0.56	1.31
Meinzer et al. (2016)	1	On	IFG	Related	24	643	88	643	87	N	0.00	- 0.55	0.55	- 5	206	0.03	- 0.36	0.42
		On	IFG	Mixed	24	606	80	616	94	Ν	- 0.11	- 0.66	0.44					
		On	STG	Related	24	643	88	625	93	Ν	0.19	- 0.36	0.74	8	198			
		On	STG	Mixed	24	606	80	608	83	Ν	- 0.02	- 0.57	0.52					
Pisoni et al. (2012)	1	Off	LSTG	Related	12	604	59	642	66	Y	- 0.56	- 1.37	0.25	- 26	198	- 0.50	- 1.06	0.07
		Off	LSTG	Mixed	12	591	55	605	62	Ν	- 0.22	- 0.98	0.53					
	2	Off	LIFG	Related	12	646	48	621	59	Ν	0.43	- 0.35	1.22	16	173	0.33	- 0.22	0.87
		Off	LIFG	Mixed	12	618	45	612	66	Ν	0.10	- 0.65	0.85					
Sparing et al. (2008)	1	On	CP5	On	15	531	367	525	306	Ν	0.09	- 0.59	0.77	6	205	0.10	- 0.38	0.58
		Off	CP5	Off	15	528	412	499	325	Y	0.40	- 0.30	1.11	29	247	0.45	- 0.05	0.96
		Off	CP5	Off(5 mins)	15	535	390	523	287	N	0.18	- 0.50	0.87	12	208	0.20	- 0.28	0.69
		Оп	CP5	Off(10 mins)	15	524	435	529	268	IN	- 0.07	- 0.75	0.60	- 5	240	- 0.08	- 0.56	0.40
Westwood et al. (2017)	1A	On	LIFG	Naming	18	896	144	894	126	Ν	0.01	- 0.61	0.64	2	824	0.02	- 0.43	0.46
		On	LIFG	Reading	18	497	82	486	71	Ν	0.14	- 0.49	0.76	11	265			
	1B	On	LIFG	Naming	20	946	118	945	106	Ν	0.01	- 0.59	0.60	1	508	0.01	- 0.41	0.43
		On	LIFG	Reading	20	541	103	537	66	Ν	0.04	- 0.55	0.64	4	340			
	1C	On	LpMTG	Naming	18	955	111	969	107	N	- 0.12	- 0.75	0.50	- 14	529	- 0.14	- 0.58	0.31
	•	On	LpMTG	Reading	18	539	55	541	63	N	- 0.03	- 0.66	0.59	- 2	158	0.00	0.00	0.10
	2	On	LIFG	Kelated	17	009 652	62 66	679 679	85 89	IN N	- 0.32	- 0.98	0.34	- 25	2/9	- 0.33	- 0.80	0.13
		OII	LIFG	wiikeu	1/	033	00	0/2	0ð	IN	- 0.23	- 0.88	0.42	- 19	304			
Wirth et al. (2011)	1	On	LdlPFC	Related	20	628	67	626	72	N	0.03	- 0.57	0.62	2	194	- 0.04	- 0.46	0.38
		On	LdlPFC	Mixed	20	584	67	589	72	N	- 0.07	- 0.66	0.53	- 5	194			
		Off	LdIPFC	Naming	20	689	65	692	73	N	- 0.04	- 0.64	0.55	- 3	193			

Legend: N = number of participants; On = online; Off = offline; LdlPFC = left dorsolateral prefrontal cortex; LpMTG = left posterior temporal gyrus; LIFG = left inferior frontal gyrus.

### Table B.2

Studies used in Primary and Moderator analyses with accuracy as the dependent variable.

