Non-Invasive Brain Stimulation to Investigate Language Production in Healthy Speakers: A Review and Meta-Analysis

Jana Klaus* Dennis J.L.G. Schutter

Radboud University

Non-invasive brain stimulation (NIBS) has become a common method to study the interrelations between the brain and language functioning. This quantitative review examined the efficacy of transcranial magnetic stimulation (TMS) and direct current stimulation (tDCS) in the study of language production in healthy volunteers. Forty-two effect sizes from 28 studies which investigated the effects of NIBS on picture naming or verbal fluency in healthy participants were meta-analysed. Further sub-analyses investigated potential influences of stimulation type, site, control, and task. Random effects modelling showed a small, but reliable effect of NIBS on language production. Subsequent analyses indicated larger weighted mean effect sizes for TMS as compared to tDCS studies. No statistical differences between stimulation of frontal and temporal regions, or between picture naming and verbal fluency tasks, were observed. We conclude that NIBS is a useful method for neuroscientific studies on language production in healthy volunteers.

Keywords: language production, meta-analysis, picture naming, verbal fluency, TMS, tDCS

Introduction

Transcranial magnetic (TMS) and direct current stimulation (tDCS) are non-invasive brain stimulation (NIBS) techniques that are increasingly used to investigate causal relationships between language functions and their underlying neuronal processes. The aim of this combined review and meta-analysis is to examine the efficacy and reliability of NIBS as an intervention method to study the neural correlates of language production in healthy volunteers. Prior meta-analyses on the effects of transcranial direct current stimulation (tDCS) on verbal fluency and picture naming have provided diverging results (Horvath, Forte, & Carter, 2015; Price, McAdams, Grossman, & Hamilton, 2015; Westwood & Romani, 2017). Our present review offers an overview and meta-analysis of studies which measured changes in verbal fluency and picture-naming performance during or following the administration of tDCS or transcranial magnetic stimulation (TMS). Furthermore, by differentiating between different experimental parameters, we aim to provide a more detailed picture with respect to the usefulness of NIBS studies that investigate language production in healthy volunteers.

The use of TMS to study language production in healthy speakers started two decades ago (Mottaghy et al., 1999; Mottaghy, Sparing, & Töpper, 2006; Sparing et al., 2001; Töpper, Mottaghy, Brügmann, Noth, & Huber, 1998). These first studies examined the effect of TMS on Broca's and Wernicke' area in relation to timing, frequency and intensity of stimulation. TMS involves an ultra-short electromagnetic pulse that creates an electric current in superficial cortical nerve tissue. Notably, the pulses can be applied during (i.e., online) or preceding the execution of a task (i.e., offline). The electric current created by the pulse is able to directly influence neural excitability levels in a relatively focal manner (Bestmann, 2008; O'Shea & Walsh, 2007; Walsh & Cowey, 1998; Walsh & Rushworth, 1999), and allows researchers to directly interfere with underlying activity of the targeted tissues and study its effects on language processes.

Töpper et al. (1998) were among the first to report shorter naming latencies when a TMS pulse to the posterior superior temporal gyrus (pSTG) preceded picture presentation by 1000 or 100 ms. Mottaghy et al. (1999) applied 20 Hz TMS for two seconds and found a decrease in picture naming latencies immediately following stimulation of Wernicke's, but not Broca's area. This finding was replicated by Sparing et al. (2001). Importantly, this study showed that low-frequency TMS (1 Hz for 40 seconds) did not affect naming latencies. The three studies contributed to the development of possible mechanisms underlying the effects of TMS on

---

* Please address correspondence to Jana Klaus (j.klaus@donders.ru.nl).

picture naming in healthy speakers: Stimulation of Wernicke's area in the pSTG facilitated naming, whereas no effect at the inferior frontal gyrus (IFG, i.e., Broca's area) was found.

Subsequent TMS studies have further established a direct relation between the left anterior temporal lobe (ATL; Pobric, Jefferies, & Lambon Ralph, 2007, 2010), left middle temporal gyrus (MTG; Acheson, Hamidi, Binder, & Postle, 2011; Schuhmann, Schiller, Goebel, & Sack, 2012), and left IFG (Schuhmann, Schiller, Goebel, & Sack, 2009; Shinshi et al., 2015; Wheat et al., 2013) in picture naming. Of note, event-related single- and triple-pulse TMS studies have provided a more fine-grained picture with respect to the temporal dynamics of picture naming, locating the involvement of the IFG at around 300 ms after picture onset, whereas MTG and STG may function as a feed-forward monitoring system around this time point. In spite of these effects, only half of the studies were sham-controlled (Schuhmann et al., 2009; Shinshi et al., 2015; Wheat et al., 2013), leaving open the possibility that the observed TMS effects are confounded by procedural effects. In addition, it remains unclear why the first studies targeting pSTG yielded a naming advantage (i.e., shorter naming latencies) while the other studies in fact reported slower naming latencies, both for STG, but also for IFG, MTG, and ATL stimulation.

Next to TMS, another means to modulate cortical excitability is to apply a constant weak electric current between two electrodes affixed on the scalp. Although the vast majority of the electric field is shunted, a small yet significant portion of the field reaches the superficial layers of the cortex (Nitsche et al., 2008). Research on the human motor cortex has shown that anodal tDCS increases spontaneous neural firing and cortical excitability, while cathodal tDCS reduced spontaneous neural firing and lowered cortical excitability (Nitsche & Paulus, 2000; Stagg & Nitsche, 2011). Its potential to modulate underlying cortical tissue together with the facts that tDCS is not associated with serious adverse advents and allows for better (double) blinding procedures as compared to TMS has contributed to its increased use in cognitive neuroscience.

Sparing, Dafotakis, Meister, Thirugnanasambandam, & Fink (2008) investigated the influence of Wernicke's area in object naming by applying anodal, cathodal, or sham tDCS to the STG. Anodal as compared to sham tDCS resulted in faster naming latencies immediately after stimulation had ended. However, this effect was not observed anymore five minutes after stimulation, suggesting that the influence of anodal tDCS on naming can be short-lived. No effects were observed for cathodal tDCS. The authors compared this observation to the null effect obtained from low-frequency rTMS found in their earlier study (Sparing et al., 2001), calling into question whether the decrease in neuronal excitability caused by cathodal tDCS is transferrable to areas outside of the motor cortex.

Fertonani, Rosini, Cotelli, Rossini, & Miniussi (2010) conducted two experiments which evaluated the effects of offline anodal, cathodal, or sham tDCS to the left dorsolateral prefrontal cortex (DLPFC) on object and action naming. Eight minutes of stimulation did not induce any direct effects in Experiment 1, whereas ten minutes of stimulation in Experiment 2 did yield a significant effect. Compared to sham stimulation, anodal stimulation reliably decreased naming latencies for both object and action naming, while no substantial effect from cathodal tDCS was found. In a follow-up study, Fertonani, Brambilla, Cotelli, & Miniussi (2014) replicated the facilitating effect of anodal tDCS in action and object naming, both in younger and older adults.

By contrast, a recent study reports a series of experiments which failed to show an effect of anodal tDCS on picture naming (Westwood, Olson, Miall, Nappo, & Romani, 2017). Factors including stimulation site, stimulation intensity, surface area of the active electrode, and position of the reference electrode could not explain the absence of effects. The authors concluded that the effectiveness of anodal tDCS as a research method in healthy participants needs further investigation. However, the findings from this study have been challenged by Gauvin, Meinzer, & de Zubicaray (2017), who argue that the null effects can at least in part be attributed to stimulating a cortical region (i.e., left IFG) which is not involved in semantic processing. Next to the classic picture naming tasks reviewed above, a number of studies have also investigated the effects of tDCS and TMS on naming latencies in the semantic blocking and picture-word interference paradigm. In semantic blocking tasks, naming latencies are compared between semantically homogeneous blocks (i.e., containing words from the same semantic category) and heterogeneous blocks (i.e., semantically unrelated words). Retrieving and producing semantically related words in a row typically results in longer naming latencies compared to producing semantically unrelated words. This semantic interference (SI) effect is taken as evidence for competitive selection of target responses (e.g., Belke, Meyer, & Damian, 2005; Damian, Vigliocco, & Levelt, 2001; Kroll & Stewart, 1994). Wirth et al. (2011) report a reduced SI effect during anodal tDCS to the DLPFC. Pisoni, Papagno, & Cattaneo (2012) found a larger SI effect following anodal tDCS to the pSTG, but the SI effect disappeared following anodal tDCS to the IFG. Averaged across conditions, naming latencies increased after pSTG, but decreased after IFG stimulation. Krieger-Redwood & Jefferies (2014) found no effect of inhibitory TMS to either the IFG or the pMTG on the difference between semantically related and unrelated blocks compared to baseline performance (i.e., prior to the application of TMS). However, for both sites, the semantic facilitation effect often observed in the first cycle of the task (i.e., a naming advantage in semantically related cycles compared to unrelated cycles; Damian & Als, 2005) was decreased after TMS. Finally, Meinzer, Yetim, McMahon, & de Zubicaray (2016) report a reduced SI effect during anodal tDCS to the IFG in the second, third and fourth naming cycle only, while anodal tDCS to the MTG reduced the SI effect from the second cycle onwards. Taken together, these studies provide first evidence that processes involving lexical selection and retrieval can be targeted using NIBS. However, it should be kept in mind that these behavioral effects were numerically small (see also Westwood et al., 2017, Experiment 2, for statistical null effects of tDCS across the left IFG in a semantic blocking task).

