


Impact of Combined Transcranial Direct Current Stimulation and Speech-language Therapy on Spontaneous Speech in Aphasia: A Randomized Controlled Double-blind Study



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Abstract

Objective: Aphasia recovery depends on neural reorganization, which can be enhanced by speech-language therapy and noninvasive brain stimulation. Several studies suggested that transcranial direct current stimulation (tDCS) associated with speech-language therapy may improve verbal performance evaluated by analytic tests, but none focused on spontaneous speech. We explored the effect of bihemispheric tDCS on spontaneous speech in patients with poststroke aphasia. **Methods:** In this multicentric controlled randomized cross-over double-blind study, we included 10 patients with poststroke aphasia (4 had aphasia >6 months and 6 with aphasia <6 months). We combined the sessions of speech-language therapy and bihemispheric tDCS (2 mA, 20 min). After three baseline speech evaluations (1/week), two different conditions were randomly consecutively proposed: active and sham tDCS over 3 weeks with 1 week of washout in between. The main outcome measure was the number of different nouns used in 2 min to answer the question “what is your job.” **Results:** There was no significant difference between conditions concerning the main outcome measure ($p = .47$) nor in the number of verbs, adjectives, adverbs, pronouns, repetitions, blank ideas, ideas, utterances with grammatical errors or paraphasias used. Other cognitive functions (verbal working memory, neglect, or verbal fluency) were not significantly improved in the tDCS group. No adverse events occurred. **Conclusion:** Our results differed from previous studies using tDCS to improve naming in patients with poststroke aphasia possibly due to bihemispheric stimulation, rarely used previously. The duration of the rehabilitation period was short given the linguistic complexity of the measure. This negative result should be confirmed by larger studies with ecological measures (*JINS*, 2020, 26, 7–18).

Keywords: Stroke, Language, tDCS, Rehabilitation, Spontaneous discourse, Ecological assessment

INTRODUCTION

Aphasia is very common after a left-hemisphere stroke. It can be described as a “disruption of the linguistic code affecting expression and/or comprehension in oral or written discourse” (Brin, 2014). Aphasia has a major impact on patients’ daily life, particularly on their psychoaffective

and socioprofessional domains (Aiach & Baumann, 2007). Few therapeutic solutions for aphasia recovery exist until now. For now, only speech rehabilitation proved its efficacy on discourse recovery but the effect size of the positive studies is quite low (Brady et al., 2016; Yu et al., 2017). Nevertheless, the previous research found that the intensity of rehabilitation and the specialization of the therapist were more important than the rehabilitation technique used (Klippi et al., 2012). Therefore, there is an urgent need to

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develop new approaches to reduce aphasia in patients with stroke. Improvement of patients with poststroke aphasia seems related to changes in neuronal activity, and it has already been shown that speech-language therapy could modulate neuronal reorganization (de Boissezon et al., 2008). But it is also possible to modulate neuronal activity using noninvasive brain stimulation techniques, such as transcranial direct current stimulation (tDCS) (ALHarbi, Armijo-Olivo, & Kim, 2017; Torres, Drebing, & Hamilton, 2013). In the context of the existing literature about aphasia and tDCS, potentiation of the effect of speech-language therapy seems possible by combining it with tDCS (Elsner, Kugler, Pohl, & Mehrholz, 2015).

Indeed, various studies in the recent literature studied the impact of tDCS on aphasia recovery. Most of them measured an improvement of language parameters after tDCS stimulation combined with speech-language therapy (Baker, Rorden, & Fridriksson, 2010; Campana, Caltagirone, & Marangolo, 2015; Cipollari et al., 2015; Jung et al., 2011; Marangolo et al., 2011, 2013a, 2014; Monti et al., 2008; Vestito, Rosellini, Mantero, & Bandini, 2014; Vines, Norton, & Schlaug, 2011; Wu, Wang, & Yuan, 2015; You, Kim, Chun, Jung, & Park, 2011). A recent systematic literature review including five meta-analyses and 48 studies found some evidence in the literature that tDCS could be effective for post-stroke aphasia rehabilitation at the chronic stages, but there is still a lot of variability between studies (Biou et al., 2019). The nature of the task, the stimulation site, the intensity and duration of the stimulation greatly differed from one study to the other (Baker et al., 2010; Branscheidt et al., 2018; Cherney et al., 2013; Ewa et al., 2013; Jung et al., 2011; Lee et al., 2013; Manenti et al., 2015; Marangolo et al., 2014, 2017; Sebastian et al., 2016; Vestito et al., 2014; Vines et al., 2011; Wu et al., 2015; You et al., 2011). Nevertheless, there is a consensus in the existing literature on the need of combining stimulation with speech-language therapy. Until now, the two intensities most commonly used in the literature are 1 and 2 mA. Indeed, 19 studies described the use of a stimulation at 1 mA and 22 at 2 mA. A stimulation intensity of 2 mA during 20 min repeated for 10 to 30 sessions has been a frequently used stimulation paradigm (Branscheidt et al., 2018; Marangolo et al., 2013b; Meinzer et al., 2016; Sebastian et al., 2016; Volpato et al., 2013; Wu et al., 2015). The electrode's placement differs from one study to another. Language recovery depends on a neural reorganization based on two major phenomena: at first, the right hemisphere takes charge of the usual left-hemispheric language abilities before its reactivation; then, the left perilesional regions restore gradually their previous activation level if possible and new neural pathways are created into the left hemisphere (Hartwigsen & Saur, 2017; Saur & Hartwigsen, 2012). This reorganization depends partly on the control of the interhemispheric inhibition balance. More precisely, if the right hemisphere inhibits the activation of the left one, language improvement will be weaker because it depends on the left hemispheric activations. On the contrary, the reactivation of the language areas in the left hemisphere correlates with an improvement of the speech function (de Boissezon

et al., 2008; Naeser et al., 2011). Therefore, it seems appropriate to set up a bihemispheric stimulation with a neuronal inhibition on the right hemisphere near Broca's homologous area and a neuronal activation on Broca's area in the left hemisphere.

Although bihemispheric stimulation has often been considered promising, there has been little empirical research on its effect on aphasia recovery (Fiori et al., 2017; Lee et al., 2013; Marangolo et al., 2014; Santos et al., 2017). Lee et al. (2013) compared the effect of bi and monohemispheric tDCS on naming and verbal fluency ability (the number of syllables produced in 1 min during an image description) in 11 patients with poststroke aphasia and found a significant improvement of naming in both conditions but a significant shorter naming response time for the group with bihemispheric stimulation.

In the recent literature, naming has been the most frequently used outcome measure for assessing aphasia recovery. The main value of this task is the ease of the evaluation, but its major disadvantage is that it does not reflect the patient's ability to communicate (Elsner, Kugler, Pohl, & Mehrholz, 2013; Elsner et al., 2015; Otal et al., 2015; Shah-Basak et al., 2016). The two main naming tasks found in the literature are naming of nouns and naming of verbs. The share is larger for nouns naming because of its use when authors use standardized language evaluation batteries (Baker et al., 2010; Branscheidt et al., 2018; Campana et al., 2015; Cherney et al., 2013; Fiori et al., 2011; Flöel et al., 2011; Fridriksson et al., 2018; Galletta et al., 2015; Kang et al., 2011; Lee et al., 2011; Marangolo et al., 2013a, 2013b, 2014, 2016, 2017, 2018; Meinzer et al., 2016; Monti et al., 2008; Pestalozzi et al., 2018; Polanowska et al., 2013; Sandars et al., 2017; Santos et al., 2013, 2017; Shah-Basak et al., 2015; Spielmann et al., 2018; Vestito et al., 2014; Vines et al., 2011; Volpato et al., 2013; You et al., 2011). Furthermore, generalization has been measured in several studies: some of them assessed the transfer of competence on an untrained task (Lee et al., 2011; Marangolo et al., 2011, 2013a, 2013b, 2014, 2016, 2017; Manenti et al., 2015; Sebastian et al., 2016; Vestito et al., 2014; Woodhead et al., 2018; Wu et al., 2015); some others showed the improvement of untrained items in addition of trained items (Baker et al., 2010; De Aguiar et al., 2015; Manenti et al., 2015; Meinzer et al., 2016; Marangolo et al., 2013a, 2013b, 2014, 2016; Sebastian et al., 2016; Vestito et al., 2014; Woodhead et al., 2018); and some others found an improvement in certain language tasks following nonspecific training of the tested tasks (Campana et al., 2015; Cipollari et al., 2015; Galletta et al., 2015; Vines et al., 2011). Some studies did not find a generalization effect in all patients (Marangolo et al., 2011; Vestito et al., 2014). Only Sandars et al. (2017) did not find a generalization effect for untreated items.

