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EFFICACY OF TDCS IN POST-STROKE APHASIA RECOVERY.

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ABSTRACT

Post-stroke aphasia, characterized by varying language deficits, typically arises following left-brain damage. Although speech-language therapy (SLT) is an effective treatment, it often fails to fully restore language functionality, underscoring the urgent need for innovative interventions. Transcranial direct current stimulation (tDCS) emerges as a promising, safe, and feasible strategy that can be smoothly integrated into SLT routines. By modulating brain activity and fostering plastic changes, tDCS is particularly effective when paired with SLT, as this combination promotes experience-dependent plasticity in relevant networks. This strategy has shown considerable efficacy in enhancing the benefits of naming therapy, a primary focus area in aphasia literature. Despite fewer studies investigating other language domains, encouraging outcomes have been observed across virtually all language areas. However, larger and more rigorously controlled trials are essential to substantiate these findings. Significant variations in study designs, including stimulation parameters such as intensity, site, and duration, must also be addressed. Furthermore, individual factors like lesion location, size, and time post-stroke must be considered for more precise and personalized results.

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While anodal tDCS over the left hemisphere has received substantial support, there is an apparent need for individualized current flow modeling to ensure accurate stimulation sites. Increased research into high-definition tDCS is advocated to facilitate more focused stimulation and reduce inter-individual variability in current flow. As research advances, rigorously designed large-scale trials are critically needed to bridge existing knowledge gaps and fully harness the therapeutic potential of this innovative technology.

Keywords: post-stroke aphasia, intervention, tDCS, recovery, naming.

INTRODUCTION

Stroke, a leading cause of disability worldwide, frequently leads to substantial language impairments commonly referred to as aphasia. This condition occurs in about 21–38% of acute left-sided stroke survivors (Berthier, 2005), constituting one of its most devastating and distressing consequences. The aftermath of aphasia is multifaceted, extending beyond the individual's ability to communicate to encompass profound effects on the overall quality of life, psychological well-being, social engagement, and the ability to return to work (Carod-Artal & Egido, 2009; Graham, Pereira, & Teasell, 2011; Mazaux et al., 2013). Despite the proven benefits of conventional rehabilitation strategies (i.e., speech and language therapy, SLT), they often fall short in restoring language abilities, indicating an unmet need in aphasia therapy.

After a stroke, language recovery is supported by distributed neuroplastic changes involving the reconfiguration of the brain networks that support different aspects of language in both hemispheres (Hamilton, Chrysikou, & Coslett, 2011; Stefaniak, Geranmayeh, & Lambon Ralph, 2022). Spontaneous recovery from post-stroke aphasia (PSA) occurs typically during the acute stage, however, it may take place even years after stroke (Hope et al., 2017), mainly aided by speech-language therapy (SLT) and biological interventions (e.g., pharmacotherapy, non-invasive brain stimulation - NIBS) (Duncan, Pradeep, & Small, 2020; Tippett, 2015). NIBS techniques like transcranial direct current stimulation (tDCS) can further enhance neuroplasticity by modulating neural activity and facilitating the rewiring of language-related neural circuits. While growing evidence suggests that tDCS can augment SLT by strengthening task-relevant neural networks, we must also acknowledge the existence of several limitations.

This chapter aims to delve into tDCS as a complementary intervention tool in PSA, offering an overview of the current scientific evidence supporting its role in aphasia recovery, its challenges and limitations, and possible future directions. We

aim to provide a balanced view, acknowledging this emerging therapy's potential benefits and complexities.

CURRENT APPROACHES TO APHASIA REHABILITATION AND NEED FOR NOVEL INTERVENTIONS

Aphasia, as a clinical condition resulting from neurological disruptions, can manifest as deficits across multiple language dimensions due to the interdependent yet independently vulnerable nature of the linguistic system. (Stefaniak et al., 2022). SLT is regarded as the gold standard in aphasia rehabilitation, crucial in managing and improving the overall severity of language impairments. These therapies involve engaging people with PSA in language tasks tailored to address their unique deficits. The overarching goal is to foster neuroplastic changes and consequently restore the function of the impaired language components.

A recent comprehensive review and meta-analysis (Brady, Kelly, Godwin, Enderby, & Campbell, 2016) underscores the efficacy of SLT in fostering language recovery in PSA, demonstrating its role as a critical tool in aphasia rehabilitation. The study, summarizing findings from 57 randomized controlled trials (RCTs), presents compelling evidence that SLT significantly enhances functional communication, reading, writing, and expressive language skills in patients receiving SLT compared to those not undergoing SLT. However, even higher-intensity interventions induce moderate improvement, with small to medium effect sizes. Therefore, while this meta-analysis crucially supports the effectiveness of SLT in facilitating post-stroke language recovery, it also indicates that despite the benefits, patients often continue to experience persistent language and communication deficits, compromising their overall communication efficiency and quality of life.

In light of these challenges, there is a pressing need to develop and integrate novel interventions that can potentiate recovery and improve residual deficits. In this line, pharmacological approaches have been explored as a potential adjunct to behavioral therapy, with some agents (e.g., donepezil and memantine) showing positive results in enhancing the effects of SLT (Berthier, 2021; Dávila, Torres-Prioris, López-Barroso, & Berthier, 2023). However, there are limitations to the use of these drugs, one being that they cannot be prescribed by speech-language pathologists who are often the sole professionals involved in aphasia care, especially during the chronic phase. Moreover, certain drugs like donepezil may not be suitable for severe aphasia cases (Woodhead et al., 2017), despite evidence of positive outcomes in less severe instances (Berthier et al., 2006; Berthier, Hinojosa, Martín, & Fernández, 2003). In this scenario, tDCS emerges as a compelling alternative for online rehabilitation during SLT. It is affordable, convenient, easy to use, safe, and portable, with mild side effects (e.g., itching,

tingling, mild burning sensation) (Lefaucheur et al., 2017). Given these advantages and the evidence supporting its efficacy, this technique offers a promising approach to augment the benefits of SLT. By integrating SLT with complementary practices, such as tDCS and pharmacological agents, synergistic effects can be achieved, and the overall recovery process in PSA can be improved.

In the next section, we will describe the action mechanisms of tDCS and the brain changes that may underlie aphasia recovery after stroke. By understanding how tDCS influences neural activity and leveraging the brain's recovery mechanisms, we can uncover new insights to enhance the effectiveness of aphasia rehabilitation.

tDCS Action Mechanisms and Neuroplasticity in Aphasia Recovery

Post-stroke recovery is attributed to neuroplastic changes comprising structural and functional adaptations within unimpaired brain regions in both hemispheres. Several mechanisms have been proposed to support language recovery after stroke (Hamilton et al., 2011; Lorca-Puls et al., 2021; Xing et al., 2016). These include the reactivation of core left hemisphere language regions over time (Saur et al., 2006), the possibility of recruiting or up-regulating the functioning of right hemisphere regions (Skipper-Kallal, Lacey, Xing, & Turkeltaub, 2017; Stefaniak, Alyahya, & Lambon Ralph, 2021) and the recruitment of domain-general networks that support language recovery (Geranmayeh, Chau, Wise, Leech, & Hampshire, 2017; Stefaniak et al., 2021).

Recent meta-analytic studies have critically summarized decades of research on the mechanisms of language recovery after stroke, highlighting their complexity (Stefaniak et al., 2021; Wilson & Schneck, 2021). In a comprehensive language Activation Likelihood Estimation (ALE) meta-analysis, (Stefaniak et al., 2021) revealed that both people with PSA and healthy subjects consistently activate shared regions in the left and right frontal and temporal lobes, the right parietal lobe, and the midline cortex, emphasizing the importance of both hemispheres in language processing. However, people with PSA exhibit a different activation pattern, with heightened activation in the right anterior insula, the right frontal operculum —both part of domain-general networks— and the right inferior frontal gyrus (pars opercularis). Further, Saur et al. (2006) proposed a three-phase model of language recovery in which the relevance, and the activity, of the left and right hemispheres evolve through the various post-stroke phases (acute, subacute, chronic). Later, Stockert et al. (2020) refined this model and provided supporting evidence highlighting the pivotal role of the right inferior frontal gyrus during recovery after left frontal lesions but not posterior (temporoparietal) lesions, which do not rely on the right hemisphere upregulation. These findings suggest that the timing post-stroke may be crucial when evaluating the efficacy of tDCS. Moreover,

the pattern of functional reorganization might also depend on factors like lesion location, size, and the particular language task involved, among other variables (Skipper-Kallal et al., 2017; Turkeltaub, Messing, Norise, & Hamilton, 2011; Wilson & Schneck, 2021).

tDCS serves as a strategic method for modulating neural activity in brain areas that are crucial for the recovery process, potentially aiding the reorganization of neural networks. This targeted regulation of cortical excitability can enhance the outcomes of SLT, promoting experience-dependent plasticity and inducing long-lasting effects. tDCS alters the resting membrane potentials of neurons (Stagg, Antal, & Nitsche, 2018), influencing spontaneous neuronal excitability and modulating neurotransmitter equilibrium (Antonenko et al., 2019). As a result, tDCS acts as a neural modulator, inducing divergent effects through both anodal and cathodal stimulation. The former facilitate action potential and, thus, behavior, and the latest reduces neural excitability and the likelihood of neuronal firing (Stagg et al., 2018).