The picture-word interference (PWI) paradigm allows for the chronometric investigation of speech production processes on the timescale of tens of milliseconds (e.g., Damian & Martin, 1999; Schriefers, Meyer, & Levelt, 1990). Participants are asked to name pictures while ignoring a visually or auditorily presented distractor word, the relatedness of which to the target word is systematically varied. Typically, a semantically related distractor (e.g., *"cow"* when the target word is *"sheep"*) increases naming latencies compared to an unrelated distractor, while a phonologically related distractor (e.g., *"sheet"*) speeds up naming latencies. Varying the onset of the distractor relative to picture presentation (stimulus-onset asynchrony, SOA) enables researchers to examine the time course of speech planning with respect to the individual representational levels involved. In recent years, a number of tDCS studies also made use of the PWI paradigm to study language production at different representational levels. Holland et al. (2011) reported faster naming latencies during anodal tDCS across Broca's area compared to sham stimulation when the presentation of the to-be-named picture was accompanied by either a noise cue or the target word itself. This behavioral facilitation effect was accompanied by a decrease in the BOLD signal measured during the production task (see also Holland, Leff, Penny, Rothwell, & Crinion, 2016). Henseler, Mädebach, Kotz, & Jescheniak (2014) report a decrease of associative facilitation (i.e., when the distractor is associatively related vs. unrelated to the target word, e.g. *"boat"* and *"port"*) under MTG as opposed to IFG and sham stimulation (anodal tDCS), but no effect of stimulation on the SI effect. Finally, Pisoni, Cerciello, Cattaneo, & Papagno (2017) found reduced phonological facilitation following anodal tDCS to the STG, but no such effect when IFG was stimulated. Notably, the two studies targeting specific representational stages (i.e., the lexical-semantic and the phonological stage, respectively) did not find a main effect of stimulation, but an interaction of stimulation and relatedness. Together these studies suggest that tDCS may be a suitable technique to study speech planning on a level that is more detailed than that provided by simple picture naming tasks.

Next to variations of picture naming tasks, a number of studies has also measured performance changes to TMS or tDCS in semantic fluency tasks (see also Horvath et al., 2015; Price et al., 2015). In semantic fluency tasks, participants are asked to produce as many words as possible from a given semantic category or starting with a given letter within a time constraint. High fluency scores reflect unimpaired speech production on the semantic or phonological level, respectively. Previous studies investigating the effect of tDCS on verbal fluency have provided ambiguous results. While some studies report increased verbal fluency during or after DC stimulation (IFG: Cattaneo, Pisoni, & Papagno, 2011; Iyer et al., 2005; Penolazzi, Pastore, & Mondini, 2013; Pisoni, Mattavelli, et al., 2017; DLPFC: Vannorsdall et al., 2012), others did not obtain such an effect (IFG: Ehlis, Haeussinger, Gastel, Fallgatter, & Plewnia, 2016; Vannorsdall et al., 2016; DLPFC: Cerruti & Schlaug, 2009).

To date, there are still many unknowns about the influence of different stimulation parameters on the behavioral (language production) effect induced by NIBS. Both TMS and tDCS have been able to alter naming performance in healthy participants using a number of different paradigms, but on the other hand, also null effects have been reported. In order to quantify the overall effect of NIBS observed across studies and to examine individual subsets contrasting different experimental parameters, we performed a meta-analysis evaluating the behavioural performance changes during language production tasks in healthy participants. With respect to language production, rather small effect sizes of tDCS treatment for clinically relevant populations (Hartwigsen & Siebner, 2013) raise the question whether this method is a useful tool in altering language production in healthy speakers, and previous meta-analyses which investigated fewer studies are inconclusive (Horvath et al., 2015; Price et al., 2015; Westwood & Romani, 2017). Here, unlike these previous studies, we investigated the absolute effect sizes obtained by the application of tDCS or TMS. The direction of behavioural effects caused by NIBS (i.e., improving or disrupting performance) is difficult to predict. We therefore were interested in the question whether NIBS changes overall performance compared to a baseline condition, regardless of whether this change is positive or negative.

Furthermore, to our knowledge, no meta-analysis has yet quantified the efficacy of TMS on inducing changes in language production in healthy speakers. Finally, by contrasting subsets of studies in regard to a number of methodological aspects (i.e., stimulation site, control condition, experimental tasks), we intend to provide a more detailed picture of the usefulness of applying NIBS in healthy speakers.

Methods

Study selection and analysis

To find eligible studies, we first conducted a literature search in PubMed, querying for the search terms "language" and "tDCS" or "TMS" published up until November 2017. This query yielded 550 results, whose abstracts and titles were screened for eligibility. Additionally, the reference lists of previous reviews and meta-analyses (Hartwigsen, 2015; Horvath et al., 2015; Monti et al., 2013; Price et al., 2015) were screened to avoid overlooking suitable studies. Eligibility criteria were the following:

(1) A single session of tDCS or TMS was applied to the left hemisphere of the cerebral cortex in right-handed participants (thus excluding the part of the study by Smirni et al., 2017, which targeted the right lateral prefrontal cortex);

(2) Participants were adult healthy, young native speakers (we thus excluded studies testing older participants; Fertonani, Brambilla, Cotelli, & Miniussi, 2014; Holland et al., 2011; Lifshitz-Ben-Basat & Mashal, 2017);

(3) The main dependent variable was either naming latency or performance in a verbal fluency task;

(4) The stimuli were either categories or letters (for the verbal fluency tasks), or pictures triggering single-word utterances (i.e., nouns or verbs, for picture-naming tasks). Studies using printed words as stimuli were omitted in order to avoid potential confounds with reading ability (Cappelletti, Fregni, Shapiro, Pascual-Leone, & Caramazza, 2008; Nozari & Thompson-Schill, 2013; Pope & Miall, 2012; Runnqvist et al., 2016; Shapiro et al., 2001; Spielmann et al., 2017; Tremblay & Gracco, 2009), as were studies that required the production of multi-word utterances (Arnold & Nozari, 2017; Nozari, Arnold, & Thompson-Schill, 2014) or in which a mixture of verbal fluency and picture naming was used (Jeon & Han, 2012);

(5) All relevant data were provided either in the paper or by the authors upon request, or could be extracted from figures in the publication. The data of four studies could not be provided in time due to technical or logistical reasons and were thus excluded from the analysis (Cerruti & Schlaug, 2009, Exp. 2; Iyer et al., 2005; Mottaghy et al., 2006; Töpper et al., 1998);

(5) The article was published in a peer-reviewed English-language journal;

(6) The study was approved by a medical ethical committee or review board.

Data synthesis and analysis

The literature search identified 28 eligible studies. For these studies, the means, standard deviations, and sample sizes for all experimental and control conditions were collected (naming latencies for the picture naming tasks and number of words generated for the verbal fluency tasks). If this information was provided in graphs rather than tables, the relevant values were extracted using the software Plot Digitizer (http://plotdigitizer.sourceforge.net/). Additionally, if the reported data were not sufficient or inconsistent, the corresponding author of the paper in question was contacted and asked to provide this information. If an experiment reported several conditions (e.g., in terms of semantic category and naming cycle for semantic blocking tasks or in terms of different distractor conditions in PWI tasks), the reported values were averaged for the stimulation and the control condition in order to receive an estimate of overall effect of stimulation. All data points were coded in terms of their treatment (TMS vs. tDCS), the task used (picture naming, semantic blocking, picture-word interference, or semantic fluency), the stimulated brain region (IFG, MTG, STG, DLPFC, IPL, or ATL), and the control condition (sham vs. no stimulation).