Kintsch et al. (1994) made the distinction between micro-linguistics and macrolinguistics. More precisely, discourse microanalyses focused on the study of lexical, syntactic, word finding, grammatical units, and characteristics of spoken language (pauses, paraphasias, and fluidity), while

macroanalyses focused on studying the coherence of discourse (local coherence at sentence level and global coherence at discourse level). The measures of main concepts and single word information in the form of C-Units (Correct Information Units) (Brookshire & Nicholas, 1994) emerged as the best measures for discourses analysis in the review of Pritchard, Hilari, Cocks, and Dipper (2017). According to Davis et al. (1997) and Bastiaanse and Jonkers (1998), microlinguistic and macrolinguistic components can be analyzed separately, but it seems useful to combine structural and functional analyses (Sherratt, 2007). All language levels come into play in the spontaneous discourse of the patients with poststroke aphasia (Chapman & Ulatowska, 1989), which is why current studies tend towards a mixed analysis that combines both sides (Falconer & Antonucci, 2012; Marini, Andretta, del Tin, & Carlomagno, 2011; Pritchard, Hilari, Cocks, & Dipper, 2018).

Until now, only few studies using tDCS explored more functional activities such as spontaneous speech, but the selected tasks remained mostly semidirected tasks of image or video clip descriptions (Campana et al., 2015; Galletta & Vogel-Eyny, 2015; Marangolo et al., 2013a, 2014; Norise, Sacchetti, & Hamilton, 2017). Marangolo et al. (2014), in a double-blind randomized controlled study including eight patients receiving 10 days of rehabilitation with a monohemispheric tDCS stimulation of 1 mA during 20 min, studied the effects of a conversational therapy on a video clip description task. They found an improvement of the average number of C-Units following a stimulation of the Broca's area significantly higher than after stimulation of the Wernicke's area or after sham stimulation. To the best of our knowledge, no study evaluated the effect of tDCS on spontaneous speech in response to an open question, yet neither used a bihemispheric stimulation to assess its effects on a speech task.

The aim of the present study was also to assess the impact of a bihemispheric tDCS stimulation coupled with speech-language therapy on spontaneous language performances of patients with poststroke aphasia answering to an open question.

MATERIALS AND METHODS

This study was a randomized, double-blind, multicentric interventional trial, comparing a bihemispheric tDCS stimulation to a sham stimulation in patients with a left-hemispheric stroke, using a cross-over design. Three neuro-rehabilitation units located in the Parisian area participated in the study by including patients.

Patients

Between November 2015 and January 2018, 14 left-hemispheric stroke patients were included in the present study. Inclusion criteria were age ≥ 18 years old (y.o.),

French language proficiency, and a first and unique stroke located in the left hemisphere of the brain (confirmed by magnetic resonance imaging or computerized tomography scan), regardless of the delay since stroke onset. The French adaptation of the Boston Diagnostic Aphasia Examination (HDAE, Mazaux and Orgogozo, 1982) score had to be one or more at the inclusion time. Indeed, we excluded patients with an aphasia severity rating scale=0, which corresponds to "no intelligible expression and no oral comprehension," because we needed to transcribe a minimum number of corpus for the speech analysis. Exclusion criteria were previous neurological disorders and the usual contraindications for tDCS (metal material or epileptic seizures occurring in 2 months before the inclusion).

Patients were in- or out-patients from three different neuro-rehabilitation units at the inclusion time. Each patient hospitalized in one of these three units and suffering from aphasia was screened by a speech and language therapist of this rehabilitation unit. If one patient fulfilled the inclusion criteria and did not present any of the exclusion criteria, one of the study investigators asked them to participate. An oral and written information was given to the patients and their relatives to explain the protocol. After a 1-week period of reflection, the patients and their relatives signed an informed consent form.

Transcranial Direct Current Stimulation

tDCS was applied with a battery-driven Eldith (NeuroConn GmbH, Ilmenau, Germany) programmable with a pair of surface-soaked sponge's electrodes (5×7 cm). Bihemispheric stimulation was administrated. Real stimulation consisted of 20 min of 2-mA direct current with the anode placed over the IFG (F7 international 10–20 system for electroencephalography (EEG)) and the cathode over the contralesional IFG (F8 international 10–20 system for EEG). The duration of fade-in and fade-out was 8 s with an increment every second. For sham stimulation, the same position was used but the current was turned off after 30 s (Gandiga, Hummel, & Cohen, 2006).

Study Design

A cross-over design was used to compare the active tDCS stimulation and the sham stimulation (Sham). The administration order of active-tDCS and sham was randomized by the Raymond Poincaré Hospital Clinical Investigation Center (CIC1429), using a stratified randomization by center. After signing informed consent, patients were included in the protocol for a period of 10 weeks.

Outcome measures were completed 6 times during the protocol: first, patients achieved as baselines three evaluations (1–2–3), one per week during 3 weeks (baseline period = P0). Just after that, began the first 3-week period of speech-language therapy combined with stimulation

		Evaluation 1 Evaluation 2 Evaluation 3	Evaluation 4	Evaluation 5	Evaluation 6 + Likert Scale	Evaluation 7
Inclusion	Randomization	Baseline (P0)	Stimulation period (P1)	Wash-out	Stimulation period (P2)	
		Weeks 1–3	Weeks 3–5	Week 6	Weeks 7–9	Week 10

Fig. 1. Overview of the study design.

(active-tDCS or sham) (P1). Outcome measures' assessments were done after P1 (evaluation 4) and just before P2 started (evaluation 5). Between the two periods of stimulation, patients had 1 week of washout without any stimulation and during which the speech-language therapy trained exclusively other cognitive processes than language. After the washout period began a second 3-week period of speech-language therapy combined with stimulation (active-tDCS or sham depending on the randomization order) (P2). At the end of the second period, outcome measures assessments were performed again (evaluation 6), in addition to the Likert scales to assess the tolerance, feasibility, and satisfaction of the patients and therapists, and then a last time (evaluation 7) after 1 week of washout (Figure 1).

The stimulation was applied 2–5 times per week during two periods of 3 weeks. Patients were blinded with respect to the administration of active-tDCS or sham stimulation. To control the blindness at the end of each session, all participants were asked about their awareness of the received stimulation, by answering the following question: “Do you think that the stimulation was on during the present session?” (The attempted answers were “yes”, “no” or “I don’t know”). The session’s number and the duration of each session were recorded. The speech therapists set the stimulation at the beginning of each speech-language therapy’s session, but the evaluators were also blinded regarding the stimulation. During both conditions (active-tDCS or sham stimulation), patients simultaneously underwent speech-language therapy. The tDCS electrodes were removed at the end of the session.

Speech-language Therapy

There is yet no consensus about the prevalence of a language rehabilitation technique over another (Brady et al., 2016), and no consensus exists in France either according to the HAS (Higher Health Authority of the country), to determine the better strategy for an optimal speech-language therapy. In the present study, speech rehabilitation was performed in accordance to the preferences of each center at the frequency of 2–5 therapy sessions per week during the entire inclusion period. The number of sessions could vary depending on the poststroke delay, according to the French recommendations (Biga, 2017).