The physiological effects of tDCS continue beyond the stimulation period, with increased cortical excitability lasting for a duration dependent on the length of stimulation. For example, a 9-minute session of anodal tDCS (A-tDCS) can lead to after-effects for up to 30 minutes, while a 13-minute session can produce effects for up to 90 minutes (Nitsche and Paulus 2001). Additionally, tDCS can induce longer-lasting impacts by promoting neuroplastic changes akin to long-term potentiation and depression. These changes, grounded in synaptic plasticity, involve the strengthening of synapses when a presynaptic neuron repeatedly fires action potentials onto a postsynaptic neuron, facilitated by increased neurotransmitter release and enhanced receptor sensitivity (Hebb 1949). This mechanism may relate to the enduring clinical benefits found in people with PSA, as noted in a recent meta-analysis (Bucur & Papagno, 2019). Additionally, tDCS has been shown to influence the Brain-Derived Neurotrophic Factor (BDNF), a crucial mediator of LTP and neuroplasticity (Chan, Yau, & Han, 2021), and crucially there is evidence suggesting that the efficacy of tDCS stimulation may be linked to BDNF polymorphisms. For instance, Fridriksson et al. (2018) demonstrated that individuals with typical BDNF genotype (val/val) respond more favorably to A-tDCS during aphasia treatment than those with atypical genotype (met/met). Hence, tDCS may promote language recovery by boosting synaptic plasticity during SLT, which requires activity-dependent BDNF secretion (Fritsch et al., 2010).

RESEARCH EVIDENCE ON TDCS AND LANGUAGE RECOVERY

The body of evidence supporting the efficacy of tDCS in enhancing language performance in PSA is steadily expanding. This trend is well documented by several reviews and meta-analyses published over the past decade, demonstrating the

increasing interest in this field and the evolution of the supporting evidence. While earlier meta-analyses, limited to a small number of studies, were unable to conclusively affirm the effectiveness of tDCS (e.g., Elsner et al., 2013), more recent reviews highlight its promising potential to improve at least some language outcomes (e.g., Elsner et al., 2019). In the subsequent sections of this chapter, we will detail pertinent information to understand the state of research on the efficacy of tDCS in PSA rehabilitation. Considering that numerous reviews, systematic reviews, and meta-analyses have been published on this topic in the last years, we provide summaries of these works in Table 1 and Table 2.

Table 1. A summary of reviews on the effectiveness of tDCS in aphasia recovery.

Study. Article type (years covered)	**Aim**	**Inclusion and exclusion criteria**	**Number of studies included and experimental designs**	**Review conclusions regarding tDCS use in PSA**
Kidwai, Sharma, Peper, & Brumberg, 2022 Scoping review (2015-2022).	To summarize research on using NIBS for improving language skills in aphasia patients.	Inclusion: (1) intervention studies (case reports and observational studies) of TMS and tDCS in aphasia. Exclusion: (1) not written in English; (2) not peer-reviewed original research; (3) population other than patients with aphasia; (4) not targeting linguistic communication skills; (5) using technology solely for assessment, not rehabilitation.	n = 36 - Randomized crossover (n = 14). - Non-randomized crossover (n = 4). - RCTs (n = 8). - Non-RCTs (n = 1). - Single case (n = 9).	- 32 of the reviewed studies reported improvement in language outcomes. - Most tDCS studies are with non-fluent chronic individuals.
Zettin, Bondesan, Nada, Varini, & Dimitri, 2021. Review.	To investigate the effectiveness of tDCS in aphasia.	Inclusion: (1) tDCS studies on persons with acquired brain lesions and aphasia. Exclusion: (1) acute stage; (2) other types of aphasia not related to acquired brain lesions; (3) < 3 participants (e.g., single case); (4) other NIBS techniques different from tDCS.	n = 46	- tDCS, in combination with SLT, promotes better recovery of impaired language functions. - Heterogeneous results regarding electrode size, electrode montage, duration of the stimulation, or current density.
Picano, Quadrini, Pisano, & Marangolo, 2021. Review.	To overview the efficacy and safety of aphasia rehabilitation methods, including tDCS.	Inclusion: (1) RCTs focused on chronic PSA. Exclusion: (1) single cases; (2) acute stage; (3) other pathologies (e.g., PPA, dementia); (4) other types of NIBS technique that are not tDCS.	n = 37 - RCTs.	- Results of tDCS are promising. Yet, it is crucial to administer it alongside SLT for optimal outcomes. - High variability in electrode location, current density, number of stimulation sessions, duration of follow-up, language protocols, and outcome measures.
Fridriksson & Hillis, 2021 Review (Last 5 years).	Review evidence of behavioral therapies and other interventions (including tDCS) to augment outcomes in PSA rehabilitation.	Inclusion: (1) RCTs	--	- Pharmaceuticals and NIBS, like tDCS, enhance SLT. - tDCS is suggested to operate via BDNF-dependent mechanism.

Marangolo, 2020. Review.	To summarize critical studies using tDCS in PSA and to discuss how tDCS may enhance recovery from aphasia.	Inclusion: (1) studies using tDCS combined with SLT in aphasia.	n = 30	- tDCS is an effective tool for language recovery in chronic PSA.
Duncan et al., 2020 Review.	To review biological interventions (including tDCS) aimed at improving symptoms of chronic PSA by directly influencing brain functions.	Inclusion: (1) chronic PSA (≥ 6 months post-onset); (2) > 5 participants; (3) stimulation paired with a behavioral task; (4) use of double blinding and a control condition (e.g., sham); (5) > 1 stimulation session. Exclusion: (1) PPA studies.	n = 19 - Crossover (n = 17). - Parallel groups (n = 2).	- Positive effects of tDCS on naming, reading, production of content units, verbs, nouns, and sentences. Those effects were found when the left frontal or left posterior areas were stimulated, the right cerebellum was inhibited, or the right IFG was stimulated paired with Melodic Intonation Therapy. - Dosing, outcome measures, and follow-up durations vary widely, with generally moderate effect sizes.
Biou et al., 2019 Systematic Review (1996-2018).	To summarize evidence on the effect of tDCS on aphasia rehabilitation.	Inclusion: (1) studies involving PSA rehabilitation with tDCS combined or not with SLT. Exclusion: (1) PPA studies; (2) TMS studies; (3) only healthy subjects.	n = 53 - 48 intervention studies: RCTs (n = 39); prospective (n = 2); single case (n = 5); sub-analyses of RCTs (n =2). - 5 meta-analyses.	- 33/39 RCTs found a positive significant effect on language performance. - 2/2 prospective studies and 5/5 case studies found an effect of tDCS combined with SLT. - 2/3 meta-analysis found positive effects of tDCS on naming. - There were no studies reporting negative effect of tDCS on language outcomes. - Heterogeneity in methodology regarding target areas, intensity and polarity of stimulation, duration, and frequency.
ALHarbi, Armijo-Olivo, & Kim, 2017 Critical review.	To overview the methodological rigor of evidence concerning the use of tDCS in PSA to improve anomia.	Inclusion: (1) unilateral stroke; (2) chronic stage (> 6 months post-stroke); (3) tDCS paired or not with behavioral therapy; (4) naming as an outcome measure; (5) published in English. Exclusion: (1) bilateral strokes; (2) naming ability not an outcome measure; (3) not original research studies.	n = 19 - Crossover (n = 16). - Single case (n = 2). - RCTs with two parallel groups (n = 1).	- The evidence for using tDCS to enhance naming ability in chronic PSA is in the pre-efficacy level. This level includes Phase I (5 studies) and Phase II (13 studies) studies, while Phase III (1 study) shows emerging evidence of efficacy, following the five-phase model of clinical outcome research.
de Aguiar, Paolazzi, & Miceli, 2015 Review.	To review existing evidence on the role of tDCS in PSA rehabilitation, focusing on the factors that may influence the effects of stimulation, such as stimulation parameters, behavioral treatments, and	Inclusion: (1) studies using tDCS to treat PSA. Exclusion: (1) tDCS used to treat a condition other than PSA; (2) only healthy subjects.	n = 11 - Crossover (n = 9). - Between groups (n = 1). - ABA design (n = 1).	- Despite the diversity in stimulation parameters, patient characteristics, and associated behavioral treatments employed in different studies, tDCS emerges as an effective tool for PSA treatment. - tDCS has proven to be safe.

	patient characteristics.			
Monti et al., 2013. Review (2005-2012).	To describe studies using tDCS to facilitate language in PSA.	--	n = 11	- tDCS can improve language function in patients with aphasia.
Holland & Crinion, 2012. Review.	To overview studies exploring the role of tDCS in treating PSA, covering recent studies, methodology, and future research gaps.	--	n = 4 - Crossover sham-controlled (n = 1). - Crossover randomized sham-controlled (n = 3).	- tDCS can be a useful tool to complement treatment in chronic PSA.