For all reported comparisons (i.e., stimulation vs. control conditions) we calculated Hedge's *d*. This is an adaptation of Hedge's *g* (Hedges & Olkin, 1985) – calculated as the difference between the mean of the experimental condition and the mean of the control condition, divided by the pooled standard deviation – which takes into account the often low sample sizes in previously published stimulation studies by multiplying the effect size with a small sample size correction. We were interested in the magnitude of the effect so we calculated the absolute effect size values. In order to avoid entering several data points from one experiment into the analysis, effect sizes originating from a single experiment were aggregated to yield a single measure per experiment. However, if several control conditions were tested which allowed for a more specific comparison of experimental variables (e.g., comparing cathodal and anodal stimulation, or different brain regions within one experiment), separate effect sizes per experiment were entered into the analysis. Two studies (Schuhmann et al., 2009, 2012) included the same results of IFG stimulation during picture naming and were only entered once into the analysis. Results from MTG and STG stimulation as compared to no stimulation were entered as two separate data points.

We computed the cumulative effect size (i.e., the aggregated magnitude of the included studies' effect sizes, $\bar{E}$) and the 95% confidence intervals (CI) using a weighted average (Hedges & Olkin, 1985). All effect sizes were entered in a random effects model. As estimates of study heterogeneity, we report total

Table 1. Overview of the studies included in the meta-analysis.

study	stimulation details	target area*	task	*N*	sham?	behavioural effect of stimulation
(1) Acheson, Hamidi, Binder, & Postle (2011)	TMS, 10 Hz, 100 ms before picture onset, 100 % MT	MTG (−69, −39, −2)	picture naming	12	no	shorter naming latencies and speech duration following TMS
(2) Acheson, Hamidi, Binder, & Postle (2011)	TMS, 10 Hz, 100 ms before picture onset, 110 % MT	STG (−64, −38, −13)	picture naming	same as (1)	no	no effect
(3) Cattaneo, Pisoni, & Papagno (2011)	tDCS, anodal, offline (20 min), 2 mA, rSO region as reference	IFG (between T3-Fz and F7-Cz)	verbal fluency (semantic and phonemic)	10	yes	higher fluency scores following tDCS
(4) Cerruti & Schlaug (2009)	tDCS, anodal and cathodal, online, 1 mA, rSO region as reference	DLPFC (F3)	verbal fluency (phonemic)	18	yes	no effect
(5) Ehlis, Haeussinger, Gastel, Fallgatter, & Plewnia (2016)	tDCS, anodal, offline (20 min), 1 mA, rSO region as reference	IFG (between C3, F3 and F7)	verbal fluency (semantic and phonemic)	23	yes	no effect
(6) Ehlis, Haeussinger, Gastel, Fallgatter, & Plewnia (2016)	tDCS, cathodal, offline (20 min), 1 mA, rSO region as reference	IFG (between C3, F3 and F7)	verbal fluency (semantic and phonemic)	23	yes	no effect
(7) Fertonani, Rosini, Cotelli, Rossini, & Miniussi (2010), Exp. 1	tDCS, anodal and cathodal, offline (8 min), 2 mA, right shoulder as reference	DLPFC (8 cm frontally and 6 cm laterally away from Cz)	picture naming	12	yes	overall no effect, when calculating difference scores to account for between-participant variability: faster naming latencies following anodal tDCS, no effect of cathodal tDCS
(8) Fertonani, Rosini, Cotelli, Rossini, & Miniussi (2010), Exp. 2	tDCS, anodal and cathodal, offline (10 min), 2 mA, right shoulder as reference	DLPFC (8 cm frontally and 6 cm laterally away from Cz)	picture naming	12	yes	faster naming latencies following anodal tDCS, no effect of cathodal tDCS
(9) Fertonani, Brambilla, Cotelli, & Miniussi (2014)	tDCS, anodal, online and offline (10 min), 2 mA, right shoulder as reference	DLPFC (8 cm frontally and 6 cm laterally away from Cz)	picture naming	20	yes	faster naming latencies during and following anodal tDCS
(10) Henseler, Mädebach, Kotz, & Jescheniak (2014)	tDCS, anodal, online, 2 mA, rSO region as reference	IFG (−50, 15, 29) MTG (−56, −48, −2)	PWI (associative and semantic)	36	yes	no main effect of tDCS associative facilitation during IFG and sham tDCS, but not during MTG tDCS no effect of tDCS on semantic interference

(11) Krieger-Redwood & Jefferies (2014)	TMS, 1 Hz, offline, 10 min, 120 % MT	IFG (−45, 19, 18)	semantic blocking	16	no	no main effect of TMS reduced semantic facilitation in first cycle following TMS
(12) Krieger-Redwood & Jefferies (2014)	TMS, 1 Hz, offline, 10 min, 120 % MT	MTG (−54, −49, −2)	semantic blocking	same as in (11)	no	no main effect of TMS reduced semantic facilitation in first cycle following TMS
(13) Meinzer et al. (2012)	tDCS, anodal, online, 1 mA, rSO region as reference	IFG (between T3-F3 and F7-C3 and midpoint between F7-F3)	verbal fluency (semantic)	20	yes	higher fluency scores during tDCS
(14) Meinzer, Yetim, McMahon, & de Zubicaray (2016)	tDCS, anodal, online, 1mA, rSO region as reference	IFG (between T3-Fz and F7-Cz) STG (−53, −46, −5)	semantic blocking	24	yes	no overall effect of tDCS reduced semantic interference during IFG tDCS in cycles 2 – 4 reduced semantic interference during MTG tDCS in cycles 2 – 6
(15) Mottaghy et al. (1999)	TMS, 20 Hz, offline (2s), 55% MSO	IFG (between F5 and F7) STG (Cp5)	picture naming	16	yes	faster naming latencies immediately after STG tDCS no effect of IFG tDCS
(16) Penolazzi, Pastore, & Mondini (2013)	tDCS, anodal, offline (20min), 2mA, varying reference positions	IFG (between T3-F3 and F7-C3)	verbal fluency (semantic)	90	yes	higher fluency scores following tDCS with rSO region as reference in second post-measurement (i.e., about 18min after stimulation)
(17) Pisoni, Papagno, & Cattaneo (2012), Exp. 1	tDCS, anodal, offline (20min), 2mA, rSO region as reference	STG (−53, −46, −5)	semantic blocking	12	yes	longer naming latencies following tDCS larger semantic interference following tDCS
(18) Pisoni, Papagno, & Cattaneo (2012), Exp.2	tDCS, anodal, offline (20 min), 2 mA, rSO region as reference	IFG (between T3-Fz and F7-Cz)	semantic blocking	12	yes	shorter naming latencies following tDCS no effect on semantic interference
(19) Pisoni, Cerciello, Cattaneo, & Papagno (2017), Exp. 1	tDCS, anodal, offline (20 min), 2 mA, rSO region as reference	STG (CP5)	PWI (phonological)	12	yes	reduced phonological facilitation following tDCS
(20) Pisoni, Cerciello, Cattaneo, & Papagno (2017), Exp. 2	tDCS, anodal, offline (20 min), 2 mA, rSO region as reference	IFG (between Fz-T3 and Cz-F7)	PWI (phonological)	12	yes	no effect of tDCS on phonological effect overall, slower naming latencies following anodal tDCS