Assessment

The main judgment criterion was the number of different nouns used during the HDAE subtest question “Describe your Job” (Goodglass & Kaplan, 2007). Patients’ oral answers were recorded during 2 min and analyzed by two different blinded speech therapists. The answers’ analyses started with the exclusion of inadequate answers (unrelated to the task). For the flow measures, the number of nouns, verbs, adjectives, adverbs, and pronouns within the patients’ answers were recorded. Regarding the quality measures, we recorded the number of repetitions, blank ideas (utterance without novel idea), ideas (utterances related to the question), utterances with grammatical errors, and paraphasias.

The secondary judgment criteria were the verbal fluency tests assessed during 2 min each [categorical (animals) and lexical (words starting with a P)] (Godefroy & Groupe de réflexion sur l’évaluation des fonctions exécutives, 2008), the time and the number of omissions on the Bells test as a measure of attention (Gauthier, Dehaut, & Joannette, 1989), and the verbal working memory span (Godefroy & Groupe de réflexion sur l’évaluation des fonctions exécutives, 2008). The description of outcome measures is available in Appendix 1 in Supplementary Material.

Furthermore, at the end of the treatment, various Likert’s scales were completed by the patients, their relatives, and the speech therapist in order to evaluate their satisfaction and the tolerability of the tDCS sessions. Likert’s scales included five levels: strongly disagree, disagree, neither agree nor disagree, agree, and strongly agree.

We expected the improvement to be better when the stimulation was active (A) compared to the sham stimulation (B).

Ethics

The study was promoted by the Garches Foundation and funded by a grant from the Bennetot Foundation (N° AP-FPB-14-002). It was authorized by the French Ethics Committee N° 15025 “Ile de France Paris XI” on 11 June 2015 and by the French National Agency for the Safety of Medicines and Health Products (ANSM, N°2014-A01773-44). Prior to inclusion, all participants received an information note. After a minimum period of 24 hr, written

consents were obtained for all participants. The Clinical Trials registration number of the study is N° NCT02612753.

Statistics

Power calculation: According to data from Marangolo (2014), we estimated the difference in the number of words when describing a video between rehabilitation alone and rehabilitation with stimulation as 17 words with a standard deviation (SD) of 10 and an effect size of 1.7. A number of six subjects per center highlight a size effect of 1.5 with a power of 80% and an α risk of 5%. In order to take into account the risk related to dropouts of around 20%, we decided to recruit eight patients per center.

The statistical analyses were performed using the SPSS (IBM corporation, USA) software version 22.

The characteristics of the population (sociodemographic, speech, characteristics of the brain damage, etc) were described using means (SD) for continuous variables and frequency for qualitative variables. We calculated the difference between the raw scores of the first poststimulation evaluation (evaluation 4) and of the last baseline measure (evaluation 3) to obtain the improvement score during the first stimulation period (P1). We also calculated a difference between the raw scores of the second poststimulation (evaluation 6) and of the post-washout (evaluation 5) to obtain the improvement score during the second stimulation period (P2). Because of the low number of participants in our study, we used nonparametric tests, that is, matched Wilcoxon tests. For Wilcoxon Signed-Rank tests, effect sizes were calculated by hand by using the following formula: $r = Z/\sqrt{N}$ as proposed by Tomczak and Tomczak (2014). A p -value $<.05$ was considered as statistically significant.

RESULTS

Description of the Study Population

We included 14 participants (4 women). The mean age was 53.8 (min = 24; max = 69; $SD = 13.1$). Ten of them had more than 12 years of education, four had 9–12 years of education (mean education duration = 2.7; min = 2; max = 3; $SD = .45$). Four patients (three in group 1) did not complete every major evaluation (two because of missing visits (one because of holidays), two because of unexpected medical events unrelated to the protocol (fracture and surgery) and could therefore not be included in the statistical analyses. All participants had a left-hemispheric stroke (ischemic for 12 and hemorrhagic for 2 of them). The delay since stroke onset ranged from 1 month to 5 years (mean = 18 months; min = 1 month; max = 68 months; $SD = 21.3$ months). The mean aphasia score on the HDAE was 2.64 (min = 1.0; max = 4.0; $SD = 1.1$).

Regarding the 10 patients who completed the whole study, 5 received active tDCS during the first period (P1) and 5 during the second period (P2). The average frequency of speech-language therapy sessions was 3.85 sessions per

week (min = 2; max = 5; $SD = 1.1$). The mean duration of speech-language therapy sessions was 72.8 min per session (min = 45 min; max = 120 min; $SD = 33.2$ min).

Table 1 shows the sociodemographic and clinical data of the 14 participants.

There was no significant difference at baseline between the patients receiving active-tDCS first (group 1) or sham first (group 2) regarding age ($p = .35$), gender ($\text{Khi}^2 = .4, p = .53$), education ($p = 1.00$), time since stroke onset ($p = .42$), and pretreatment aphasia severity measured using the HDAE ($p = .79$). There was no significant difference concerning the main judgment criterion between the patients receiving active tDCS first or active tDCS second ($z = -.67$, partial $\eta^2 = -.30, p = .50$).

Effect on the Primary Outcome Measure

There was no significant difference between active-tDCS and sham tDCS regarding the raw improvement scores of the primary outcome measure (the number of different nouns used during the HDAE job description subtest) ($z = -.71$, partial $\eta^2 = -.22, p = .48$) (Figure 2).

Effect on the Secondary Outcome Measures

There was no significant difference between active-tDCS and sham tDCS conditions concerning the secondary outcome measures (i.e., for verbs, adjectives, adverbs, pronouns, words, repetitions, blank ideas, ideas, utterances with grammatical errors, paraphasias, verbal working memory span direct, verbal working memory span reverse, number of omissions during the Bells test, total duration of the Bells test in seconds, and verbal fluency tests; Table 2).

Patient's Acceptability and Satisfaction

We asked participants about their acceptability of the tDCS stimulation, using a five-level Lickert scale. Regarding the following statement: "there are no concerns about the use of this technique", 3/9 (33%) of patients strongly agreed, 5/9 (56%) agreed, and 1/9 (11%) were undecided. In response to this same statement, 1/5 (20%) of relatives strongly agreed, 1/5 (20%) agreed, 1/5 (20%) were undecided, and 2/5 (40%) disagreed. Regarding therapists', 1/9 (90%) of them strongly agreed and 1/10 (10%) of them agreed. Afterwards, participants were asked to give their opinion concerning the following statement: "I am satisfied with this new therapeutic approach," 4/9 (44%) of patients strongly agreed, 3/9 (33%) agreed, 1/9 (11%) were undecided, and 1/9 (11%) disagreed. In response to this same statement, 1/5 (20%) of relatives strongly agreed, 3/5 (60%) agreed, and 1/5 (20%) were undecided. Regarding the therapists, 9/10 (90%) of them strongly agreed with the statement and 1/10 (10%) of them agreed. And finally, 9/10 (90%) of therapists strongly agreed and 1/10 (10%) agreed that the technique is easily used in rehabilitation (Table 3).