Notes. PSA: post-stroke aphasia. NIBS: non-invasive brain stimulation; TMS: transcranial magnetic stimulation; SLT: speech-language therapy; RCT: Randomized-controlled trial; PPA: primary progressive aphasia; BDNF: brain-derived neurotrophic factor.

Table 2. A summary of published meta-analyses reviews on the effects of tDCS in aphasia recovery.

Study (years covered)	**Aim and outcome measures**	**Inclusion and exclusion criteria**	**Number of studies included and results**	**Study conclusions**
Ding et al., 2022 (up to January 2022)	Aim: To compare and rank the efficacy of various NIBS approaches (tDCS and TMS) for enhancing different language domains and to explore the impact of modulators (e.g., sociodemographic factors, therapy characteristics) on their efficacy. POM: global aphasia severity (WAB-AQ) and other subdomains of speech (comprehension, repetition, naming, spontaneous speech). SOM: reading and writing, and other linguistic variables (prosody, phonematic, syntactic processes).	Inclusion: (1) participants with diagnosed PSA; (2) NIBS interventions; (3) compared to placebo o sham condition; (4) include a measure of the change in language abilities post-therapy; (5) RCTs. Exclusion: (2) non-appropriate participants (e.g., healthy or pediatric subjects); (3) other interventions than NIBS; (4) not appropriate control group; (5) low-quality studies (e.g., case reports).	n = 69 (1670 participants) POM: - Global aphasia severity. A-tDCS showed efficacy (SMD = 0.38; CI = 0.05, 0.71). - Naming. Improvement with all types of tDCS (dual: SMD = 1.11; CI = 0.40, 1.81; C-tDCS: SMD = 0.84; CI = 0.30, 1.39; A-tDCS: SMD = 0.67; CI = 0.34, 1.01). - Repetition. Dual-tDCS showed superior effect size (SMD = 1.50; CI = 0.82, 2.16) and improvements (SMD = 0.54; CI = 0.02, 1.06). - Spontaneous speech. A-tDCS (SMD = 1.06; CI = 0.49, 1.64) and dual tDCS (SMD = 1.05; CI = 0.22, 1.87) resulted in improvements.	- Dual-tDCS and A-tDCS were more effective at improving naming and repetition than TMS, while TMS was better at improving the global severity of aphasia. A-tDCS was the best technique to enhance spontaneous speech. - The therapy duration may modulate NIBS's effects on naming and spontaneous speech.
Cheng et al., 2021 (Up to July 2020)	Aim: To investigate the impacts of right-hemispheric tDCS application on naming ability in PSA compared to sham-tDCS. POM: naming accuracy.	Inclusion: (1) adults with PSA diagnosis; (2) > 4 participants; (3) tDCS applied over the right hemisphere;(4) naming accuracy as an outcome measure; (5) RCT or crossover design; (6) peer-reviewed publications in English.	n = 4 (42 participants) - Clinically significant difference between active tDCS vs sham-tDCS (SMD = 0.71; 95% CI = 0.24, 1.19; p = 0.003, I^2 = 16%). - Statistically significant differences between A-tDCS and sham-tDCS (SMD = 1.35; 95% CI = 0.60, 2.10; p = 0.0004; I^2 = 0%).	- A-tDCS over the right hemisphere may have clinically significant therapeutic effects on patients with PSA on naming abilities.
Elsner, Kugler, &	Aim: To overview the evidence regarding the efficacy and	Inclusion: (1) adult people with stroke; (2) use of any	n = 25 (471 participants)	- A-tDCS is the most promising technique to

Study (years covered)	Aim and outcome measures	Inclusion and exclusion criteria	Number of studies included and results	Study conclusions
Mehrholz, 2020 (Up to February 2020)	safety of different tDCS stimulation types for improving functional communication and language in post-stroke aphasia. POM: functional communication. SOM: naming nouns, naming verbs, and safety.	kind of active tDCS (anodal, cathodal, or dual); (3) RCTs and randomized controlled crossover trials which compared tDCS with other interventions.	SOM: - Evidence of effect for A-tDCS (SMD = 0.51; 95% CI = 0.11, 0.9) in naming nouns. - No differences in safety between tDCS conditions (A-tDCS, C-tDCS, dual-tDCS).	improve performance in naming nouns in PSA. - No evidence of an effect of active tDCS on functional communication or performance in naming verbs. - No difference between the different types of tDCS regarding safety (number of dropouts and adverse effects).
Bucur & Papagno, 2019 (2004-2019)	Aim: To investigate the long-term efficacy of NIBS (TMS and tDCS) and its effectiveness and reliability for naming recovery. POM: picture naming accuracy (if unavailable, the explicitly reported POM was used.)	Inclusion: (1) adults with PSA; (2) repetitive TMS or tDCS intervention studies; (3) cephalic stimulation designs; (4) > 4 weeks of follow-up; (5) > 4 participants; (6) peer-reviewed publications published in English; (7) RCT or crossover design. Exclusion: (1) other disorders; (2) other brain stimulation techniques; (3) open-label studies, case reports, or studies with < 4 participants; (4) studies administering < 3 stimulation sessions; (5) non-cephalic stimulation sites; (6) < 4 weeks follow-up period; (7) other publication types or languages different than English (e.g., non-peer-reviewed articles); (8) articles with insufficient information.	n = 16 (8 tDCS and 8 TMS) - Efficacy at follow-up. tDCS resulted in a significant but small effect (SMD = 0.33; 95% CI = 0.03, 0.62; p = 0.02; I^2 =18.32%). - Maintenance of gains. No significant differences between after-therapy vs follow-up. tDCS studies (t (7) = 0.14, p = 0.88; 99% CI = −0.16, 0.17).	- NIBS improves aphasia recovery and produces durable results, especially for naming. - The magnitude treatment effect size was higher for TMS (medium to large) than tDCS (small to medium). - Feasibility is higher for tDCS than TMS, given its user-friendliness, portability, and lower cost.
Elsner et al., 2019 (Update of Elsner et al. 2015; up to June 2018)	Aim: To evaluate the efficacy of tDCS on improving PSA. POM: functional communication. SOM: receptive or expressive language, or both (e.g., accuracy of picture naming), as well as dropouts and adverse effects. Measures of other cognitive functions (working memory, executive functions, attention, intelligence, visual-auditory recognition, visual-spatial abilities).	Inclusion: (1) RCTs and randomized controlled crossover trials (analyses only the first phase); (2) people ≥ 18 years old; (3) use tDCS alone or combined with SLT vs. sham-tDCS (or other control condition). Exclusion: studies that do not match the inclusion criteria.	n = 15 (421 participants) in the qualitative synthesis. n = 14 (153 participants) in quantitative synthesis. SOM: - Evidence of effect for accuracy of naming nouns at post-intervention evaluation (SMD = 0.42; 95% CI = 0.19, 0.66; p = 0.0005; I^2= 0%) and follow-up evaluation (SMD = 0.87; 95% CI = 0.25, 1.48; p = 0.006; I^2 = 32%).	- No evidence of effectiveness of any type of tDCS compared to sham for improving functional communication in PSA. - Moderate evidence that tDCS can improve the naming of nouns at post-intervention and follow-up.