(21) Pisoni, Mattavelli, et al. (2017)	tDCS, anodal, offline (20 min), 0.75 mA, rSO as reference	IFG (n/a)	verbal fluency (phonemic and semantic)	18	yes	higher fluency rate following tDCS
(22) Pobric, Jefferies, & Lambon Ralph (2007)	TMS, 1Hz, offline (10 min), 120 % MT	ATL (−53, 4, −32)	picture naming	10	no	slower naming latencies following TMS
(23) Pobric, Jefferies, & Lambon Ralph (2010)	TMS, 1Hz, offline (10 min), 120 % MT	ATL (−53, 4, −32)	picture naming	9	no	slower naming latencies following TMS
(24) Pobric, Jefferies, & Lambon Ralph (2010)	TMS, 1Hz, offline (10 min), 120 % MT	IPL (−49, −44, 48)	picture naming	9	no	slower naming latencies following TMS
(25) Schuhmann, Schiller, Goebel, & Sack (2009)	triple-pulse TMS 150, 225, 300, 400, or 525 ms after picture onset, 40 Hz, online, 120 % MT	IFG (−51, 13, 24)	picture naming	10	yes	no main effect of stimulation increased naming latencies following TMS at 300ms after picture onset
(26) Schuhmann, Schiller, Goebel, & Sack (2012)	triple-pulse TMS 150, 225, 300, 400, or 525 ms after picture onset, 40 Hz, online, 120 % MT	MTG (−59, −45, 16)	picture naming	same as (25)	no	no main effect of stimulation increased naming latencies following TMS at 225 ms and 400 ms after picture onset
(27) Schuhmann, Schiller, Goebel, & Sack (2012)	triple-pulse TMS 150, 225, 300, 400, or 525 ms after picture onset, 40 Hz, online, 120 % MT	STG (−57, −45, 16)	picture naming	same as in (25)	no	no main effect of TMS increased naming latencies following TMS at 400 ms after picture onset
(28) Shinshi et al. (2015)	triple-pulse TMS 150, 225, 300, 375, or 450 ms after picture onset, 40 Hz, online, 100 % MT	IFG (−49, 24, 19)	picture naming	12	yes	no main effect of TMS increased naming latencies following TMS 300 and 375 ms after picture onset
(29) Smirni et al. (2017)	TMS, 1 Hz, offline, 90 % MT	~IFG (F7)	verbal fluency (phonemic)	22	yes	lower fluency rate following TMS
(30) Sparing et al. (2001), Exp. 1	TMS, 1 Hz, offline (40 s), 55 % MSO	IFG (between F5 and F7) STG (CP5)	picture naming	10	yes	no effect
(31) Sparing et al. (2001), Exp. 2	TMS, 20 Hz, offline (2 s), 35 %, 45 %, and 55 % MSO	STG (CP5)	picture naming	6	yes	shorter naming latencies 1 min after TMS at 55% MSO
(32) Sparing, Dafotakis, Meister,	tDCS, anodal, online (7 min) and offline, 2 mA,	STG (CP5)	picture naming	15	yes	no main effect of tDCS shorter naming latencies directly after

Thirugnanasambandam, & Fink (2008)	right frontopolar cortex as reference					anodal tDCS
(33) Vannorsdall et al. (2012)	tDCS, anodal, online, 1 mA, vertex as reference	DLPFC (F3)	verbal fluency (phonemic and semantic)	12	yes	no main effect of tDCS higher fluency rate in semantic task during stimulation
(34) Vannorsdall et al. (2012)	tDCS, cathodal, online, 1 mA, vertex as reference	DLPFC (F3)	verbal fluency (phonemic and semantic)	12	yes	no main effect of tDCS descriptively, lower fluency rate in phonemic task during tDCS
(35) Vannorsdall et al. (2016)	tDCS, anodal, offline (20 min), 2 mA, rSO as reference	IFG (between T3-Fz and F7-Cz)	verbal fluency (phonemic and semantic)	14	yes	no effect
(36) Westwood, Olson, Miall, Nappo, & Romani (2016), Exp. 1A	tDCS, anodal, online, 1 mA, rSO region as reference	IFG (F7)	picture naming	18	yes	no effect
(37) Westwood, Olson, Miall, Nappo, & Romani (2016), Exp. 1B	tDCS, anodal, online, 1.5 mA, rSO region as reference	IFG (F7)	picture naming	20	yes	no effect
(38) Westwood, Olson, Miall, Nappo, & Romani (2016), Exp. 1B	tDCS, anodal, online, 1.5 mA, right cheek as reference	MTG (between T3 and T5)	picture naming	18	yes	no effect
(39) Westwood, Olson, Miall, Nappo, & Romani (2016), Exp. 2	tDCS, anodal, online, 1.5 mA, rSO region as reference	IFG (F7)	semantic blocking	17	yes	no effect
(40) Wheat et al. (2013)	single-pulse TMS 75, 100, 125, 225, 300, or 500 ms after picture onset, online, 150 % MT	IFG (−40, 5, −7)	picture naming	10	yes	no main effect of TMS longer naming latencies following stimulation at 225 and 300 ms after picture onset
(41) Wirth et al. (2011)	tDCS, anodal, online, 1.5 mA, right shoulder as reference	DLPFC (between F3 and AF3)	semantic blocking	20	yes	no main effect of stimulation smaller semantic interference during stimulation
(42) Wirth et al. (2011)	tDCS, anodal, offline (≈37 min, i.e., following experiment (41)), 1.5 mA, right shoulder as reference	DLPFC (between F3 and AF3)	picture naming	same as (41)	yes	no effect

Note. All target areas refer to the left hemisphere. IFG = inferior frontal gyrus; STG = superior temporal gyrus; MTG = medial temporal gyrus; ATL = anterior temporal lobe; DLPFC = dorsolateral prefrontal cortex; IPL = inferior parietal lobule; rSO region = right supraorbital region. MT = motor threshold; MSO = maximum stimulator output. PWI = picture-word interference.

* MNI coordinates or positions according to the 10-20 EEG referencing system are provided.

heterogeneity of the effect sizes (Q_T), which is tested against the χ^2 distribution with $n - 1$ degrees of freedom.

All effect size calculations and summary analyses were conducted using *MetaWin* (version 2.1, Rosenberg, Adams, & Gurevitch, 2000) and the *metafor* package (version 1.9-9, Viechtbauer, 2010) in *R* (version 3.3.3, R Core Team, 2017). Additional ANOVAs were run using the *ez* package (version 4.4.0, Lawrence, 2016).

Results

In total, 42 effect sizes originating from 28 studies including 642 healthy participants were analysed (Table 1). None of the studies reported any adverse events after applying stimulation. A significant effect of NIBS was found for behavioural performance ($Z = 4.780$, $p < .0001$), indicating that applying NIBS is capable of modulating speech production processes in healthy speakers. The overall weighted mean effect size for all included studies was 0.271 (95% CI: 0.160 – 0.382). The test for heterogeneity was not significant ($Q_T = 20.724$, $p = .997$), showing that the variance between studies was not larger than is to be expected when including random sample error. Rosenberg's fail-safe number for all studies was 208, implying that at least 208 studies publishing null effects would be required to invalidate the significant effect of NIBS on behavioural performance in language production. Figure 1 displays the effect sizes and 95% confidence intervals for all included studies.

Overall, our results suggest that NIBS appears to be an effective tool to modulate behaviour even in healthy participants. It should however be noted that the applied tDCS and TMS parameters used in the studies vary considerably. We therefore performed additional analyses to examine differences between stimulation type (tDCS vs. TMS), stimulation area (frontal vs. temporal), the applied control condition (sham vs. no stimulation), and task (picture naming vs. verbal fluency). The results for these sub-analyses are summarised in Table 2.

TMS vs. tDCS

In order to investigate the efficacy of stimulation separately for TMS ($N = 16$) and tDCS ($N = 26$), respectively, separate meta-analyses were performed for the two stimulation techniques. The outcomes revealed significant weighted mean effect sizes of 0.225 (95% CI: 0.094 – 0.356) for the tDCS studies and 0.388 (95% CI: 0.178 – 0.598) for the TMS studies. Furthermore, an ANOVA comparing the effect sizes yielded a significant main effect of stimulation type ($F(1,40) = 5.394$, $p = .025$, $\eta^2_G = .119$), indicating that the effect sizes for the TMS studies were significantly higher than those for the tDCS studies. Importantly, for the TMS group, we pooled studies applying low-frequency (1 Hz) rTMS