Table 1. Sociodemographic and clinical data at baseline of the 14 patients included in the study

Subjects (Number)	Group distribution	Gender (M = male, F = female)	Age (Years old)	Frequency of speech-language therapy sessions (Time \times frequency/week)	Delay between stroke and inclusion (Months + weeks)	Type of stroke	Type of aphasia	Score at the HDAE	Educational level
1	Group 1	M	54	1 hr 30 \times 5/week	2 months, 1 week	Left sylvic ischemic stroke	Mixed	1	3
2	Group 2	F	53	2 hr \times 3/week	17 months, 1 week	Left sylvic ischemic stroke	Mixed	2	3
3	Group 1	F	29	2 hr \times 3/week	44 months, 1 week	Left sylvic ischemic stroke	Broca	4	3
4	Group 2	M	65	2 hr \times 3/week	68 months	Left sylvic ischemic stroke	Wernicke	2	3
5	Group 1	M	56	1 hr \times 2/week	24 months	Left sylvic ischemic stroke	Anomic	4	2
6	Group 2	F	52	45 min \times 5/week	3 months	Left sylvic ischemic stroke	Motor transcortical	3	3
7	Group 2	M	24	1 hr \times 3/week	10 months, 3 weeks	Left hemorrhagic stroke	Motor transcortical	4	2
8	Group 1	M	66	2 hr \times 3/week	48 months	Left sylvic ischemic stroke	Mixed	1	3
9	Group 2	M	52	45 min \times 5/week	4 months	Left sylvic ischemic stroke	Broca	1	2
10	Group 2	F	57	45 min \times 5/week	24 months	Left hemorrhagic stroke	Motor transcortical	3	3
11	Group 1	M	57	45 min \times 5/week	4 months	Left sylvic ischemic stroke	Broca	3	3
12	Group 1	F	68	45 min \times 5/week	1 month, 2 weeks	Left sylvic ischemic stroke	Conduction	2	3
13	Group 1	M	52	45 min \times 5/week	1 months, 2 weeks	Left sylvic ischemic stroke	Conduction	3	2
14	Group 2	M	69	1 hr \times 4/week	2 months, 1 week	Left sylvic ischemic stroke	Broca	4	3

Note: The first column shows the number of the participants' inclusion. The second column shows group distribution (Group 1 = active t-DCS first (P1); Group 2 = active t-DCS during period 2 (P2)). The next columns show, respectively, gender, age, frequency of the speech-language therapy sessions, time since stroke onset, type of stroke, type of aphasia, pretreatment HDAE score, and educational level (3 = more than 12 years, 2 = 9–12 years; 1 = 8 years or less).

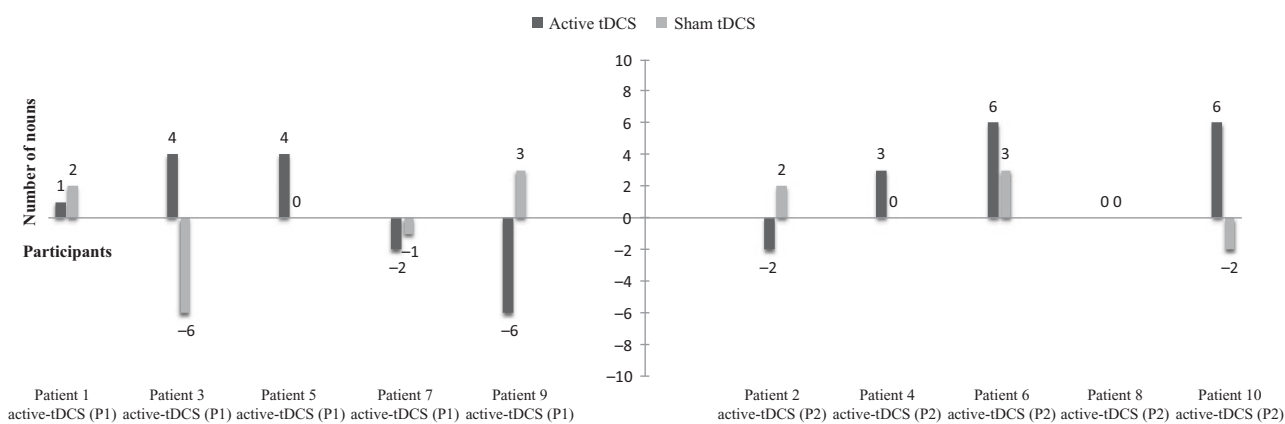


Fig. 2. Raw improvement scores for the number of nouns of the 10 participants who completed the study.

The figure's axis represents each patient included in the study. The improvement score at the end of the active tDCS is represented in dark grey, and the improvement score at the end of the sham tDCS is represented in light grey. Patients on the left part of the figure received active tDCS first, and those on the right part received sham stimulation first.

Side Effects

No side effects appeared during the treatment, which was well tolerated by each participant.

DISCUSSION

The aim of our study was to determine if tDCS combined with speech-language therapy in routine clinical practice improved spontaneous speech in response to an open question in patients with poststroke aphasia. No significant difference was found between the two conditions (active-tDCS and sham-tDCS) regarding the primary outcome measure, that is, the number of different nouns used during the HDAE subtest question "Describe your Job," and regarding the secondary outcome measures (flow measures, quality measures, verbal working memory, Bells test, and fluency tests). No adverse effects occurred and patients and speech therapists were satisfied with the use of the tDCS device.

Comparison with Previous Studies

Some studies compared the effect of mono- and bihemispheric tDCS on a learning task in healthy controls. For example, Lindenberg et al. (2010) found a larger improvement on a choice reaction time task when using bihemispheric stimulation in elderly subjects, just like Fiori et al. (2017) using a verbal learning task. But only few studies explored the impact of bihemispheric tDCS on language performances in patients with poststroke aphasia (Lee et al., 2013; Marangolo et al., 2013b, 2016). Yet Lee et al. (2013) found a larger improvement of reaction time in naming pictures, using a bi- rather than a monohemispheric stimulation in 11 patients with poststroke aphasia. Furthermore, Marangolo et al. (2013b) found in nine patients an increase of accuracy and speed during an articulatory task but also an improvement in other language tasks. More recently, a systematic review (Biou et al., 2019) concluded on the effectiveness of tDCS on poststroke aphasia

rehabilitation at the chronic stages. Faced with these promising results, we chose to evaluate the impact of a bihemispheric stimulation on spontaneous speech in patients with poststroke aphasia. Our results are in accordance with Norise et al. (2017) who recently evaluated in a randomized study in nine patients with poststroke aphasia, the effect of monohemispheric tDCS in a patient-dependent optimal response site (2 mA, 20 min) on verbal fluency. They did not find any significant improvement of the number of nouns generated, the sentence length, the proportion of well-formed sentences, and the proportion of pronouns during the Cookie Theft Picture Description Task after active stimulation. But the task used was semidirected (which means that the discourse is guided by the question asked and that the expected elements are explicit (e.g., the characters or the scenario in the image) and also not similar to ours which used an open question (where the theme (professional activity) is guided, but the form and content are different and specific to each patient). But Marangolo et al. (2013b, 2014), in two double-blind randomized studies, found a significantly higher number of C-units, verbs, mean percentage of correct, and number of sentences for trained items after a Broca's area stimulation than a Wernicke's area or a sham stimulation. Concerning untrained items, the results were more heterogeneous depending on the clip for C-Units (Content Units are clusters of elements and/or isolated phrases not always accompanied by a verb but with high communicative value (Loban, 1963), numbers of verbs and sentences). The mean percentage of endophoric's references was also significantly higher (endophoric's references are words referring to concepts that have been previously mentioned in the flow of discourse, anaphoras, conjunctions, ellipses, word repetition, etc. Halliday & Hasan, 2009). But these studies did not evaluate the effect of tDCS stimulation on the number of nouns and the outcome measures were trained specifically during the speech-language therapy sessions, which differs from our study. Lastly, the stimulation parameters used in these studies (a monohemispheric stimulation

Table 2. Main and secondary outcome measures between the active tDCS group and the sham-tDCS group