Study (years covered)	Aim and outcome measures	Inclusion and exclusion criteria	Number of studies included and results	Study conclusions
Rosso, Arbizu, Dhennain, Lamy, & Samson, 2018	Aim: To explore the effects of tDCS on naming abilities in individuals with PSA. POM: picture naming accuracy	Inclusion: (1) sham-controlled experimental design; (2) > 1 tDCS session; (3) aphasia after left hemisphere stroke; (4) naming as an outcome measure; (5) > 3 patients; (5) individual data reported. Exclusion: (1) a parallel group design; (2) risk of multiplicity.	n = 7 (68 participants) - Mean statistically significant improvement of 35% in the active vs. 25% in the sham condition (SMD = 0.8; 95% CI = 0.27, 1.33). A dose-dependent effect was also found (5 sessions vs. > 5 sessions; p = 0.02) - A-tDCS ($p < 0.0001$) and C-tDCS ($p = 0.02$) polarities were effective. Greater effects after left vs. right stimulation ($p = 0.005$), although both were better than sham condition ($p < 0.001$, and $p < 0.002$). No effect of stimulation site (frontal vs. temporoparietal), but a statistically significant interaction between site and hemisphere was found ($F(3,83) = 4.03$; $p = 0.04$). tDCS was beneficial regardless of the severity of aphasia, comprehension deficits, and time post-stroke.	- tDCS applied over repetitive sessions can enhance picture naming accuracy in PSA.
Shah-Basak, Wurzman, Purcell, Gervits, & Hamilton, 2016 (1960-2014)	Aim: To evaluate the efficacy of TMS and tDCS treatment studies in PSA and compare the effects between both NIBS techniques. POM: accuracy in picture naming	Inclusion: (1) adults diagnosed with PSA; (2) NIBS (including tDCS); (3) picture naming as part of the outcome measures; (4) between-subject or RCTs, crossover trials, within-subject or pre-post trial designs; (5) published between 1960-2014. Exclusion: (1) non-stroke patients; (2) including NIBS but not as a treatment (single sessions, multiple sessions over different sites); (3) non-English articles.	n = 16 [8 tDCS (140 participants) and 8 TMS (143 participants) - Statistically significant and moderate effect of tDCS on picture naming (SMD = 0.39; 95% CI = 0.28,0.51).	- tDCS treatment is an effective tool in the treatment of PSA. - Larger clinical trials are required.
Elsner, Kugler, Pohl, & Mehrholz, 2015 (Update of Elsner et al. 2013; up to November 2014)	Aim: To evaluate the efficacy of tDCS on improving PSA. POM: functional communication. SOM: receptive and expressive language (e.g., accuracy of picture naming) as well as dropouts and adverse effects. Measure of other cognitive functions (e.g., attention and working memory).	Inclusion:(1) RCTs and randomized controlled crossover trials (analyses only the first phase); (2) people ≥ 18 years old;(3) use tDCS alone or combined with SLT vs sham-tDCS (or other control condition). Exclusion: (1) studies that do not match the inclusion criteria.	n = 12 (136 participants) in the qualitative synthesis n = 8 (115 participants) in the quantitative synthesis - No statistically significant effects were found.	- None of the included studies reported functional communication measures formally evaluated. - None of the studies examined the effect of tDCS on cognition in PSA. - No evidence supports the effectiveness of tDCS (anodal, cathodal, or bihemispheric) compared to sham in

Study (years covered)	Aim and outcome measures	Inclusion and exclusion criteria	Number of studies included and results	Study conclusions
				enhancing SLT outcomes.
Otal, Olma, Flöel, & Wellwood, 2015	Aim: To assess the clinical efficacy of inhibitory NIBS techniques (including C-tDCS) targeting the right hemisphere as an adjunct to SLT for PSA rehabilitation. POM: accuracy in naming.	Inclusion: (1) RCTs or randomized controlled crossover trials; (2) adult patients with ischemic stroke and aphasia; (3) C-tDCS or repetitive TMS applied over the unaffected hemisphere paired with SLT; (4) control group (sham NIBS with SLT); (5) outcome measures including accuracy in naming.	n = 3 (32 participants) - Accuracy in naming score was improved in patients receiving active NIBS paired with SLT compared with sham (SMD = 0.51; 95% CI = 0.24, 0.79); p = 0.0003).	- C-tDCS applied over the unaffected (non-language dominant) hemisphere can be a promising rehabilitation tool.
Elsner et al., 2013 (Up to 2012)	Aim: To evaluate the efficacy of tDCS on improving PSA. POM: functional communication. SOM: receptive and expressive language (e.g., accuracy of picture naming) as well as dropouts and adverse effects.	Inclusion: (1) RCTs and randomized controlled crossover trials (analyses only the first phase); (2) ≥ 18 years old; (3) use tDCS alone or combined with SLT vs. sham-tDCS (or other control condition). Exclusion: studies that do not match the inclusion criteria.	n = 5 (54 participants) - No statistically significant effects were found.	- None of the included studies reported functional communication measures formally evaluated. - No evidence of tDCS enhancing SLT outcomes. No adverse events were reported. The proportion of dropouts was comparable between groups.

Notes. PSA: post-stroke aphasia. POM: primary outcome measures; SOM: secondary outcome measures; NIBS: non-invasive brain stimulation; TMS: transcranial magnetic stimulation; SLT: speech-language therapy; RCT: Randomized-controlled trial; SMD: standard mean difference; CI: confidence interval; PPA: primary progressive aphasia; A-tDCS: anodal tDCS; C-tDCS: cathodal tDCS. For space constraints, only the statistically significant results of the reported outcome measures are included in the "Number of studies included and results" column.

Stimulation parameters and montages

Aphasia studies employing tDCS exhibit marked heterogeneity in the montages and stimulation parameters. Three key types of stimulation are typically implemented in aphasia: A-tDCS mainly to left hemisphere areas, but occasionally to right ones (Flöel et al., 2011; Vines, Norton, & Schlaug, 2011); cathodal tDCS (C-tDCS) over the undamaged right hemisphere, and dual stimulation (dual-tDCS) employing A-tDCS and C-tDCS simultaneously, typically targeting a left frontal or temporoparietal area with the return electrode over the right homologous area. In both A-tDCS and C-tDCS, the return electrode can be positioned in a non-cephalic location (e.g., shoulder) or a cephalic position (areas of no interest, for instance, the orbitofrontal region). While A-tDCS aims to facilitate the recruitment of undamaged perilesional areas or right hemisphere structures, C-tDCS typically intends to inhibit right hemispheric regions. The rationale for using C-tDCS over

the right hemisphere stems from the interhemispheric competition model (Cook, 1984). This model postulates that, under normal circumstances, the two hemispheres inhibit each other through the corpus callosum to allow functional lateralization and specialization. Then, after a brain damage in the left hemisphere, there is a consequent release of right hemisphere activity that can inhibit left hemisphere activity and prevent optimal recovery. Nevertheless, this model oversimplifies the complexity of aphasia recovery and lacks full validation by recent evidence showing that bilateral brain changes support recovery and that the importance of each hemisphere may change over time (Geranmayeh et al., 2017; Saur et al., 2006; Stefaniak et al., 2021). Furthermore, positive outcomes following right hemisphere C-tDCS do not necessarily endorse the interhemispheric competition model, mainly because of the low focality of standard tDCS montages, especially when the return electrode is placed in a cephalic position. Indeed, most studies do not include individualized modeling of the distribution of electric field strength to optimize the location of the tDCS electrodes. This raises the possibility that even when the cathode is positioned over right hemisphere structures, current flow could generate hotspots in the vicinity, rendering the interpretation of results more complex (see Figure 1).

A-tDCS is the primary method used in aphasia interventions, typically targeting the left hemisphere to boost its activity. Key focus areas often include the inferior frontal gyrus, the posterior superior temporal gyrus—known more commonly as Wernicke's area—and the motor cortex. Despite these prevalent practices, significant gaps persist within our understanding of this field. One fundamental issue is the "one-size-fits-all" approach adopted by most studies, targeting the same brain area for all participants, neglecting to account for possible lesions in the target area. This approach fails to consider the unique individual characteristics and interindividual anatomical and functional variability. For example, even if the regions stimulated are structurally intact, they may not necessarily play a role in a particular individual in the specific linguistic processes targeted by the accompanying SLT. As a result, modulation of unrelated areas may inadvertently reduce the therapy's effectiveness. To circumvent these obstacles, a handful of studies have employed individualized targets. These are usually chosen to stimulate undamaged areas, as determined by structural MRI (de Aguiar et al., 2015) or functional MRI data. For example, some studies have targeted individualized

preserved left temporal regions that show the highest activation during a naming task (Fridriksson, Elm, et al., 2018; Fridriksson, Rorden, et al., 2018).