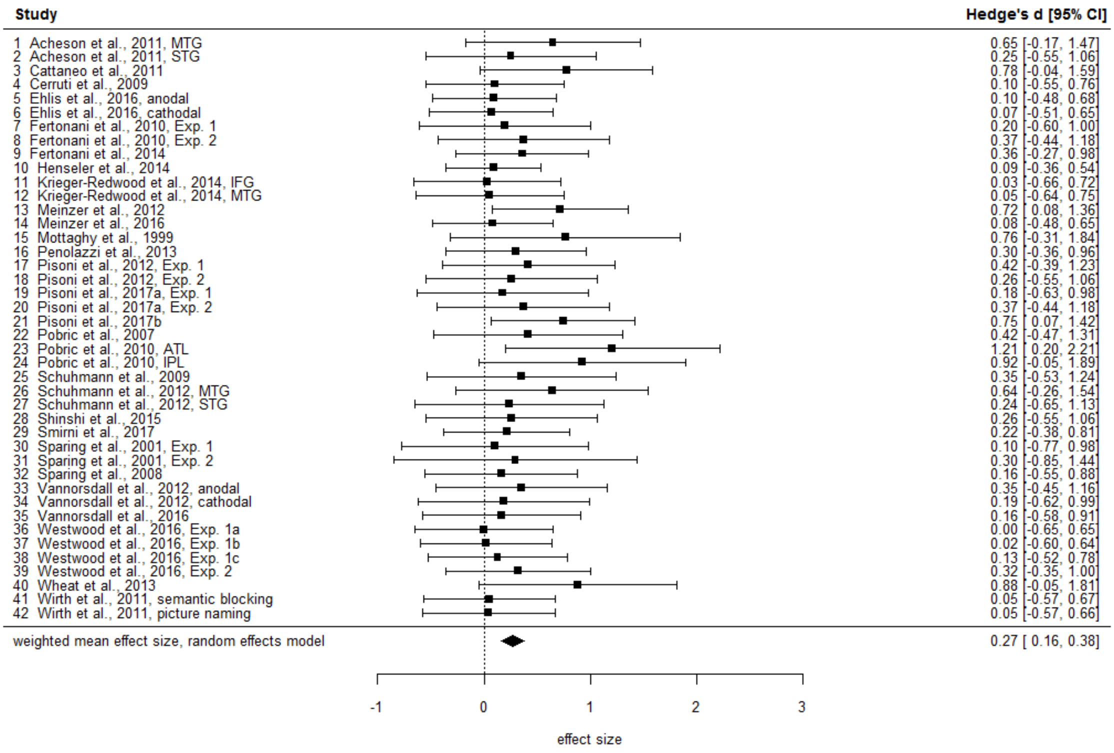

Figure 1. Forest plot of the effect sizes of the studies included in the meta-analysis investigating the efficacy of non-invasive brain stimulation as a tool of investigating language production in healthy participants.

with studies using high-frequency (≥ 10 Hz) single- or triple-pulse TMS, which have different effects on cortical excitability. However, further subdividing the TMS studies was not meaningful given the very small sample sizes. Despite the larger effect sizes of TMS as to tDCS, this finding should be thus treated with caution.

Frontal vs. temporal NIBS

The majority of the studies targeted areas within the left frontotemporal language network. To investigate whether one of these regions is more susceptible to NIBS, we selected studies targeting frontal regions including the left dorsolateral prefrontal cortex and the left inferior frontal gyrus ($N = 25$), and temporal regions including the left middle and superior temporal gyrus and left anterior temporal lobe ($N = 15$). An ANOVA comparing the effect of brain stimulation on these two regions provided no evidence for differences in effect sizes ($F(1,38) = 0.940$, $p = .338$, $\eta^2_G = .024$). That is, both frontal and temporal NIBS influence language production in healthy speakers, but there is no quantitative difference in the magnitude of the effect between the two target locations (for frontal regions: $\bar{E} = 0.252$, 95% CI: 0.113 – 0.391; for temporal regions: $\bar{E} = 0.289$, 95% CI: 0.090 – 0.489).

Sham vs. no stimulation as a control condition

To investigate a possible difference in NIBS efficacy depending on type of control condition, we compared studies that were sham-controlled ($N = 33$) to those that were not ($N = 9$). An ANOVA yielded a significant main effect of control condition ($F(1,40) = 3.778$, $p = .059$, $\eta^2_G = .086$), and separate summary analyses revealed a larger effect size for studies which were not sham-controlled ($\bar{E} = 0.409$, 95% CI: 0.132 – 0.687) compared to those that were ($\bar{E} = 0.245$, 95% CI: 0.123 – 0.366). Notably, the variance of the studies without a sham condition was much higher. Overall, this suggests that a sham condition is needed in order to detect the often subtle effects of real stimulation.

Picture naming vs. verbal fluency

To examine whether NIBS is more efficient for verbal fluency or picture naming tasks, we compared studies measuring verbal fluency ($N = 8$) with pure picture naming studies ($N = 20$; excluding picture-word interference and semantic blocking tasks to avoid potential confounds due to additional experimental conditions). An ANOVA provided no evidence for a difference in effect sizes between these types of tasks ($F < 1$). Separate summary analyses yielded descriptively comparably effect sizes and confidence intervals for verbal fluency tasks ($\bar{E} = 0.316$, 95% CI: 0.114 – 0.518) and picture naming tasks ($\bar{E} = 0.319$, 95% CI: 0.146 - 493).

Discussion

The current combined review and meta-analysis evaluated the efficacy of non-invasive brain stimulation on performance changes in language production tasks in healthy speakers. As we have reviewed in the first part, a number of studies which investigated the effects of NIBS on language production performance in healthy speakers show mixed results. Importantly, the methodological

Table 2. Results of meta-analysis, for all studies and specific subsets.

Comparison	N	$\bar{E}$	95% CI	Z	p	Q_T	$p(\chi^2)$	Fail-safe
overall	**42**	**0.271**	**0.160 – 0.382**	**4.780**	**< .0001**	**20.724**	**.997**	**208**
				by method				
tDCS only	26	0.225	0.094 – 0.356	3.369	< .001	10.120	.997	51
TMS only	16	0.388	0.178 – 0.598	3.627	< .001	8.943	.881	39
				by region				
frontal stimulation	25	0.252	0.113 – 0.391	3.556	< .001	11.579	.984	58
temporal stimulation	15	0.289	0.090 – 0.489	2.844	.005	7.291	.923	17
				by control condition				
sham-controlled	33	0.245	0.123 – 0.366	3.951	< .0001	13.079	.999	102
not sham-controlled	9	0.409	0.132 – 0.687	2.895	.004	6.505	.591	11
				by task				
picture naming	21	0.319	0.146 – 0.493	3.607	< .001	11.220	.940	51
verbal fluency	11	0.316	0.114 – 0.518	3.066	.002	6.371	.783	16

approaches vary substantially between studies as well, for example, with respect to the stimulation technique, site, duration, control condition and behavioural paradigm. While there is study-specific evidence for the efficacy of NIBS in language production research, the methodological variability between studies is large. As a result, it is not clear to what extent these differences affect the behavioural outcome.

To this end, we meta-analysed the effect sizes from studies measuring picture naming latencies or verbal fluency scores in healthy participants in which either TMS or tDCS was applied to probe the causal involvement of specific cortical areas in unimpaired language production. The overall effect size for all studies combined was small, but comparable to the results found in other meta-analyses investigating the influence of NIBS on cognitive function in healthy participants (e.g., Brunoni & Vanderhasselt, 2014; Dedoncker, Brunoni, Baeken, & Vanderhasselt, 2016; Hill, Fitzgerald, & Hoy, 2016; Mancuso, Ilieva, Hamilton, & Farah, 2016; Schutter & Wischnewski, 2016). A potential reason for this relatively small effect size is that no clear-cut experimental standards exist. This introduces a large methodological variability between studies, which hampers both their comparability as well as the efficacy of the stimulation to effectively induce performance changes. For instance, for TMS studies, no valid threshold procedure (like motor-evoked potentials for the motor cortex or phosphene induction for the visual cortex) exists to reliably determine individual thresholds. Previous research on language production used stimulation intensities between 100 and 120 % MT or fixed stimulation output for all participants. In both cases, however, it is unclear if such a measure is the most reliable way to stimulate areas outside of the motor cortex. Inducing speech arrest may be a possible way of quantifying individual "speech thresholds". Following Pascual-Leone, Gates, & Dhuna (1991), who had successfully induced speech arrest in epileptic patients by applying rTMS to Broca's area, Epstein et al. (1996) contrasted the effect of stimulation frequencies between 4 and 32 Hz in a counting task. They found that applying 20 or 40 pulses over a period of five seconds (i.e., at 4 and 8 Hz, respectively) allowed for the induction of complete speech arrest without excessive muscle disturbances or pain sensations of the participants, which led the authors to conclude that this frequency was suitable for widespread application, e.g., to measure speech lateralization (see also Epstein et al., 1999). However, to the best our knowledge, none of the TMS studies that investigated language production in healthy participants has used this procedure. Similarly, for tDCS studies, individual cortical susceptibility to stimulation may differ (Parazzini, Fiocchi, Liorni, & Ravazzani, 2015), inducing different levels of excitability between participants. Also, the placement of the reference electrode, the size of both the active and the reference electrode, as well as the stimulation frequencies vary substantially between studies, which hampers comparability between studies because different montages and intensities cause different electric field distributions across the cortex.