	A	B	Wilcoxon results
<i>Primary outcome measure: different nouns</i>	2 (-1.5, 4)	0 (-.75, 2)	($z = -.71$, partial $\eta^2 = -.22$, $p = .48$)
Flow measures			
Different verbs	0 (-.75, 1)	0 (0, 1)	($z = .36$, partial $\eta^2 = .11$, $p = .72$)
Different adjectives	0 (0, 1.75)	.5 (-2, .75)	($z = -1.20$, partial $\eta^2 = -.38$, $p = .23$)
Different adverbs	0 (-1, .75)	.5 (-.75, 1.75)	($z = .42$, partial $\eta^2 = .13$, $p = .67$)
Different pronouns	.5 (0, 2.75)	-.5 (-1, 1)	($z = -1.01$, partial $\eta^2 = .32$, $p = .31$)
Quality measures			
Repetitions	0 (0, .75)	0 (0, .75)	($z = -.08$, partial $\eta^2 = -.03$, $p = .93$)
Blank idea	0(-2.5, 1)	0 (-1.75, .75)	($z = .14$, partial $\eta^2 = .04$, $p = .89$)
Ideas	.5 (-2.5, 2)	.5 (-1.75, 1)	($z = .06$, partial $\eta^2 = .02$, $p = .95$)
Utterances with grammatical errors	-.5 (-1, .75)	1.5 (-1.25, 2)	($z = .84$, partial $\eta^2 = .27$, $p = .40$)
Paraphasias	.5 (-3.25, 2.75)	1 (0, 3.5)	($z = .66$, partial $\eta^2 = .21$, $p = .51$)
Other measures			
Verbal working memory span (direct)	0 (0, 0)	0 (-1, 0)	($z = -1.41$, partial $\eta^2 = -.45$, $p = .16$)
Verbal working memory span (reverse)	0 (-1, 0)	-.5 (-1.75, 0)	($z = -.42$, partial $\eta^2 = -.13$, $p = .67$)
Number of omissions during the Bells test	-.5 (-1, .75)	0 (-1, 1.75)	($z = -.67$, partial $\eta^2 = .21$, $p = .50$)
Total duration of the Bells test (seconds)	-5 (-34.5, 8.75)	-1 (-38.75, 11.25)	($z = -.15$, partial $\eta^2 = .05$, $p = .88$)
Categorical fluency (animals)	1 (-.5, 2.75)	0 (-3.75, 3)	($z = -.65$, partial $\eta^2 = -.21$, $p = .51$)
Litteral fluency (p)	0 (-1, 2)	.5 (-1, 2.5)	($z = .70$, partial $\eta^2 = .22$, $p = .48$)

Note: The first column shows the primary and secondary outcome measures; the second column shows the raw improvement score after the active tDCS condition [median (Quartile 1, Quartile 3)]; the third column shows the raw improvement score after the sham tDCS condition [median (Quartile 1, Quartile 3)]; the fourth column presents the Wilcoxon test. $p < .05$ was considered as statistically significant.

Table 3. Acceptability and satisfaction results

	Results of the Lickert scales			
	Strongly agreed	Agreed	Undecided	Disagreed
Answer to the statement: "There are no concerns about the use of this technique"				
Patients' answers	3/9 (33%)	5/9 (56%)	1/9 (11%)	0/9
Relatives' answers	1/5 (20%)	1/5 (20%)	1/5 (20%)	2/5 (40%)
Therapists' answers	1/9 (90%)	1/10 (10%)	0/10	0/10
Statement: "I am satisfied with this new therapeutic approach"				
Patients' answers	4/9 (44%)	3/9 (33%)	1/9 (11%)	1/9 (11%)
Relatives' answers	0/5	1/5 (20%)	3/5 (60%)	1/5 (20%)
Therapists' answers	9/10 (90%)	9/10 (90%)	0/10	0/10
Statement: "The technique is easily used in rehabilitation"				
Therapists' answers	9/10 (90%)	9/10 (90%)	0/10	0/10

Note: The first column specifies the statement and the respondents (9 patients, 5 relatives, and 10 Speech and Language Therapists). The next columns present the number of answers by level on the Lickert scales with the corresponding percentage into brackets.

with an intensity of 1 mA) differed from ours. Campana et al. (2015) assessed in a randomized controlled study the impact of tDCS combined with speech conversational therapy on various language abilities (picture description, nouns, and verbs naming) in 20 nonfluent chronic patients with poststroke aphasia. The main assessment criterion was the difference of percentage of correct answers before and after treatment (percentage of correct nouns and verbs in naming and of correct sentences in picture description). They found a significant improvement of the three outcome measures but only after anodic tDCS. The stimulation modality was similar to ours but with a monohemispheric configuration. However, 9/20 patients did not improve on

the picture description task. Moreover, the percentage of improvement for a picture description task is a questionable measure as it depends on the total number of sentences.

Discursive Language Measurement and Task Training

Two studies made by Marangolo et al. (2013a, 2014) moved towards a discursive approach. The first one showed an improvement of verb denomination, nouns, and image description after active-tDCS stimulation. The rehabilitation used was pragmatic, with a dialogue between the patient and the therapist about cartoons. The purpose of this rehabilitation

was to make the patient more and more informative. In this study, the evaluated task was not specifically trained. However, the outcome measures included paraphasias, which may be misleading. In opposition, in our study, we removed all language and speech deviations, therefore paraphasias were not considered as correct responses. The second study found an improvement of the number of endophoric references after active-tDCS stimulation. In this latter study, conversational improvement was analyzed through the description of video clips. However, such a task could be considered as a semidirected and not a spontaneous discourse, such as the open-ended question used in our study. In addition, it should be emphasized that three video clips were used during training sessions, and language improvement was significant on these trained “T-video clips,” while there was no significant improvement on the two untrained clips, which were used only for evaluations. This suggests that the beneficial effect could be due, at least in part, to task learning.

In most other studies that reported a naming improvement after tDCS stimulation, the patients were trained with the outcome assessment task.

Strengths and Limitations of the Present Study

To the best of our knowledge, no previous study addressed the effect of tDCS on a spontaneous language task such as the answer to an open question. Previous research relied mainly on semidirected speech tasks through video clips (Marangolo et al., 2013a, 2014) or picture’s description (Campana et al., 2015; Norise et al., 2017). Ecological tasks such as answering an open question could be assumed to reflect more accurately the daily life functioning of patients with poststroke aphasia. In our study, we had to deal with both methodological and clinical practice constraints. One of the strength of the present study is its multicentric, randomized, double-blind cross-over controlled design. Each cross-over period lasted 3 weeks which corresponded to the longer duration found in the previous research with tDCS (Cipollari et al., 2015; Manenti et al., 2015; Marangolo et al., 2016). However, in our current practice, progress observed clinically appears mainly more often after months than after weeks. Unfortunately, the administrative constraints of our protocol did not allow us to follow our population longer, which is a limitation of our study. Contrary to previous studies, we used three baseline evaluations in order to control the intraindividual variability of speech production, which is widely known in patients with poststroke aphasia (Duncan, Schmah, & Small, 2016; Villard & Kiran, 2018). Nevertheless, in order for multiple baselines to be relevant and meaningful, the Single-Case Experimental Design (SCED) methodology would have required optimally five baselines at least. Furthermore, two assessors translated and analyzed the audio records until reaching a consensus in order to avoid an evaluation bias. Finally, to facilitate reproducibility, we tried to stay as close as possible to the

number, duration, and content of speech-language therapy sessions usually done in rehabilitation centers in our country. Hospitalization times, budget allocations for speech and language rehabilitation, number of sessions that could be performed taking into account the number of speech and language therapists, and patient attendance days could not be completely objectively adapted to the specific requirements of a clinical study (i.e., a precise homogeneity of the duration and frequency of sessions between subjects for example).

But our study has some limitations. Although the sample size is similar to most of the previously published studies in the field, our small number of patients limited the statistical power. We included only 14 patients, while we had planned to include 24 participants. French rehabilitations centers receive very heterogeneous patients, and it is often difficult to find patients respecting inclusions criteria and moreover the duration of hospitalization is often insufficient to follow a study of 10 weeks. Additionally, our sample was quite heterogeneous in terms of poststroke delay, type of aphasia, and age, but it was representative of the population of most of the French rehabilitation centers. We observe that there is a factual limit between the need for homogeneous and specific samples for a specific clinical study, and the varied profiles actually present in our services, all the more so within a defined time range.

CONCLUSION

Our study evaluated the impact of bihemispheric tDCS combined with speech-language therapy on an ecological language production task and did not find any significant improvement in 10 patients with poststroke aphasia. The small number of patients, even if similar to most previous studies, and the limited time of therapy, should be taken into account in the interpretation of our results. Further studies using a SCED methodology may increase statistical power and reduce intra- and intervariability of patients with poststroke aphasia assessment and may help obtaining a better understanding of tDCS effectiveness in clinical practice to facilitate learning or to improve speech function in patients with poststroke aphasia.

SUPPLEMENTARY MATERIAL

To view supplementary material for this article, please visit <https://doi.org/10.1017/S1355617719001036>

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CONFLICTS OF INTEREST

The authors have nothing to disclose.