Author	Exp	Timing	Loci	Condition	N	Sham		tDCS		Sig.	Hedges' g	95%CI		М	Variance	Hedges' g	95%CI	
						М	SD	м	SD			Lower	Upper	(Sham - tDCS)			Lower	Upper
Fertonani et al. (2014)	1	Off	LdlPFC	Actions	20	6	7	5	7	N	0.1	- 0.5	0.7	0.5	1.0	0.1	- 0.3	0.5
	1	Off	LdlPFC	Object	20	1	4	1	4	Ν	0.0	- 0.6	0.6					
	1	On	LdlPFC	Actions	20	6	7	6	7	Ν	0.0	- 0.6	0.6	0	0.9	0.0	- 0.4	0.4
	1	On	LdlPFC	Object	20	1	4	1	2	Ν	0.0	- 0.6	0.6					
Henseler et al. (2014)	1	On	LIFG	Associated	36	2.2	0.8	2.4	3.0	Ν	- 0.1	- 0.5	0.4	- 0.575	0.2	- 0.2	- 0.6	0.1
		On	LIFG	Unrelated	36	2.4	0.9	3.3	3.6	Ν	- 0.3	- 0.7	0.2					
		On	LIFG	Semantic	36	3.6	1.3	3.6	3.6	Ν	0.0	- 0.5	0.5					
		On	LIFG	Unrelated	36	2.5	0.7	2.0	3.0	Ν	0.2	- 0.3	0.6					
		On	LMTG	Associated	36	2.2	3	2.6	2.4	Ν	- 0.1	- 0.6	0.3					
		On	LMTG	Unrelated	36	2.4	3	2.2	3	Ν	0.1	- 0.4	0.5					
		On	LMTG	Semantic	36	3.6	4.2	3.7	4.2	Ν	0.0	- 0.4	0.5					
		On	LMTG	Unrelated	36	2.5	3	2.8	3	Ν	0.1	- 0.4	0.6					
Jeon and Han (2012)	1	Off	LdlPFC	BNT	8	12	10	6.58	6.33	N	0.6	- 0.4	1.5	5.24	17.1	0.6	- 0.4	
Ross et al. (2010)	1	On	LATL	Faces	15	73	19	70	28	Ν	0.1	- 0.6	0.8	0	23.8	0.0	- 0.5	0.5
		On	LATL	Places	15	68	22	71	22	Ν	- 0.1	- 0.8	0.6					
Turkeltaub et al. (2012)	1	Off	LpTC	Reading	25	97.5	9.8	100.7	9.2	Y	0.3	- 0.2	0.9	1.15	1.6	0.2	- 0.2	0.6
		Off	LpTC	Decoding	25	92.8	9.6	94.4	7.8	Ν	0.2	- 0.4	0.7					
		Off	LpTC	Word ID	25	100.4	5.6	99.8	5.6	Ν	- 0.1	- 0.6	0.4					
		Off	LpTC	Attack	25	99.6	9.7	100	7.5	Ν	0.0	- 0.5	0.6					
Westwood et al. (2017)	1A	On	LIFG	Naming	18	15	8.9	16	7.2	Ν	- 0.1	- 0.7	0.5	- 1	3.0	- 0.1	- 0.6	0.3
Westwood et al. (2017)	1B	On	LIFG	Naming	20	13	7	12	4.4	Ν	0.2	- 0.4	0.8	1	1.7	0.2	- 0.3	0.6
Westwood et al. (2017)	1C	On	LpMTG	Naming	18	10	6	11	5	Ν	- 0.2	- 0.8	0.5	- 1	1.4	- 0.2	- 0.6	0.3

# Table B.3

Studies used in Semantic Interference analysis using reaction times as the dependent measure.

Author	Exp	Timing	Loci	N	Sha	m	tDC	S	Sig.	Hedges' g	95%CI		Μ	Variance	Hedges' g	95%CI	
					М	SD	м	SD			Lower	Upper	(Sham - tDCS)			Lower	Upper
Henseler et al. (2014)	1	Online	LIFG	36	33	36	30	42	Ν	0.08	- 0.38	0.53	3	35	0.08	- 0.24	0.40
		Online	LMTG	36	33	36	37	42	Ν	- 0.10	- 0.55	0.35	- 4	35	- 0.11	- 0.43	0.21
	1	Online	IFG	24	37	34	28	28	Ν	0.28	- 0.28	0.84	9	33	0.31	- 0.09	0.70
		Online	STG	24	37	34	17	36	Y	0.55	- 0.04	1.14	20	41	0.62	0.19	1.04
Pisoni et al. (2012)	1	Offline	LSTG	12	13	14	38	14	Y	- 1.66	- 2.86	- 0.46	- 25	13	- 1.85	- 2.76	- 0.95
	2	Offline	LIFG	12	29	21	9	17	Y	0.97	0.05	1.90	20	25	1.07	0.39	1.75
Westwood et al. (2017)	1 A	Online	LIFG	18	72	38	95	59	Ν	- 0.44	- 1.10	0.21	- 23	124	- 0.46	- 0.93	0.00
Westwood et al. (2017)	1B	Online	LIFG	20	76	58	57	56	Ν	0.32	- 0.29	0.93	19	130	0.36	- 0.08	0.79
Westwood et al. (2017)	1 C	Online	LpMTG	18	48	80	41	70	Ν	0.09	- 0.54	0.71	7	254	0.10	- 0.34	0.54
Westwood et al. (2017)	2	Online	LIFG	17	54	85	92	69	Ν	- 0.47	- 1.15	0.21	- 38	291	- 0.51	- 1.00	- 0.03
Wirth et al. (2011)	1	Online	LdlPFC	20	44	11	37	12	Y	0.58	- 0.06	1.23	7	5	0.65	0.19	1.12