On another note, different tasks might be differentially sensitive to performance changes induced by NIBS. We have shown that performance in both verbal fluency and pure picture naming tasks can be effectively modulated using NIBS. However, we cannot make a conclusive point with respect to the efficacy of NIBS in more specific picture naming paradigms (i.e., PWI, semantic blocking), as we have focused our analysis on the *overall* effect of NIBS as opposed to more specific experimental conditions. Westwood & Romani (2017) provide some evidence that at least tDCS may not be useful for examining semantically specific effects during language production. However, it should be noted that their analysis is based on a small number of experiments, so clearly more studies are needed before definitive conclusions can be drawn.

It needs to be noted that the apparent advantage of TMS over tDCS is confounded with the application of a proper sham condition. While the case numbers show that applying sham stimulation as a control condition is more common practice, the current finding underlines the importance of including an appropriate control condition to properly evaluate the effect of real stimulation. While some studies use so-called placebo coils or stimulate several areas (i.e., including at least one control region which is not expected to affect the outcome), many studies so far have only compared performance with real TMS to performance *without* the application of TMS. As we have shown, not applying sham, which in fact was only the case for TMS studies, substantially inflates the effect size while decreasing the reliability of the stimulation. Evidently, in these cases, participants know when they are being stimulated and this could bias the results. These results further underline the necessity to apply a sham stimulation or an active control site as control conditions.

In conclusion, NIBS is a viable method to investigate the relations between cortical regions and language production in healthy volunteers and can contribute to the understanding of the neurobiology underlying unimpaired language production.

Acknowledgments

We wish to thank Barry Gordon, Beth Jefferies, Katya Krieger-Redwood, Felix Mottaghy, Marcus Meinzer, Gottfried Schlaug, Teresa Schuhmann, Rudolf Töpper, Tracy Vannorsdall, Eric Wassermann, and Greig de Zubicaray for their support in providing additional data. This work was supported by the German Research Council (KL 2933/2).

References

Acheson, D., Hamidi, M., Binder, J., & Postle, B. (2011). A common neural substrate for language production and verbal working memory. *Journal of Cognitive Neuroscience*, *23*(6), 1358–1367. https://doi.org/10.1162/jocn.2010.21519

Arnold, J. E., & Nozari, N. (2017). The effects of utterance timing and stimulation of left prefrontal cortex on the production of referential expressions. *Cognition*, *160*, 127–144. https://doi.org/10.1016/j.cognition.2016.12.008

Belke, E., Meyer, A. S., & Damian, M. F. (2005). Refractory effects in picture naming as assessed in a semantic blocking paradigm. *The Quarterly Journal of Experimental Psychology Section A*, *58*(4), 667–692. https://doi.org/10.1080/02724980443000142

Bestmann, S. (2008). The physiological basis of transcranial magnetic stimulation. *Trends in Cognitive Sciences*, *12*(3), 81–83. https://doi.org/10.1016/j.tics.2007.12.002

Brunoni, A. R., & Vanderhasselt, M.-A. (2014). Working memory improvement with non-invasive brain stimulation of the dorsolateral prefrontal cortex: A systematic review and meta-analysis. *Brain and Cognition*, *86*, 1–9. https://doi.org/10.1016/j.bandc.2014.01.008

Cappelletti, M., Fregni, F., Shapiro, K., Pascual-Leone, A., & Caramazza, A. (2008). Processing Nouns and Verbs in the Left Frontal Cortex: A Transcranial Magnetic Stimulation Study. *Journal of Cognitive Neuroscience*, *20*(4), 707–720. https://doi.org/10.1162/jocn.2008.20045

Cattaneo, Z., Pisoni, A., & Papagno, C. (2011). Transcranial direct current stimulation over Broca's region improves phonemic and semantic fluency in healthy individuals. *Neuroscience*, *183*, 64–70. https://doi.org/10.1016/j.neuroscience.2011.03.058

Cerruti, C., & Schlaug, G. (2009). Anodal transcranial direct current stimulation of the prefrontal cortex enhances complex verbal associative thought. *Journal of Cognitive Neuroscience*, *21*(10), 1980–7. https://doi.org/10.1162/jocn.2008.21143

Damian, M. F., & Als, L. C. (2005). Long-Lasting Semantic Context Effects in the Spoken Production of Object Names. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *31*(6), 1372–1384. https://doi.org/10.1037/0278-7393.31.6.1372

Damian, M. F., & Martin, R. (1999). Semantic and phonological codes interact in single word production. *Journal of Experimental Psychology: Learning, Memory, and Cognition*, *25*, 1–18. https://doi.org/10.1037/0278-7393.25.2.345

Damian, M. F., Vigliocco, G., & Levelt, W. J. M. (2001). Effects of semantic context in the naming of pictures and words. *Cognition*, *81*(3), B77–B86. https://doi.org/10.1016/S0010-0277(01)00135-4

Dedoncker, J., Brunoni, A. R., Baeken, C., & Vanderhasselt, M.-A. (2016). A Systematic Review and Meta-Analysis of the Effects of Transcranial Direct Current Stimulation (tDCS) Over the Dorsolateral Prefrontal Cortex in Healthy and Neuropsychiatric Samples: Influence of Stimulation Parameters. *Brain Stimulation*, *9*(4), 501–517. https://doi.org/10.1016/j.brs.2016.04.006

Ehlis, A.-C., Haeussinger, F. B., Gastel, A., Fallgatter, A. J., & Plewnia, C. (2016). Task-dependent and polarity-specific effects of prefrontal transcranial direct current stimulation on cortical activation during word fluency. *NeuroImage*, *140*, 134–140. https://doi.org/10.1016/j.neuroimage.2015.12.047

Epstein, C. M., Lah, J. J., Meador, K. J., Weissman, J. D., Gaitan, L. E., & Dihenia, B. (1996). Optimum stimulus parameters for lateralized suppression of speech with magnetic brain stimulation. *Neurology*, *47*(6), 1590–3. https://doi.org/10.1212/WNL.47.6.1590

Epstein, C. M., Meador, K. J., Loring, D. W., Wright, R. J., Weissman, J. D., Sheppard, S., … Davey, K. R. (1999). Localization and characterization of speech arrest during transcranial magnetic stimulation. *Clinical Neurophysiology*, *110*(6), 1073–1079. https://doi.org/10.1016/S1388-2457(99)00047-4

Fertonani, A., Brambilla, M., Cotelli, M., & Miniussi, C. (2014). The timing of cognitive plasticity in physiological aging: a tDCS study of naming. *Frontiers in Aging Neuroscience*, *6*, 131. https://doi.org/10.3389/fnagi.2014.00131

Fertonani, A., Rosini, S., Cotelli, M., Rossini, P. M., & Miniussi, C. (2010). Naming facilitation induced by transcranial direct current stimulation. *Behavioural Brain Research*, *208*(2), 311–318. https://doi.org/10.1016/j.bbr.2009.10.030

Gauvin, H. S., Meinzer, M., & de Zubicaray, G. (2017). tDCS effects on word production: Limited by design? Comment on Westwood et al. (2017). *Cortex*, *96*, 137–142. https://doi.org/10.1016/J.CORTEX.2017.06.017

Hartwigsen, G. (2015). The neurophysiology of language: Insights from non-invasive brain stimulation in the healthy human brain. *Brain and Language*, *148*, 81–94. https://doi.org/10.1016/j.bandl.2014.10.007

Hartwigsen, G., & Siebner, H. R. (2013). Novel methods to study aphasia recovery after stroke.

Frontiers in Neurology and Neuroscience, *32*, 101–11. https://doi.org/10.1159/000346431

Hedges, L. V., & Olkin, I. (1985). *Statistical methods for meta-analysis*. San Diego, CA: Academic Press.