REFERENCES

- Aïach, P. & Baumann, Mi. (2007). L'aphasie, principal facteur aggravant du vécu d'un AVC par les proches. *Médecine*, 3(3), 130–135. doi: [10.1684/med.2007.0093](https://doi.org/10.1684/med.2007.0093)
- 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. doi: [10.1016/j.bbr.2017.05.050](https://doi.org/10.1016/j.bbr.2017.05.050)
- Baker, J.M., Rorden, C., & Fridriksson, J. (2010). Using transcranial direct-current stimulation to treat stroke patients with aphasia. *Stroke*, 41(6), 1229–1236. doi: [10.1161/STROKEAHA.109.576785](https://doi.org/10.1161/STROKEAHA.109.576785)
- Bastiaanse, R. & Jonkers, R. (1998). Verb retrieval in action naming and spontaneous speech in agrammatic and anomia aphasia. *Aphasiology*, 12(11), 951–969.
- Biga, J. (2017). Haute Autorité de Santé – Rééducation de la voix, du langage et de la parole. Retrieved September 23, 2018, from https://www.has-sante.fr/portail/jcms/r_1498794/fr/reeducation-de-la-voix-du-langage-et-de-la-parole.
- Biou, E., Cassouesalle, H., Cogne, M., Sibon, I., Gabory, I.D., Dehail, P., Aupy, J., & 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. doi: [10.1016/j.rehab.2019.01.003](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. *The Cochrane Database of Systematic Reviews*, (6), CD000425. doi: [10.1002/14651858.CD000425.pub4](https://doi.org/10.1002/14651858.CD000425.pub4)
- Branscheidt, M., Hoppe, J., Zwitserlood, P., & Liuzzi, G. (2018). tDCS over the motor cortex improves lexical retrieval of action words in poststroke aphasia. *Journal of Neurophysiology*, 119(2), 621–630. doi: [10.1152/jn.00285.2017](https://doi.org/10.1152/jn.00285.2017)
- Brin, F. (2014). *Dictionnaire d'orthophonie*. Isbergues: Ortho éd.
- Brookshire, R.H. & Nicholas, L.E. (1994). Speech sample size and test-retest stability of connected speech measures for adults with aphasia. *Journal of Speech and Hearing Research*, 37(2), 399–407.
- Campana, S., Caltagirone, C., & Marangolo, P. (2015). Combining voxel-based lesion-symptom mapping (VLSM) with A-tDCS language treatment: Predicting outcome of recovery in nonfluent chronic aphasia. *Brain Stimulation*, 8(4), 769–776. doi: [10.1016/j.brs.2015.01.413](https://doi.org/10.1016/j.brs.2015.01.413)
- Chapman, S.B. & Ulatowska, H.K. (1989). Discourse in aphasia: Integration deficits in processing reference. *Brain and Language*, 36(4), 651–668.
- Cherney, L.R., Babbitt, E.M., Hurwitz, R., Rogers, L.M., Stinear, J., Wang, X., Harvey, R.L., & Parrish, T. (2013). Transcranial direct current stimulation and aphasia: The case of Mr. C. *Topics in Stroke Rehabilitation*, 20(1), 5–21. doi: [10.1310/tsr2001-5](https://doi.org/10.1310/tsr2001-5)
- Cipollari, S., Veniero, D., Razzano, C., Caltagirone, C., Koch, G., & Marangolo, P. (2015). Combining TMS-EEG with transcranial direct current stimulation language treatment in aphasia. *Expert Review of Neurotherapeutics*, 15(7), 833–845. doi: [10.1586/14737175.2015.1049998](https://doi.org/10.1586/14737175.2015.1049998)
- Davis, G., O'Neil-Pirozzi, T.M., & Coon, M. (1997). Referential cohesion and logical coherence of narration after right hemisphere stroke. *Brain and Language*, 56(2), 183–210. doi: [10.1006/brln.1997.1741](https://doi.org/10.1006/brln.1997.1741)
- 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. doi: [10.3389/fnbeh.2015.00190](https://doi.org/10.3389/fnbeh.2015.00190)
- de Boissezon, X., Raboyeau, G., Simonetta-Moreau, M., Puel, M., Démonet, J.F., & Cardebat, D. (2008). Imagerie fonctionnelle cérébrale et prise en charge thérapeutique de l'aphasie : Orthophonie et stimulation magnétique transcrânienne répétitive [Functional neuroimaging and the treatment of aphasia: Speech therapy and repetitive transcranial magnetic stimulation]. *Revue Neurologique*, 164 Suppl 3, S45–S48. doi: [10.1016/S0035-3787\(08\)73290-9](https://doi.org/10.1016/S0035-3787(08)73290-9)
- Duncan, E.S., Schmah, T., & Small, S.L. (2016). Performance variability as a predictor of response to aphasia treatment. *Neurorehabilitation and Neural Repair*, 30(9), 876–882. doi: [10.1177/1545968316642522](https://doi.org/10.1177/1545968316642522)
- 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. doi: [10.1002/14651858.CD009760.pub2](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. doi: [10.1002/14651858.CD009760.pub3](https://doi.org/10.1002/14651858.CD009760.pub3)
- Ewa, P.K., Maciej, L.M., Barbara, S.J., Wojciech, C., & Anna, C. (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. doi: [10.3233/RNN-130333](https://doi.org/10.3233/RNN-130333)
- Falconer, C. & Antonucci, S.M. (2012). Use of semantic feature analysis in group discourse treatment for aphasia: Extension and expansion. *Aphasiology*, 26(1), 64–82. doi: [10.1080/02687038.2011.602390](https://doi.org/10.1080/02687038.2011.602390)
- Fiori, V., Coccia, M., Marinelli, C.V., Vecchi, V., Bonifazi, S., Ceravolo, M.G., Provinciali, L., Tomaiuolo, F., & Marangolo, P. (2011). Transcranial direct current stimulation improves word retrieval in healthy and nonfluent aphasic subjects. *Journal of Cognitive Neuroscience*, 23(9), 2309–2323. doi: [10.1162/jocn.2010.21579](https://doi.org/10.1162/jocn.2010.21579)
- Fiori, V., Nitsche, M., Iasevoli, L., Cucuzza, G., Caltagirone, C., & Marangolo, P. (2017). Differential effects of bihemispheric and unihemispheric transcranial direct current stimulation in young and elderly adults in verbal learning. *Behavioural Brain Research*, 321, 170–175. doi: [10.1016/j.bbr.2016.12.044](https://doi.org/10.1016/j.bbr.2016.12.044)
- 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. doi: [10.1161/STROKEAHA.110.609032](https://doi.org/10.1161/STROKEAHA.110.609032)
- 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. doi: [10.1001/jamaneurol.2018.2287](https://doi.org/10.1001/jamaneurol.2018.2287)