<b>Table B.4</b> Studies used in <i>Secondary A</i>	Inalysis v	vith reaction	on times an	d accuracy	as dependent varial	oles.													
Author	Exp	Polar	Timing	Loci	Condition	N	Sham	Ð	SC	s	Sig. He	edges' g	95%CI		M (Sham - tDCS)	Variance	Hedges' g	95%CI	
							M SI	- M	S	Ð									
Boehringer et al. (2013)	1	C	Off	Cereb	Reading	39	13.2 1.	9 13	3.2 1.	.3	N 0.(	00	- 0.44	0.44	0	0.06	0.00	- 0.31	0.31
Fertonani et al. (2010)	1	υ	Off	LdIPFC	Object	12	739 81	1 7£	51 8.	4	N 0.2	25	- 0.51	1.01	15.5	547			
		U	Off	LdIPFC	Action	12	907 1(	04 91	.6 1.	29 N	N 0.(	07	- 0.67	0.82			0.18	- 0.35	0.72
	2	U	Off	LdlPFC	Object	12	617 5.	1 61	16 5	1	 7	0.02	- 0.76	0.73	- 16.5	268	- 0.28	- 0.82	0.26
		υ	Off	LdIPFC	Action	12	789 1(	00 7E	57 6.	0	۱ ۲	0.36	- 1.13	0.41					
Jeon and Han (2012)	1	A	Off	RdIPFC	Naming	8	5.57 4.	33 5.	42 7.	.22 Y	- λ	0.02	- 0.95	06.0	- 0.15	6	- 0.02	- 0.95	0.90
Jeon and Han (2012)	1	A	Off	RdIPFC	Stroop; neutral	8	10 4	6	3	4	- 7	0.27	- 1.20	0.66	- 1	3	- 0.02	- 0.95	06.0
Pope and Miall (2012)	1	А	Off	Cereb	Nouns	22	0.52 0.	07 0.	48 0.	.04 N	 	0.69	- 1.29	- 0.09	- 0.04	0.0003			
		А	Off	Cereb	Verbs	22	0.52 0.	10 0.	48 0.	.04 N	 	0.52	- 1.11	0.07			- 0.68	- 1.28	- 0.09
Pope and Miall (2012)	1	U	Off	Cereb	Nouns	22	0.52 0.	07 0.	44 0.	.05 N	N 1.:	29	0.65	1.93	0.08	0.0004			
		U	Off	Cereb	Verbs	22	0.52 0.	10 0.	45 0.	.05 N	N 0.1	87	0.26	1.48			1.37	0.72	2.01
Ross et al. (2010)	1	А	On	RATL	Faces	15	73 19	62	2	4 Y	- λ	0.62	- 1.37	0.12	0	15			
		Α	On	RATL	Places	15	68 2.	2 75	9 1.	5	N 0.5	55	- 0.18	1.28			0.00	- 0.48	0.48
Sparing et al. (2008)	1	U	On	CP5	On	15	531 62	2 52	25 6:	2	 7	0.15	- 0.83	0.53	- 9	158			
		U	Off	CP5	Off	15	528 7(	0 52	28 5	8	 7	0.13	- 0.81	0.55			-0.17	- 0.65	0.31
		υ	Off	CP5	Off(5 mins)	15	535 6t	5 51	16 5	8	 7	0.37	- 1.07	0.34					
		U	Off	CP5	Off(10 mins)	15	524 7-	4 51	14 6.	6 V	I Z	0.26	- 0.95	0.43					
Sparing et al. (2008)	1	Α	On	CP6	On	15	531 3(	57 52	22 5	4	 7	0.09	- 0.77	0.59	- 14	145			
		А	Off	CP6	Off	15	528 4	12 51	9	8	N 0.(	00	- 0.68	0.68			- 0.29	- 0.78	0.20
		А	Off	CP6	Off(5 mins)	15	535 39	90 51	13 4	9 9	 7	0.29	- 0.98	0.40					
		A	Off	CP6	Off(10 min)	15	524 4:	35 5(	7 4	6 N	 Z	0.13	- 0.81	0.55					
Younger et al. (2016)	1	A	Off	LIPL	Reading	11	91.7 8.	2 92	2.2 8	ł	Y 0.(	06	- 0.71	0.82	7	21	0.60	- 0.18	1.39
Younger et al. (2016)	1	A	Off	RIPL	Reading	11	91.7 8.	2 96	3.8 1.	4	N 0.(	61	- 0.17	1.39	1	11	0.06	- 0.71	0.82

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