Henseler, I., Mädebach, A., Kotz, S. A., & Jescheniak, J. D. (2014). Modulating Brain Mechanisms Resolving Lexico-semantic Interference during Word Production: A Transcranial Direct Current Stimulation Study. *Journal of Cognitive Neuroscience*, *26*(7), 1403–1417. https://doi.org/10.1162/jocn_a_00572

Hill, A. T., Fitzgerald, P. B., & Hoy, K. E. (2016). Effects of Anodal Transcranial Direct Current Stimulation on Working Memory: A Systematic Review and Meta-Analysis of Findings From Healthy and Neuropsychiatric Populations. *Brain Stimulation*, *9*(2), 197–208. https://doi.org/10.1016/j.brs.2015.10.006

Holland, R., Leff, A. P., Josephs, O., Galea, J. M., Desikan, M., Price, C. J., … Crinion, J. (2011). Speech Facilitation by Left Inferior Frontal Cortex Stimulation. *Current Biology*, *21*(16), 1403–1407. https://doi.org/10.1016/j.cub.2011.07.021

Holland, R., Leff, A. P., Penny, W. D., Rothwell, J., & Crinion, J. (2016). Modulation of frontal effective connectivity during speech. *NeuroImage*, *140*, 126–133. https://doi.org/10.1016/j.neuroimage.2016.01.037

Horvath, J. C., Forte, J. D., & Carter, O. (2015). Quantitative Review Finds No Evidence of Cognitive Effects in Healthy Populations From Single-session Transcranial Direct Current Stimulation (tDCS). *Brain Stimulation*, *8*(3), 535–550. https://doi.org/10.1016/j.brs.2015.01.400

Iyer, M. B., Mattu, U., Grafman, J., Lomarev, M., Sato, S., & Wassermann, E. M. (2005). Safety and cognitive effect of frontal DC brain polarization in healthy individuals. *Neurology*, *64*(5), 872–5. https://doi.org/10.1212/01.WNL.0000152986.07469.E9

Jeon, S. Y., & Han, S. J. (2012). Improvement of the Working Memory and Naming by Transcranial Direct Current Stimulation. *Ann Rehabil Med*, *36*(5), 585–595. https://doi.org/10.5535/arm.2012.36.5.585

Krieger-Redwood, K., & Jefferies, E. (2014). TMS interferes with lexical-semantic retrieval in left inferior frontal gyrus and posterior middle temporal gyrus: Evidence from cyclical picture naming. *Neuropsychologia*, *64*, 24–32. https://doi.org/10.1016/j.neuropsychologia.2014.09.014

Kroll, J. F., & Stewart, E. (1994). Category Interference in Translation and Picture Naming: Evidence for Asymmetric Connections Between Bilingual Memory Representations. *Journal of Memory and Language*, *33*(2), 149–174. https://doi.org/10.1006/jmla.1994.1008

Lawrence, M. A. (2016). *ez: Easy Analysis and Visualization of Factorial Experiments. R package version 4.4-0.* Retrieved from https://cran.r-project.org/package=ez

Lifshitz-Ben-Basat, A., & Mashal, N. (2017). Improving Naming Abilities Among Healthy Young-Old Adults Using Transcranial Direct Current Stimulation. *Journal of Psycholinguistic Research*, 1–12. https://doi.org/10.1007/s10936-017-9516-9

Mancuso, L. E., Ilieva, I. P., Hamilton, R. H., & Farah, M. J. (2016). Does Transcranial Direct Current Stimulation Improve Healthy Working Memory?: A Meta-analytic Review. *Journal of Cognitive Neuroscience*, *28*(8), 1063–1089. https://doi.org/10.1162/jocn_a_00956

Meinzer, M., Antonenko, D., Lindenberg, R., Hetzer, S., Ulm, L., Avirame, K., … Flöel, A. (2012). Electrical Brain Stimulation Improves Cognitive Performance by Modulating Functional Connectivity and Task-Specific Activation. *The Journal of Neuroscience*, *32*(5), 1859–1866. https://doi.org/10.1523/JNEUROSCI.4812-11.2012

Meinzer, M., Yetim, Ö., McMahon, K., & de Zubicaray, G. (2016). Brain mechanisms of semantic interference in spoken word production: An anodal transcranial Direct Current Stimulation (atDCS) study. *Brain and Language*, *157*, 72–80. https://doi.org/10.1016/j.bandl.2016.04.003

Monti, A., Ferrucci, R., Fumagalli, M., Mameli, F., Cogiamanian, F., Ardolino, G., & Priori, A. (2013). Transcranial direct current stimulation (tDCS) and language. *Journal of Neurology, Neurosurgery & Psychiatry*, *84*(8), 832–842. https://doi.org/10.1136/jnnp-2012-302825

Mottaghy, F. M., Hungs, M., Brügmann, M., Sparing, R., Boroojerdi, B., Foltys, H., … Töpper, R. (1999). Facilitation of picture naming after repetitive transcranial magnetic stimulation. *Neurology*, *53*(8), 1806–12. https://doi.org/10.1212/WNL.53.8.1806

Mottaghy, F. M., Sparing, R., & Töpper, R. (2006). Enhancing Picture Naming with Transcranial Magnetic Stimulation. *Behavioural Neurology*, *17*(3–4), 177–186. https://doi.org/10.1155/2006/768413

Nitsche, M. A., Cohen, L. G., Wassermann, E. M., Priori, A., Lang, N., Antal, A., … Pascual-Leone, A. (2008). Transcranial direct current stimulation: State of the art 2008. *Brain Stimulation*, *1*(3), 206–223. https://doi.org/10.1016/j.brs.2008.06.004

Nitsche, M. A., & Paulus, W. (2000). Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *The Journal of Physiology*, *527*(3), 633–639. https://doi.org/10.1111/j.1469-7793.2000.t01-1-

00633.x

Nozari, N., Arnold, J. E., & Thompson-Schill, S. L. (2014). The effects of anodal stimulation of the left prefrontal cortex on sentence production. *Brain Stimulation*, *7*(6), 784–92. https://doi.org/10.1016/j.brs.2014.07.035

Nozari, N., & Thompson-Schill, S. L. (2013). More attention when speaking: Does it help or does it hurt? *Neuropsychologia*, *51*(13), 2770–2780. https://doi.org/10.1016/j.neuropsychologia.2013.08.019

O'Shea, J., & Walsh, V. (2007). Transcranial magnetic stimulation. *Current Biology*, *17*(6), R196–R199. https://doi.org/10.1016/j.cub.2007.01.030

Parazzini, M., Fiocchi, S., Liorni, I., & Ravazzani, P. (2015). Effect of the Interindividual Variability on Computational Modeling of Transcranial Direct Current Stimulation. *Computational Intelligence and Neuroscience*, *2015*, 963293. https://doi.org/10.1155/2015/963293

Pascual-Leone, A., Gates, J. R., & Dhuna, A. (1991). Induction of speech arrest and counting errors with rapid-rate transcranial magnetic stimulation. *Neurology*, *41*(5), 697–702. https://doi.org/10.1212/WNL.41.5.697

Penolazzi, B., Pastore, M., & Mondini, S. (2013). Electrode montage dependent effects of transcranial direct current stimulation on semantic fluency. *Behavioural Brain Research*, *248*, 129–135. https://doi.org/10.1016/j.bbr.2013.04.007

Pisoni, A., Cerciello, M., Cattaneo, Z., & Papagno, C. (2017). Phonological facilitation in picture naming: When and where? A tDCS study. *Neuroscience*, *352*, 106–121. https://doi.org/10.1016/j.neuroscience.2017.03.043

Pisoni, A., Mattavelli, G., Papagno, C., Rosanova, M., Casali, A. G., & Romero Lauro, L. J. (2017). Cognitive Enhancement Induced by Anodal tDCS Drives Circuit-Specific Cortical Plasticity. *Cerebral Cortex*. https://doi.org/10.1093/cercor/bhx021

Pisoni, A., Papagno, C., & Cattaneo, Z. (2012). Neural correlates of the semantic interference effect: New evidence from transcranial direct current stimulation. *Neuroscience*, *223*, 56–67. https://doi.org/10.1016/j.neuroscience.2012.07.046

Pobric, G., Jefferies, E., & Lambon Ralph, M. A. (2007). Anterior temporal lobes mediate semantic representation: mimicking semantic dementia by using rTMS in normal participants. *Proceedings of the National Academy of Sciences of the United States of America*, *104*(50), 20137–41. https://doi.org/10.1073/pnas.0707383104

Pobric, G., Jefferies, E., & Lambon Ralph, M. A. (2010). Category-Specific versus Category-General Semantic Impairment Induced by Transcranial Magnetic Stimulation. *Current Biology*, *20*(10), 964–968. https://doi.org/10.1016/j.cub.2010.03.070

Pope, P. A., & Miall, R. C. (2012). Task-specific facilitation of cognition by cathodal transcranial direct current stimulation of the cerebellum. *Brain Stimulation*, *5*, 84–94. https://doi.org/10.1016/j.brs.2012.03.006

Price, A. R., McAdams, H., Grossman, M., & Hamilton, R. H. (2015). A Meta-analysis of Transcranial Direct Current Stimulation Studies Examining the Reliability of Effects on Language Measures. *Brain Stimulation*, *8*(6), 1093–1100. https://doi.org/10.1016/j.brs.2015.06.013

Rosenberg, M. S., Adams, D. C., & Gurevitch, J. (2000). MetaWin. Statistical Software for Meta-Analysis. Sunderland, MA: Sinauer Associates.