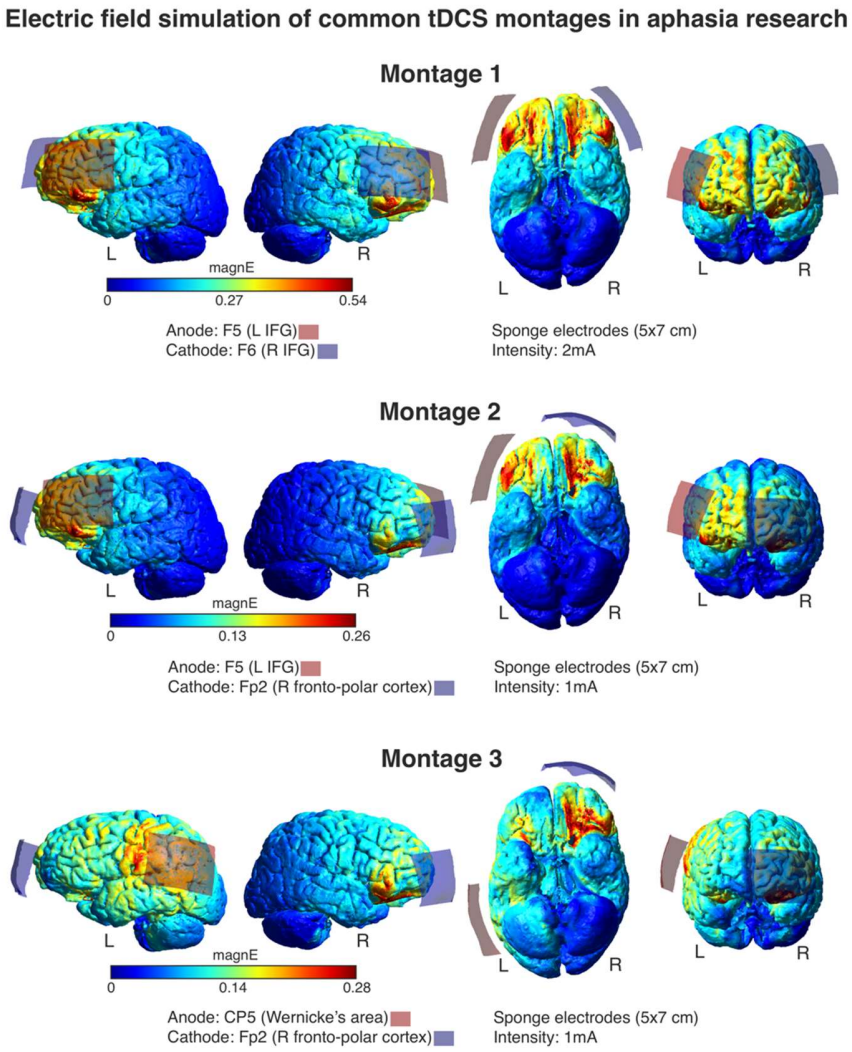

Figure 1. **Simulation of the electric field distribution in three commonly used tDCS montages in aphasia research.** These montages aim to modulate the activity of the inferior frontal gyrus (IFG) or posterior superior temporal gyrus areas (Wernicke's area). The anode located over: the left IFG (L IFG) and the right IFG (R IFG) (Montage 1); the L IFG and the right fronto-polar cortex (Montage 2); Wernicke's area and the right fronto-polar cortex (Montage 3), respectively. Multiple studies have used one of these three setups or similar ones (see for example, Table 4 of Biou et al. 2019). Sponge electrodes were used for the simulation, and the computational

modeling of the electric field was performed using the SimNIBS 4.01 software. mangE refers to the magnitude of the electric field visualized on the grey matter surface, measured in V/m. L: left; R: right.

The efficacy of tDCS can also be significantly influenced by parameters such as current intensity and stimulation duration, which have shown considerable variation across aphasia studies. The duration of each stimulation session in these studies typically ranges from 10 to 30 minutes, with most studies opting for a 20-minute duration and a current intensity between 1 and 2 mA (Biou et al., 2019). Notably, the characteristics and placement of electrodes significantly impact stimulation intensity and current distribution. Traditional sponge electrodes, usually of dimensions 5 x 5 cm or 5 x 7 cm, are used in most aphasia studies. However, a few studies have explored high-definition tDCS (HD-tDCS) (Richardson et al. 2015; Fiori et al. 2019).

Contrary to the presumption that traditional tDCS using large sponge electrodes focuses the modulatory effect directly under the electrode, computational modeling of electric fields proposes a more complex scenario. To illustrate this complexity, Figure 1 depicts an electric field modeling of three of the most frequently used montages, as summarized in Biou et al. (2019), using the software package SimNIBS (version 4.01, https://simnibs.github.io/simnibs). Conventional tDCS montages often yield multiple peak clusters not restricted to the area directly beneath the target electrode. In fact, the electrode position can influence the emergence of these electric fields peak, with potential hotspots occurring in regions between or even near the return electrodes rather than exclusively underneath them (Datta, Truong, Minhas, Parra, & Bikson, 2012; Truong, Magerowski, Blackburn, Bikson, & Alonso-Alonso, 2013; Wiethoff, Hamada, & Rothwell, 2014). These peaks' distribution and scattering can significantly vary among individuals, depending on electrode placement and individual anatomical variations. Opitz, Paulus, Will, Antunes, & Thielscher (2015) demonstrated through a multiple regression model that the electric field distribution systematically depends on anatomical factors, such as the thickness and composition of the overlying skull, the cerebrospinal fluid layer's thickness between the cortex and skull, and the depth of the sulci. This underscores the significance of individualized modeling to ensure control over the modulated brain area.

The implications of the less-focused nature of standard montages, commonly used in aphasia studies, are far-reaching for our comprehension of the neural mechanisms underpinning recovery. HD-tDCS, as opposed to conventional tDCS, employs small electrodes positioned around a central electrode situated in the target area. This configuration produces a current distribution with a maximum electric field under the anode electrode (located in the target areas), leading to a more substantial and focused electric field. This characteristic reduces the influence of

individual differences in cortical current flow (Datta et al., 2012), potentially bringing about a higher degree of consistency in research results. Only two intervention studies have, to our knowledge, utilized HD-tDCS in PSA (Fiori, Nitsche, Cucuzza, Caltagirone, & Marangolo, 2019; Richardson, Datta, Dmochowski, Parra, & Fridriksson, 2015). Richardson et al. (2015) revealed an improvement in naming accuracy under both C-tDCS and HD-tDCS conditions, with most patients showing a higher, albeit statistically insignificant, improvement with HD-tDCS. Moreover, Fiori et al., 2019 found that HD-tDCS efficacy in enhancing verb recovery in PSA is current intensity-dependent, with significant improvement seen at 2 mA stimulation but not at 1 mA.

Stroke phase: subacute vs. chronic

The stroke stage, whether subacute or chronic, significantly influences the brain's condition and ongoing plastic changes, potentially affecting treatment outcomes. Most of the intervention studies in PSA have been conducted in the chronic stage, generally defined as more than three to six months after stroke. A recent meta-analytic study supports the efficacy of these interventions in the chronic phase, although the level of evidence remains low (Bucur & Papagno, 2019). This limited evidence is partly attributed to the variability in stimulation parameters, stimulation site, and the small sample size across studies. The larger RCT performed in chronic aphasia resulting from a single left hemisphere stroke involved a three-week computerized anomia treatment (15 sessions of 45 minutes each) combined with either A-tDCS or a sham-tDCS applied to preserved left temporal lobe regions, individualized based on functional fMRI peaks. The primary outcome measure was the ability to name common objects correctly. The findings demonstrated a relative 70% increase in correct naming for those treated with A-tDCS compared to the sham group.

Contrarily, studies focusing on the subacute phase of stroke have yielded mixed results. While some have indicated considerable improvements over a control condition in domains like auditory verbal comprehension and discourse skills (as seen in the content and efficiency of picture descriptions) (Stockbridge et al., 2023; You, Kim, Chun, Jung, & Park, 2011), others found no difference from the control condition (Polanowska, Leśniak, Seniów, Czepiel, & Członkowska, 2013; Polanowska, Leśniak, Seniów, & Członkowska, 2013; Spielmann, van de Sandt-Koenderman, Heijenbrok-Kal, & Ribbers, 2018). In the largest RCT on acute-subacute aphasia to date, Stockbridge et al. 2023 administered to 58 patients either A-tDCS or sham-tDCS over an undamaged brain area (frontal or temporal) paired with fifteen 45-minute sessions of naming treatment. They found that A-tDCS did not significantly improve picture naming accuracy but enhanced discourse content and efficiency compared to sham. However, the body of research in the subacute phase remains relatively sparse compared to the chronic phase, with a recent meta-

analysis suggesting that tDCS's primary benefits may lie in treating chronic aphasia, while its efficacy for subacute aphasia is still under examination (Bucur & Papagno, 2019).