- Galletta, E.E. & Vogel-Eyny, A. (2015). Translational treatment of aphasia combining neuromodulation and behavioral intervention for lexical retrieval: Implications from a single case study. *Frontiers in Human Neuroscience*, 9, 447. doi: [10.3389/fnhum.2015.00447](https://doi.org/10.3389/fnhum.2015.00447)
- Gandiga, P.C., Hummel, F.C., & Cohen, L.G. (2006). Transcranial DC stimulation (tDCS): A tool for double-blind sham-controlled clinical studies in brain stimulation. *Clinical Neurophysiology: Official Journal of the International Federation of Clinical Neurophysiology*, 117(4), 845–850. doi: [10.1016/j.clinph.2005.12.003](https://doi.org/10.1016/j.clinph.2005.12.003)
- Gauthier, L., Dehaut, F., & Joanette, Y. (1989). The bells test: A quantitative and qualitative test for visual neglect. *International Journal of Clinical Neuropsychology*, 11(2), 49–54.
- Godefroy, O. & Groupe de réflexion sur l'évaluation des fonctions exécutives. (2008). *Fonctions exécutives et pathologies neurologiques et psychiatriques: Évaluation en pratique clinique*. Marseille: Solal.
- Goodglass, H. & Kaplan, E. (2007). *HDAE, échelle d'évaluation de l'aphasie: Adaptation française du Boston diagnostic aphasia examination de* (Vols 1–1). Paris: ECPA, les Éd. du Centre de psychologie appliquée.
- Halliday, M.A.K. & Hasan, R. (2009). *Cohesion in English (Nachdr.)*. London: Longman.
- Hartwigsen, G. & Saur, D. (2017). Neuroimaging of stroke recovery from aphasia – Insights into plasticity of the human language network. *NeuroImage*, 190, 14–31. doi: [10.1016/j.neuroimage.2017.11.056](https://doi.org/10.1016/j.neuroimage.2017.11.056)
- Jung, I.-Y., Lim, J.Y., Kang, E.K., Sohn, H.M., & Paik, N.-J. (2011). The factors associated with good responses to speech therapy combined with transcranial direct current stimulation in post-stroke aphasic patients. *Annals of Rehabilitation Medicine*, 35(4), 460. doi: [10.5535/arm.2011.35.4.460](https://doi.org/10.5535/arm.2011.35.4.460)
- Kang, E.K., Kim, Y.K., Sohn, H.M., Cohen, L.G., & Paik, N.-J. (2011). Improved picture naming in aphasia patients treated with cathodal tDCS to inhibit the right Broca's homologue area. *Restorative Neurology and Neuroscience*, 29(3), 141–152. doi: [10.3233/RNN-2011-0587](https://doi.org/10.3233/RNN-2011-0587)
- Kintsch, W. (1994). Text comprehension, memory, and learning. *The American Psychologist*, 49(4), 294–303.
- Klippi, A., Sellman, J., Heikkinen, P., & Laine, M. (2012). Current clinical practices in aphasia therapy in Finland: Challenges in moving towards National Best Practice. *Folia Phoniatrica et Logopaedica*, 64(4), 169–178. doi: [10.1159/000341106](https://doi.org/10.1159/000341106)
- Lee, J. & Thompson, C.K. (2011). Real-time production of unergative and unaccusative sentences in normal and agrammatic speakers: An eyetracking study. *Aphasiology*, 25(6–7), 813–825. doi: [10.1080/02687038.2010.542563](https://doi.org/10.1080/02687038.2010.542563)
- Lee, S.Y., Cheon, H.-J., Yoon, K.J., Chang, W.H., & Kim, Y.-H. (2013). Effects of dual transcranial direct current stimulation for Aphasia in Chronic stroke patients. *Annals of Rehabilitation Medicine*, 37(5), 603–610. doi: [10.5535/arm.2013.37.5.603](https://doi.org/10.5535/arm.2013.37.5.603)
- Lindenberg, R., Renga, V., Zhu, L.L., Nair, D., & Schlaug, G. (2010). Bihemispheric brain stimulation facilitates motor recovery in chronic stroke patients. *Neurology*, 75(24), 2176–2184. doi: [10.1212/WNL.0b013e318202013a](https://doi.org/10.1212/WNL.0b013e318202013a)
- Loban, W. (1963). *The language of elementary school children*. Ed. Champaign, IL: National Council of Teachers of English.
- Manenti, R., Petesi, M., Brambilla, M., Rosini, S., Miozzo, A., Padovani, A., Miniussi, C., & Cotelli, M. (2015). Efficacy of semantic-phonological treatment combined with tDCS for verb retrieval in a patient with aphasia. *Neurocase*, 21(1), 109–119. doi: [10.1080/13554794.2013.873062](https://doi.org/10.1080/13554794.2013.873062)
- Marangolo, P., Fiori, V., Calpagnano, M.A., Campana, S., Razzano, C., Caltagirone, C., & Marini, A. (2013a). tDCS over the left inferior frontal cortex improves speech production in aphasia. *Frontiers in Human Neuroscience*, 7, 539. doi: [10.3389/fnhum.2013.00539](https://doi.org/10.3389/fnhum.2013.00539)
- Marangolo, P., Fiori, V., Caltagirone, C., Pisano, F., & Priori, A. (2018). Transcranial cerebellar direct current stimulation enhances verb generation but not verb naming in poststroke aphasia. *Journal of Cognitive Neuroscience*, 30(2), 188–199. doi: [10.1162/jocn_a_01201](https://doi.org/10.1162/jocn_a_01201)
- Marangolo, P., Fiori, V., Campana, S., Calpagnano, M.A., Razzano, C., Caltagirone, C., & Marini, A. (2014). Something to talk about: Enhancement of linguistic cohesion through tDCS in chronic non fluent aphasia. *Neuropsychologia*, 53, 246–256. doi: [10.1016/j.neuropsychologia.2013.12.003](https://doi.org/10.1016/j.neuropsychologia.2013.12.003)
- Marangolo, P., Fiori, V., Cipollari, S., Campana, S., Razzano, C., Di Paola, M., ... Caltagirone, C. (2013b). Bihemispheric stimulation over left and right inferior frontal region enhances recovery from apraxia of speech in chronic aphasia. *The European Journal of Neuroscience*, 38(9), 3370–3377. doi: [10.1111/ejn.12332](https://doi.org/10.1111/ejn.12332)
- Marangolo, P., Fiori, V., Sabatini, U., De Pasquale, G., Razzano, C., Caltagirone, C., & Gili, T. (2016). Bilateral transcranial direct current stimulation language treatment enhances functional connectivity in the left hemisphere: Preliminary data from aphasia. *Journal of Cognitive Neuroscience*, 28(5), 724–738. doi: [10.1162/jocn_a_00927](https://doi.org/10.1162/jocn_a_00927)
- Marangolo, P., Fiori, V., Shofany, J., Gili, T., Caltagirone, C., Cucuzza, G., & Priori, A. (2017). Moving beyond the brain: Transcutaneous spinal direct current stimulation in post-stroke aphasia. *Frontiers in Neurology*, 8, 400. doi: [10.3389/fneur.2017.00400](https://doi.org/10.3389/fneur.2017.00400)
- Marangolo, P., Marinelli, C.V., Bonifazi, S., Fiori, V., Ceravolo, M.G., Provinciali, L., & Tomaiuolo, F. (2011). Electrical stimulation over the left inferior frontal gyrus (IFG) determines long-term effects in the recovery of speech apraxia in three chronic aphasics. *Behavioural Brain Research*, 225(2), 498–504. doi: [10.1016/j.bbr.2011.08.008](https://doi.org/10.1016/j.bbr.2011.08.008)
- Marini, A., Andreetta, S., del Tin, S., & Carlomagno, S. (2011). A multi-level approach to the analysis of narrative language in aphasia. *Aphasiology*, 25(11), 1372–1392. doi: [10.1080/02687038.2011.584690](https://doi.org/10.1080/02687038.2011.584690)
- Mazaux, J.M. & Orgogozo, J.M. (1982). Etude analytique et quantitative des troubles du langage par lesion du thalamus gauche: L'aphasie thalamique. *Cortex*, 18(3), 403–416. doi: [10.1016/S0010-9452\(82\)80039-7](https://doi.org/10.1016/S0010-9452(82)80039-7)
- Meinzer, M., Darkow, R., Lindenberg, R., & Flöel, A. (2016). Electrical stimulation of the motor cortex enhances treatment outcome in post-stroke aphasia. *Brain*, 139(4), 1152–1163. doi: [10.1093/brain/aww002](https://doi.org/10.1093/brain/aww002)
- Monti, A., Cogiamanian, F., Marceglia, S., Ferrucci, R., Mameli, F., Mrakic-Sposta, S., Vergari, M., Zago, S., & Priori, A. (2008). Improved naming after transcranial direct current stimulation in aphasia. *Journal of Neurology, Neurosurgery, and Psychiatry*, 79(4), 451–453. doi: [10.1136/jnnp.2007.135277](https://doi.org/10.1136/jnnp.2007.135277)
- Naeser, M.A., Martin, P.I., Theoret, H., Kobayashi, M., Fregni, F., Nicholas, M., Tormos, J.M., Steven, M.S., Baker, E.H., & Pascual-Leone, A. (2011). TMS suppression of right pars triangularis, but not pars opercularis, improves naming in aphasia. *Brain and Language*, 119(3), 206–213. doi: [10.1016/j.bandl.2011.07.005](https://doi.org/10.1016/j.bandl.2011.07.005)