Runnqvist, E., Bonnard, M., Gauvin, H. S., Attarian, S., Trébuchon, A., Hartsuiker, R. J., & Alario, F.-X. (2016). Internal modeling of upcoming speech: A causal role of the right posterior cerebellum in non-motor aspects of language production. *Cortex*, *81*, 203–214. https://doi.org/10.1016/j.cortex.2016.05.008

Schriefers, H., Meyer, A. S., & Levelt, W. J. M. (1990). Exploring the time course of lexical access in language production: Picture-word interference studies. *Journal of Memory and Language*, *29*(1), 86–102. https://doi.org/10.1016/0749-596X(90)90011-N

Schuhmann, T., Schiller, N. O., Goebel, R., & Sack, A. T. (2009). The temporal characteristics of functional activation in Broca's area during overt picture naming. *Cortex*, *45*(9), 1111–1116. https://doi.org/10.1016/j.cortex.2008.10.013

Schuhmann, T., Schiller, N. O., Goebel, R., & Sack, A. T. (2012). Speaking of which: dissecting the neurocognitive network of language production in picture naming. *Cerebral Cortex*, *22*(3), 701–709. https://doi.org/10.1093/cercor/bhr155

Schutter, D. J. L. G., & Wischnewski, M. (2016). A meta-analytic study of exogenous oscillatory electric potentials in neuroenhancement. *Neuropsychologia*, *86*, 110–118. https://doi.org/10.1016/j.neuropsychologia.2016.04.011

Shapiro, C., Alfred, K., Pascual-Leone, A., Mottaghy, F. M., Gangitano, M., Shapiro, K. A., & Caramazza, A. (2001). Grammatical Distinctions in the Left Frontal Cortex. *Journal of Cognitive Neuroscience*, *13*(6), 713–720. https://doi.org/10.1162/08989290152541386

Shinshi, M., Yanagisawa, T., Hirata, M., Goto, T., Sugata, H., Araki, T., … Yorifuji, S. (2015). Temporospatial identification of language-related cortical function by a combination of transcranial magnetic stimulation and magnetoencephalography. *Brain and Behavior*, *5*(3), e00317. https://doi.org/10.1002/brb3.317

Smirni, D., Turriziani, P., Mangano, G. R., Bracco, M., Oliveri, M., & Cipolotti, L. (2017). Modulating phonemic fluency performance in healthy subjects with transcranial magnetic stimulation over the left or right lateral frontal cortex. *Neuropsychologia*, *102*, 109–115. https://doi.org/10.1016/j.neuropsychologia.2017.06.006

Sparing, R., Dafotakis, M., Meister, I. G., Thirugnanasambandam, N., & Fink, G. R. (2008). Enhancing language performance with non-invasive brain stimulation—A transcranial direct current stimulation study in healthy humans. *Neuropsychologia*, *46*(1), 261–268. https://doi.org/10.1016/j.neuropsychologia.2007.07.009

Sparing, R., Mottaghy, F. M., Hungs, M., Bruegmann, M., Foltys, H., Huber, W., & Toepper, R. (2001). Repetitive transcranial magnetic stimulation effects on language function depend on the stimulation parameters. *Journal of Clinical Neurophysiology*, *18*(4), 326–330. https://doi.org/10.1097/00004691-200107000-00004

Spielmann, K., van der Vliet, R., van de Sandt-Koenderman, W. M. E., Frens, M. A., Ribbers, G. M., Selles, R. W., … Holland, P. (2017). Cerebellar Cathodal Transcranial Direct Stimulation and Performance on a Verb Generation Task: A Replication Study. *Neural Plasticity*, *2017*, 1–12. https://doi.org/10.1155/2017/1254615

Stagg, C. J., & Nitsche, M. A. (2011). Physiological Basis of Transcranial Direct Current Stimulation. *The Neuroscientist*, *17*(1), 37–53. https://doi.org/10.1177/1073858410386614

Töpper, R., Mottaghy, F. M., Brügmann, M., Noth, J., & Huber, W. (1998). Facilitation of picture naming by focal transcranial magnetic stimulation of Wernicke's area. *Experimental Brain Research*, *121*(4), 371–378. https://doi.org/10.1007/s002210050471

Tremblay, P., & Gracco, V. L. (2009). Contribution of the pre-SMA to the production of words and non-speech oral motor gestures, as revealed by repetitive transcranial magnetic stimulation (rTMS). *Brain Research*, *1268*, 112–124. https://doi.org/10.1016/j.brainres.2009.02.076

Vannorsdall, T. D., Schretlen, D. J., Andrejczuk, M., Ledoux, K., Bosley, L. V, Weaver, J. R., … Gordon, B. (2012). Altering automatic verbal processes with transcranial direct current stimulation. *Frontiers in Psychiatry*, *3*, 73. https://doi.org/10.3389/fpsyt.2012.00073

Vannorsdall, T. D., van Steenburgh, J. J., Schretlen, D. J., Jayatillake, R., Skolasky, R. L., & Gordon, B. (2016). Reproducibility of tDCS Results in a Randomized Trial. *Cognitive And Behavioral Neurology*, *29*(1), 11–17. https://doi.org/10.1097/WNN.0000000000000086

Viechtbauer, W. (2010). Conducting meta-analyses in R with the metafor package. *Journal of Statistical Software*, *36*(3), 1–48. Retrieved from http://www.jstatsoft.org/v36/i03/

Walsh, V., & Cowey, A. (1998). Magnetic stimulation studies of visual cognition. *Trends in Cognitive Sciences*, *2*(3), 103–110. https://doi.org/10.1016/S1364-6613(98)01134-6

Walsh, V., & Rushworth, M. (1999). A primer of magnetic stimulation as a tool for neuropsychology. *Neuropsychologia*, *37*(2), 125–35. https://doi.org/10.1016/S0028-3932(98)00087-6

Westwood, S. J., Olson, A., Miall, R. C., Nappo, R., & Romani, C. (2017). Limits to tDCS effects in language: Failures to modulate word production in healthy participants with frontal or temporal tDCS. *Cortex*, *86*, 64–82. https://doi.org/10.1016/j.cortex.2016.10.016

Westwood, S. J., & Romani, C. (2017). Transcranial direct current stimulation (tDCS) modulation of picture naming and word reading: A meta-analysis of single session tDCS applied to healthy participants. *Neuropsychologia*. https://doi.org/10.1016/j.neuropsychologia.2017.07.031

Wheat, K. L., Cornelissen, P. L., Sack, A. T., Schuhmann, T., Goebel, R., & Blomert, L. (2013). Charting the functional relevance of Broca's area for visual word recognition and picture naming in Dutch using fMRI-guided TMS. *Brain and Language*, *125*(2), 223–230. https://doi.org/10.1016/j.bandl.2012.04.016

Wirth, M., Rahman, R. A., Kuenecke, J., Koenig, T., Horn, H., Sommer, W., & Dierks, T. (2011). Effects of transcranial direct current stimulation (tDCS) on behaviour and electrophysiology of language production. *Neuropsychologia*, *49*(14), 3989–3998. https://doi.org/10.1016/j.neuropsychologia.2011.10.015