Effectiveness of online vs. offline tDCS in language outcomes

Most studies utilizing tDCS for the treatment of PSA have implemented online stimulation, in which stimulation is paired with linguistic training, predominantly demonstrating the advantages of active stimulation compared to sham. As highlighted in the systematic review by Biou et al. (2019), nearly all of the 34 reviewed tDCS RCTs using online stimulation yielded positive effects on language outcomes. The only exception was a study performed in subacute aphasia (<3 months post-onset) (Spielmann et al., 2018). Nevertheless, at least one other recent RCT yielded null results, with no observed impact of tDCS when coupled with personalized SLT in chronic PSA (Guillouët et al., 2020).

Although tDCS was used alongside various tasks tapping into almost all linguistic processes —including production (naming, spontaneous speech), comprehension, repetition, and lexical decision—, recent reviews (Biou et al., 2019; Kidwai et al., 2022; Marangolo, 2020; Picano et al., 2021) indicate that interventions were primarily aimed at enhancing naming abilities. Indeed, 40 to 60% of RCTs covered in these recent reviews utilized confrontation naming as a training and outcome task. Consequently, the most convincing evidence for the efficacy of tDCS in language recovery primarily revolves around enhancing naming performance. There are critical reasons for naming being the central metric in tDCS studies of PSA: first, word retrieval problems are the most common deficit observed in PSA irrespective of the severity and, therefore, they are often the focus of aphasia therapy; and second, naming outcomes and the generalization from trained to untrained items are relatively simple to measure. In fact, multiple recent meta-analytic studies endorse tDCS as a beneficial intervention for naming rehabilitation, despite the small to medium reported effect sizes (Bucur & Papagno, 2019; Elsner et al., 2020, 2019; Rosso et al., 2018). Further, a recent study also points towards its superiority over sham-tDCS in improving global aphasia severity and repetition abilities (Ding et al., 2022). Nevertheless, a dose-dependent effect has been suggested (Rosso et al., 2018), with therapies extending beyond five sessions reporting superior outcomes than their shorter counterparts. The duration of interventions in aphasia studies ranges from a single session to as many as 30, although most studies typically utilize repeated stimulation over 5 to 10 sessions. It is worth noting that improvements in naming abilities have been observed to persist

for a period ranging from one to six months after the final stimulation session (Bucur & Papagno, 2019).

In contrast, offline tDCS, which involves administering stimulation independently without simultaneous SLT (although language training can occur before or after), is ineffective. Several studies have shown no significant differences when compared to a control condition (Polanowska, Leśniak, Seniów, Czepiel, et al., 2013; Polanowska, Leśniak, Seniów, & Członkowska, 2013; Santos et al., 2017; Silva, Mac-Kay, Chao, Santos, & Gagliadi, 2018; Volpato et al., 2013). Given the modulatory effect of tDCS, these findings suggest that when stimulation is combined with linguistic training, it triggers relevant neuroplastic changes in the stimulated areas, hence improving recovery to a greater extent than when SLT is applied alone. This combination may be particularly important in facilitating impactful changes in brain configuration.

In conclusion, the pairing of repeated tDCS sessions with naming tasks appears to significantly and durably improve naming accuracy in PSA, and may also reduce overall aphasia severity and enhance repetition. However, evidence regarding other linguistic domains remains sparse. For instance, current research does not sufficiently support a positive effect of tDCS on functional communication (Elsner et al., 2020, 2019), a key aspect for evaluating the impact of interventions on patients' everyday communication abilities. This deficiency may largely be attributed to the limited number of studies incorporating functional communication as an outcome; for instance, only 6 out of 25 studies reviewed in Elsner, Kugler, and Mehrholz (2020) included these measures.

LIMITATIONS AND FUTURE DIRECTIONS

Despite the potential of tDCS in aphasia treatment, significant limitations need to be addressed in future research. Considerable heterogeneity exists among the montages and stimulation parameters used in current tDCS studies. To optimize the benefits of this methodology, additional research is needed to determine the most effective parameters for tDCS, including specific stimulation location, intensity, duration, and frequency. This research should focus on understanding how individual factors (e.g., lesion characteristics and brain structure and function), and technical aspects (e.g., montage configuration and intensity), interact to modulate the therapeutic response to tDCS. Understanding these interactions is critical to developing more personalized therapeutic interventions for PSA.

Further, HD-tDCS presents an exciting avenue for future research, as this technique may allow for more focal stimulation. With its potential for enhanced precision, HD-tDCS may facilitate the design of more controlled studies, providing

more reliable and replicable evidence regarding the efficacy of tDCS in treating aphasia and other language impairments.

The current body of evidence primarily supports the use of tDCS to enhance naming abilities in the chronic phase of aphasia recovery. There is a lack of robust evidence demonstrating benefits in other linguistic domains or during the acute-subacute phase of the condition. This gap in the research is partly due to the significant heterogeneity among studies, coupled with the typically small sample sizes employed. Preliminary findings suggest potential efficacy for virtually all linguistic domains, underlining the need for larger, rigorous RCTs incorporating functional communication outcomes, among other language measures.

Another crucial limitation lies in our incomplete understanding of the specific language components (e.g., phonology, semantics) modulated by tDCS. Previous studies have shown that different language components follow different recovery trajectories and are associated with activation changes in distinct neural regions (Stefaniak et al., 2022). This suggests that a given stimulation protocol might improve some components of language but not others. Optimally, the regions chosen for stimulation should be individualized to each patient accounting for the specific deficits and targeting areas functionally related to the specific language component to be improved. Thus, future investigations should seek to individualize stimulation sites to target relevant areas and differentiate the language components modulated by tDCS.

In sum, while tDCS offers significant potential for aphasia rehabilitation, a comprehensive understanding of its capabilities, limitations, and optimal implementation is still a work in progress. Rigorous, well-designed future research will be instrumental in fully realizing the therapeutic potential of this promising technology.

REFERENCES

ALHarbi, M. F., Armijo-Olivo, S., & Kim, E. S. (2017). Transcranial direct current stimulation (tDCS) to improve naming ability in post-stroke aphasia: a critical review. *Behavioural Brain Research*, *332*, 7–15.

Antonenko, D., Thielscher, A., Saturnino, G. B., Aydin, S., Ittermann, B., Grittner, U., & Flöel, A. (2019). Towards precise brain stimulation: Is electric field simulation related to neuromodulation? *Brain Stimulation*, *12*(5), 1159–1168.

Berthier, M. L. (2005). Poststroke Aphasia. *Drugs & Aging*, *22*(2), 163–182. https://doi.org/10.2165/00002512-200522020-00006

Berthier, M. L., Green, C., Higueras, C., Fernández, I., Hinojosa, J., & Martín, M. del

C. (2006). A randomized, placebo-controlled study of donepezil in poststroke aphasia. *Neurology*, *67*(9), 1687–1689.

Berthier, M. L., Hinojosa, J., Martín, M. del C., & Fernández, I. (2003). Open-label study of donepezil in chronic poststroke aphasia. *Neurology*, *60*(7), 1218–1219. https://doi.org/10.1212/01.WNL.0000055871.82308.41

Berthier, M. L. (2021). Ten key reasons for continuing research on pharmacotherapy for post-stroke aphasia. *Aphasiology*, *35*(6), 824–858.

Biou, E., Cassoudesalle, H., Cogné, M., Sibon, I., De Gabory, I., Dehail, P., … Glize, B. (2019). Transcranial direct current stimulation in post-stroke aphasia rehabilitation: A systematic review. *Annals of Physical and Rehabilitation Medicine*, *62*(2), 104–121. https://doi.org/10.1016/j.rehab.2019.01.003

Brady, M. C., Kelly, H., Godwin, J., Enderby, P., & Campbell, P. (2016). Speech and language therapy for aphasia following stroke. *Cochrane Database of Systematic Reviews*, *2016*(6), CD000425. https://doi.org/10.1002/14651858.CD000425.pub4

Bucur, M., & Papagno, C. Are transcranial brain stimulation effects long-lasting in post-stroke aphasia? A comparative systematic review and meta-analysis on naming performance. *Neuroscience and Biobehavioral Reviews*, Vol. 102, pp. 264–289. Elsevier Ltd. https://doi.org/10.1016/j.neubiorev.2019.04.019

Carod-Artal, F. J., & Egido, J. A. (2009). Quality of life after stroke: the importance of a good recovery. *Cerebrovascular Diseases*, *27*(Suppl. 1), 204–214.