- Norise, C., Sacchetti, D., & Hamilton, R. (2017). Transcranial direct current stimulation in post-stroke chronic aphasia: The impact of baseline severity and task specificity in a pilot sample. *Frontiers in Human Neuroscience*, *11*, 260. doi: [10.3389/fnhum.2017.00260](https://doi.org/10.3389/fnhum.2017.00260)
- 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*, 236. doi: [10.3389/fnhum.2015.00236](https://doi.org/10.3389/fnhum.2015.00236)
- Pestalozzi, M.I., Di Pietro, M., Martins Gaytanidis, C., Spierer, L., Schneider, A., Chouiter, L., Colombo, F., Annoni, J.M., & Jost, L.B. (2018). Effects of prefrontal transcranial direct current stimulation on lexical access in chronic poststroke aphasia. *Neurorehabilitation and Neural Repair*, *32*(10), 913–923. doi: [10.1177/1545968318801551](https://doi.org/10.1177/1545968318801551)
- 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.
- Pritchard, M., Hilari, K., Cocks, N., & Dipper, L. (2017). Reviewing the quality of discourse information measures in aphasia. *International Journal of Language & Communication Disorders*, *52*(6), 689–732. doi: [10.1111/1460-6984.12318](https://doi.org/10.1111/1460-6984.12318)
- Pritchard, M., Hilari, K., Cocks, N., & Dipper, L. (2018). Psychometric properties of discourse measures in aphasia: Acceptability, reliability, and validity. *International Journal of Language & Communication Disorders*, *53*(6), 1078–1093. doi: [10.1111/1460-6984.12420](https://doi.org/10.1111/1460-6984.12420)
- Sandars, M., Cloutman, L., & Woollams, A. (2017). Manipulating laterality and polarity of transcranial direct current stimulation to optimise outcomes for anomia therapy in an individual with chronic Broca's aphasia. *Aphasiology*, *32*(7), 1–25. doi: [10.1080/02687038.2017.1350631](https://doi.org/10.1080/02687038.2017.1350631)
- Santos, M.D., Gagliardi, R.J., Mac-Kay, A.P.M.G., Boggio, P.S., Lianza, R., & Fregni, F. (2013). Transcranial direct-current stimulation induced in stroke patients with aphasia: A prospective experimental cohort study. *Sao Paulo Medical Journal*, *131*(6), 422–426. doi: [10.1590/1516-3180.2013.1316595](https://doi.org/10.1590/1516-3180.2013.1316595)
- Santos, M.D.D., Cavenaghi, V.B., Mac-Kay, A.P.M.G., Serafim, V., Venturi, A., Truong, D.Q., Huang, Y., Boggio, P.S., Fregni, F., Bikson, M., & Gagliardi, R.J. (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 = Revista Paulista De Medicina*, *135*(5), 475–480. doi: [10.1590/1516-3180.2016.0194060617](https://doi.org/10.1590/1516-3180.2016.0194060617)
- Saur, D. & Hartwigsen, G. (2012). Neurobiology of language recovery after stroke: Lessons from neuroimaging studies. *Archives of Physical Medicine and Rehabilitation*, *93*(1 Suppl), S15–S25. doi: [10.1016/j.apmr.2011.03.036](https://doi.org/10.1016/j.apmr.2011.03.036)
- Sebastian, R., Saxena, S., Tsapkini, K., Faria, A.V., Long, C., Wright, A., Davis, C., Tippett, D.C., Mourdoukoutas, A.P., Bikson, M., Celnik, P., & Hillis, A.E. (2016). Cerebellar tDCS: A novel approach to augment language treatment post-stroke. *Frontiers in Human Neuroscience*, *10*, 695. doi: [10.3389/fnhum.2016.00695](https://doi.org/10.3389/fnhum.2016.00695)
- Shah-Basak, P.P., Norise, C., Garcia, G., Torres, J., Faseyitan, O., & Hamilton, R.H. (2015). Individualized treatment with transcranial direct current stimulation in patients with chronic non-fluent aphasia due to stroke. *Frontiers in Human Neuroscience*, *9*, 201. doi: [10.3389/fnhum.2015.00201](https://doi.org/10.3389/fnhum.2015.00201)
- 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. doi: [10.3233/RNN-150616](https://doi.org/10.3233/RNN-150616)
- Sherratt, S. (2007). Multi-level discourse analysis: A feasible approach. *Aphasiology*, *21*(3–4), 375–393. doi: [10.1080/02687030600911435](https://doi.org/10.1080/02687030600911435)
- Spielmann, K., van de Sandt-Koenderman, W.M., Heijnenbrok-Kal, M.H., & Ribbers, G.M. (2018). Comparison of two configurations of transcranial direct current stimulation for aphasia treatment. *Journal of Rehabilitation Medicine*, *50*(6), 527–533. doi: [10.2340/16501977-2338](https://doi.org/10.2340/16501977-2338)
- Tomczak, M. & Tomczak, E. (2014). The need to report effect size estimates revisited. An overview of some recommended measures of effect size. *Trends in Sport Sciences*, *1*(21), 19–25.
- Torres, J., Drebing, D., & Hamilton, R. (2013). TMS and tDCS in post-stroke aphasia: Integrating novel treatment approaches with mechanisms of plasticity. *Restorative Neurology and Neuroscience*, *31*(4), 501–515. doi: [10.3233/RNN-130314](https://doi.org/10.3233/RNN-130314)
- Vestito, L., Rosellini, S., Mantero, M., & Bandini, F. (2014). Long-term effects of transcranial direct-current stimulation in chronic post-stroke aphasia: A pilot study. *Frontiers in Human Neuroscience*, *8*, 785. doi: [10.3389/fnhum.2014.00785](https://doi.org/10.3389/fnhum.2014.00785)
- Villard, S. & Kiran, S. (2018). Between-session and within-session intra-individual variability in attention in aphasia. *Neuropsychologia*, *109*, 95–106. doi: [10.1016/j.neuropsychologia.2017.12.005](https://doi.org/10.1016/j.neuropsychologia.2017.12.005)
- Vines, B.W., Norton, A.C., & Schlaug, G. (2011). Non-invasive brain stimulation enhances the effects of melodic intonation therapy. *Frontiers in Psychology*, *2*, 230. doi: [10.3389/fpsyg.2011.00230](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. doi: [10.1016/j.bbr.2013.03.029](https://doi.org/10.1016/j.bbr.2013.03.029)
- Woodhead, Z.V.J., Kerry, S.J., Aguilar, O.M., Ong, Y.-H., Hogan, J.S., Pappa, K., Leff, A.P., & Crinion, J.T. (2018). Randomized trial of iReadMore word reading training and brain stimulation in central alexia. *Brain: A Journal of Neurology*, *141*(7), 2127–2141. doi: [10.1093/brain/awy138](https://doi.org/10.1093/brain/awy138)
- Wu, D., Wang, J., & Yuan, Y. (2015). Effects of transcranial direct current stimulation on naming and cortical excitability in stroke patients with aphasia. *Neuroscience Letters*, *589*, 115–120. doi: [10.1016/j.neulet.2015.01.045](https://doi.org/10.1016/j.neulet.2015.01.045)
- 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. doi: [10.1016/j.bandl.2011.05.002](https://doi.org/10.1016/j.bandl.2011.05.002)
- Yu, Z.-Z., Jiang, S.-J., Jia, Z.-S., Xiao, H.-Y., & Zhou, M.-Q. (2017). Study on language rehabilitation for aphasia. *Chinese Medical Journal*, *130*(12), 1491–1497. doi: [10.4103/0366-6999.207465](https://doi.org/10.4103/0366-6999.207465)