Chan, M. M. Y., Yau, S. S. Y., & Han, Y. M. Y. (2021). The neurobiology of prefrontal transcranial direct current stimulation (tDCS) in promoting brain plasticity: A systematic review and meta-analyses of human and rodent studies. *Neuroscience & Biobehavioral Reviews*, *125*, 392–416.

Cheng, W., Li, Y., Cheng, B., Chen, Y., Chen, Z., Cui, L., … Chen, Z. (2021). Effects of transcranial direct current stimulation over the right hemisphere on naming ability in patients with poststroke aphasia: A meta-analysis. *Journal of Neurolinguistics*, *58*, 100986. https://doi.org/10.1016/j.jneuroling.2021.100986

Cook, N. D. (1984). Homotopic callosal inhibition. *Brain and Language*, *23*(1), 116–125.

Datta, A., Truong, D., Minhas, P., Parra, L. C., & Bikson, M. (2012). Inter-individual variation during transcranial direct current stimulation and normalization of dose using MRI-derived computational models. *Frontiers in Psychiatry*, *3*, 91.

Dávila, G., Torres-Prioris, M. J., López-Barroso, D., & Berthier, M. L. (2023). Turning

the Spotlight to Cholinergic Pharmacotherapy of the Human Language System. *CNS Drugs*, 1–39.

de Aguiar, V., Bastiaanse, R., Capasso, R., Gandolfi, M., Smania, N., Rossi, G., & Miceli, G. (2015). Can tDCS enhance item-specific effects and generalization after linguistically motivated aphasia therapy for verbs? *Frontiers in Behavioral Neuroscience*, *9*, 190.

de Aguiar, V., Paolazzi, C. L., & Miceli, G. (2015). tDCS in post-stroke aphasia: The role of stimulation parameters, behavioral treatment and patient characteristics. *Cortex*, *63*, 296–316. https://doi.org/10.1016/j.cortex.2014.08.015

Ding, X., Zhang, S., Huang, W., Zhang, S., Zhang, L., Hu, J., … Zhang, J. (2022). Comparative efficacy of non-invasive brain stimulation for post-stroke aphasia: A network meta-analysis and meta-regression of moderators. *Neuroscience and Biobehavioral Reviews*, *140*, 104804. https://doi.org/10.1016/j.neubiorev.2022.104804

Duncan, E. S., Pradeep, A. A., & Small, S. L. (2020). A review of biological interventions in chronic aphasia. *Annals of Indian Academy of Neurology*, *23*(Suppl 2), S82.

Elsner, B., Kugler, J., & Mehrholz, J. (2020). Transcranial direct current stimulation (tDCS) for improving aphasia after stroke: A systematic review with network meta-analysis of randomized controlled trials. *Journal of NeuroEngineering and Rehabilitation*, *17*(1), 1–11. https://doi.org/10.1186/s12984-020-00708-z

Elsner, B., Kugler, J., Pohl, M., & Mehrholz, J. (2013). Transcranial direct current stimulation (tDCS) for improving aphasia in patients after stroke. *The Cochrane Database of Systematic Reviews*, (6), CD009760. https://doi.org/10.1002/14651858.CD009760.pub2

Elsner, B., Kugler, J., Pohl, M., & Mehrholz, J. (2015). Transcranial direct current stimulation (tDCS) for improving aphasia in patients with aphasia after stroke. *The Cochrane Database of Systematic Reviews*, (5), CD009760. https://doi.org/10.1002/14651858.CD009760.pub3

Elsner, B., Kugler, J., Pohl, M., & Mehrholz, J. (2019). Transcranial direct current stimulation (tDCS) for improving aphasia in adults with aphasia after stroke. *Cochrane Database of Systematic Reviews*, (5).

Fiori, V., Nitsche, M. A., Cucuzza, G., Caltagirone, C., & Marangolo, P. (2019). High-definition transcranial direct current stimulation improves verb recovery in aphasic patients depending on current intensity. *Neuroscience*, *406*, 159–166.

Flöel, A., Meinzer, M., Kirstein, R., Nijhof, S., Deppe, M., Knecht, S., & Breitenstein,

C. (2011). Short-term anomia training and electrical brain stimulation. *Stroke*, *42*(7), 2065–2067.

Fridriksson, J., Elm, J., Stark, B. C., Basilakos, A., Rorden, C., Sen, S., … Bonilha, L. (2018). BDNF genotype and tDCS interaction in aphasia treatment. *Brain Stimulation*, *11*(6), 1276–1281.

Fridriksson, J., & Hillis, A. E. (2021). Current approaches to the treatment of post-stroke aphasia. *Journal of Stroke*, *23*(2), 183–201.

Fridriksson, J., Rorden, C., Elm, J., Sen, S., George, M. S., & Bonilha, L. (2018). Transcranial Direct Current Stimulation vs Sham Stimulation to Treat Aphasia After Stroke: A Randomized Clinical Trial. *JAMA Neurology*, *75*(12), 1470–1476. https://doi.org/10.1001/JAMANEUROL.2018.2287

Fritsch, B., Reis, J., Martinowich, K., Schambra, H. M., Ji, Y., Cohen, L. G., & Lu, B. (2010). Direct current stimulation promotes BDNF-dependent synaptic plasticity: potential implications for motor learning. *Neuron*, *66*(2), 198–204.

Geranmayeh, F., Chau, T. W., Wise, R. J. S., Leech, R., & Hampshire, A. (2017). Domain-general subregions of the medial prefrontal cortex contribute to recovery of language after stroke. *Brain*, *140*(7), 1947–1958. https://doi.org/https://doi.org/10.1093/brain/awx134

Graham, J. R., Pereira, S., & Teasell, R. (2011). Aphasia and return to work in younger stroke survivors. *Aphasiology*, *25*(8), 952–960.

Guillouët, E., Cogné, M., Saverot, E., Roche, N., Pradat-DIehl, P., Weill-Chounlamountry, A., … Charveriat, S. (2020). Impact of Combined Transcranial Direct Current Stimulation and Speech-language Therapy on Spontaneous Speech in Aphasia: A Randomized Controlled Double-blind Study. *Journal of the International Neuropsychological Society*, *26*(1), 7–18. https://doi.org/10.1017/S1355617719001036

Hamilton, R. H., Chrysikou, E. G., & Coslett, B. (2011). Mechanisms of aphasia recovery after stroke and the role of noninvasive brain stimulation. *Brain and Language*, *118*(1–2), 40–50. https://doi.org/10.1016/j.bandl.2011.02.005

Hebb, D. O. (1949). The first stage of perception: growth of the assembly. *The Organization of Behavior*, *4*(60), 60–78.

Holland, R., & Crinion, J. (2012). Can tDCS enhance treatment of aphasia after stroke? *Aphasiology*, *26*(9), 1169–1191.

Hope, T. M. H., Leff, A. P., Prejawa, S., Bruce, R., Haigh, Z., Lim, L., … Crinion, J. (2017). Right hemisphere structural adaptation and changing language skills

years after left hemisphere stroke. *Brain*, *140*(6), 1718–1728.

Kidwai, J., Sharma, S., Peper, M., & Brumberg, J. (2022). Investigating NIBS for language rehabilitation in aphasia. *Aphasiology*, *00*(00), 1–30. https://doi.org/10.1080/02687038.2022.2089972

Lefaucheur, J.-P., Antal, A., Ayache, S. S., Benninger, D. H., Brunelin, J., Cogiamanian, F., … Langguth, B. (2017). Evidence-based guidelines on the therapeutic use of transcranial direct current stimulation (tDCS). *Clinical Neurophysiology*, *128*(1), 56–92.

Lorca-Puls, D. L., Gajardo-Vidal, A., Team, P., Oberhuber, M., Prejawa, S., Hope, T. M. H., … Price, C. J. (2021). Brain regions that support accurate speech production after damage to Broca's area. *Brain Communications*, *3*(4), fcab230.

Marangolo, P. (2020). The potential effects of transcranial direct current stimulation (tDCS) on language functioning: Combining neuromodulation and behavioral intervention in aphasia. *Neuroscience Letters*, *719*(September 2017), 133329. https://doi.org/10.1016/j.neulet.2017.12.057

Mazaux, J.-M., Lagadec, T., de Sèze, M., Zongo, D., Asselineau, J., Douce, E., … Darrigrand, B. (2013). Communication activity in stroke patients with aphasia. *Journal of Rehabilitation Medicine*, *45*(4), 341–346.

Monti, A., Ferrucci, R., Fumagalli, M., Mameli, F., Cogiamanian, F., Ardolino, G., … Sforza, V. F. (2013). *Transcranial direct current stimulation (tDCS) and language*. 832–842. https://doi.org/10.1136/jnnp-2012-302825

Nitsche, M. A., & Paulus, W. (2001). Sustained excitability elevations induced by transcranial DC motor cortex stimulation in humans. *Neurology*, *57*(10), 1899–1901.

Opitz, A., Paulus, W., Will, S., Antunes, A., & Thielscher, A. (2015). Determinants of the electric field during transcranial direct current stimulation. *Neuroimage*, *109*, 140–150.

Otal, B., Olma, M. C., Flöel, A., & Wellwood, I. (2015). Inhibitory non-invasive brain stimulation to homologous language regions as an adjunct to speech and language therapy in post-stroke aphasia: A meta-analysis. *Frontiers in Human Neuroscience*, *9*. https://doi.org/10.3389/fnhum.2015.00236

Picano, C., Quadrini, A., Pisano, F., & Marangolo, P. (2021). Adjunctive approaches to aphasia rehabilitation: A review on efficacy and safety. *Brain Sciences*, *11*(1), 1–29. https://doi.org/10.3390/brainsci11010041

Polanowska, K. E., Leśniak, M. M., Seniów, J. B., Czepiel, W., & Członkowska, A.

(2013). Anodal transcranial direct current stimulation in early rehabilitation of patients with post-stroke non-fluent aphasia: a randomized, double-blind, sham-controlled pilot study. *Restorative Neurology and Neuroscience*, *31*(6), 761–771.

Polanowska, K. E., Leśniak, M., Seniów, J. B., & Członkowska, A. (2013). No effects of anodal transcranial direct stimulation on language abilities in early rehabilitation of post-stroke aphasic patients. *Neurologia i Neurochirurgia Polska*, *47*(5), 414–422.

Richardson, J., Datta, A., Dmochowski, J., Parra, L. C., & Fridriksson, J. (2015). Feasibility of using high-definition transcranial direct current stimulation (HD-tDCS) to enhance treatment outcomes in persons with aphasia. *NeuroRehabilitation*, *36*(1), 115–126.

Rosso, C., Arbizu, C., Dhennain, C., Lamy, J.-C., & Samson, Y. (2018). Repetitive sessions of tDCS to improve naming in post-stroke aphasia: Insights from an individual patient data (IPD) meta-analysis. *Restorative Neurology and Neuroscience*, *36*(1), 107–116.

Santos, M. D. dos, Cavenaghi, V. B., Mac-Kay, A. P. M. G., Serafim, V., Venturi, A., Truong, D. Q., … Simis, M. (2017). Non-invasive brain stimulation and computational models in post-stroke aphasic patients: single session of transcranial magnetic stimulation and transcranial direct current stimulation. A randomized clinical trial. *Sao Paulo Medical Journal*, *135*, 475–480.

Saur, D., Lange, R., Baumgaertner, A., Schraknepper, V., Willmes, K., Rijntjes, M., & Weiller, C. (2006). Dynamics of language reorganization after stroke. *Brain*, *129*(6), 1371–1384. https://doi.org/10.1093/brain/awl090

Shah-Basak, P. P., Wurzman, R., Purcell, J. B., Gervits, F., & Hamilton, R. (2016). Fields or flows? A comparative metaanalysis of transcranial magnetic and direct current stimulation to treat post-stroke aphasia. *Restorative Neurology and Neuroscience*, *34*(4), 537–558.

Silva, F. R. da, Mac-Kay, A. P. M. G., Chao, J. C., Santos, M. D. dos, & Gagliadi, R. J. (2018). Transcranial direct current stimulation: a study on naming performance in aphasic individuals. *Codas*, *30*. SciELO Brasil.

Skipper-Kallal, L. M., Lacey, E. H., Xing, S., & Turkeltaub, P. E. (2017). Right Hemisphere Remapping of Naming Functions Depends on Lesion Size and Location in Poststroke Aphasia. *Neural Plasticity*, *2017*, 1–17. https://doi.org/10.1155/2017/8740353

Spielmann, K., van de Sandt-Koenderman, W. M. E., Heijenbrok-Kal, M. H., & Ribbers, G. M. (2018). Transcranial Direct Current Stimulation Does Not Improve Language Outcome in Subacute Poststroke Aphasia. *Stroke*,

STROKEAHA.117.020197. https://doi.org/10.1161/STROKEAHA.117.020197

Stagg, C. J., Antal, A., & Nitsche, M. A. (2018). Physiology of transcranial direct current stimulation. *The Journal of ECT*, *34*(3), 144–152.

Stefaniak, J. D., Alyahya, R. S. W., & Lambon Ralph, M. A. (2021). Language networks in aphasia and health: A 1000 participant activation likelihood estimation meta-analysis. *Neuroimage*, *233*, 117960.

Stefaniak, J. D., Geranmayeh, F., & Lambon Ralph, M. A. (2022). The multidimensional nature of aphasia recovery post-stroke. *Brain : A Journal of Neurology*, *145*(4), 1354–1367. https://doi.org/10.1093/brain/awab377

Stockbridge, M. D., Elm, J., Breining, B. L., Tippett, D. C., Sebastian, R., Cassarly, C., … Vitti, E. (2023). Transcranial direct-current stimulation in subacute aphasia: a randomized controlled trial. *Stroke*, *54*(4), 912–920.

Stockert, A., Wawrzyniak, M., Klingbeil, J., Wrede, K., Kümmerer, D., Hartwigsen, G., … Saur, D. (2020). Dynamics of language reorganization after left temporo-parietal and frontal stroke. *Brain*, *143*(3), 844–861.

Tippett, D. C. (2015). Update in aphasia research. *Current Neurology and Neuroscience Reports*, *15*, 1–8.

Truong, D. Q., Magerowski, G., Blackburn, G. L., Bikson, M., & Alonso-Alonso, M. (2013). Computational modeling of transcranial direct current stimulation (tDCS) in obesity: impact of head fat and dose guidelines. *NeuroImage: Clinical*, *2*, 759–766.

Turkeltaub, P. E., Messing, S., Norise, C., & Hamilton, R. H. (2011). Are networks for residual language function and recovery consistent across aphasic patients? *Neurology*, *76*(20), 1726–1734. https://doi.org/10.1212/WNL.0b013e31821a44c1

Vines, B. W., Norton, A. C., & Schlaug, G. (2011). Non-invasive brain stimulation enhances the effects of melodic intonation therapy. *Frontiers in Psychology*, *2*, 1–10. https://doi.org/10.3389/fpsyg.2011.00230

Volpato, C., Cavinato, M., Piccione, F., Garzon, M., Meneghello, F., & Birbaumer, N. (2013). Transcranial direct current stimulation (tDCS) of Broca's area in chronic aphasia: a controlled outcome study. *Behavioural Brain Research*, *247*, 211–216.

Wiethoff, S., Hamada, M., & Rothwell, J. C. (2014). Variability in response to transcranial direct current stimulation of the motor cortex. *Brain Stimulation*, *7*(3), 468–475.

Wilson, S. M., & Schneck, S. M. (2021). Neuroplasticity in Post-Stroke Aphasia: A Systematic Review and Meta-Analysis of Functional Imaging Studies of Reorganization of Language Processing. *Neurobiology of Language*, *2*(1), 22–82. https://doi.org/10.1162/NOL_A_00025

Woodhead, Z. V. J., Crinion, J., Teki, S., Penny, W., Price, C. J., & Leff, A. P. (2017). Auditory training changes temporal lobe connectivity in 'Wernicke's aphasia': A randomized trial. *Journal of Neurology, Neurosurgery and Psychiatry*, *88*(7), 586–594. https://doi.org/10.1136/jnnp-2016-314621

Xing, S., Lacey, E. H., Skipper-Kallal, L. M., Jiang, X., Harris-Love, M. L., Zeng, J., & Turkeltaub, P. E. (2016). Right hemisphere grey matter structure and language outcomes in chronic left hemisphere stroke. *Brain*, *139*(1), 227–241. https://doi.org/10.1093/brain/awv323

You, D. S., Kim, D.-Y., Chun, M. H., Jung, S. E., & Park, S. J. (2011). Cathodal transcranial direct current stimulation of the right Wernicke's area improves comprehension in subacute stroke patients. *Brain and Language*, *119*(1), 1–5.

Zettin, M., Bondesan, C., Nada, G., Varini, M., & Dimitri, D. (2021). Transcranial Direct-Current Stimulation and Behavioral Training, a Promising Tool for a Tailor-Made Post-stroke Aphasia Rehabilitation: A Review. *Frontiers in Human Neuroscience*, *15*(December), 1–18. https://doi.org/10.3389/fnhum.2021.742136