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Efficacy of Bihemispheric tDCS in Rehabilitation of Non-Fluent Aphasia: A Single-subject Pilot Study

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ABSTRACT

Objective: Transcranial direct current stimulation (tDCS) has emerged as a potentially effective complementary tool in rehabilitation of aphasia. However, there is no consensus regarding the optimal tDCS montage to augment language outcomes in aphasia. Against this background, the present study aimed to examine efficacy of tDCS combined with language therapy in aphasia rehabilitation and to compare two different montages.

Methods: A right-handed participant suffering from chronic, non-fluent aphasia following stroke affecting the left hemisphere underwent a 5-week procedure involving tDCS coupled with language therapy. The procedure comprised two 5-day treatments of bihemispheric tDCS (over inferior frontal and posterior temporal sites determined using the international 10-20 EEG system). As part of both treatments, the left hemispheric targets were excited through anodal tDCS while simultaneously inhibiting their right-hemispheric homologues through cathodal tDCS. Baseline, post-treatment and follow-up assessments were obtained using a comprehensive language assessment tool.

Results: An increase in language outcomes, particularly in repetition, was observed following the treatments. It was also found that therapy gains were more robust following bihemispheric stimulation of the posterior temporal sites compared to the inferior frontal targets.

Conclusion: Bihemispheric tDCS coupled with language therapy appears to be effective in remediating language symptoms, particularly in terms of the repetition ability, in aphasia.

Keywords: Aphasia, stroke, tDCS, brain stimulation, rehabilitation

1. INTRODUCTION

Aphasia is an acquired neurogenic language disorder resulting from damage to specific brain regions especially in the left hemisphere and affecting oral and/or written, expressive and/or receptive language skills (1,2). Speech and language therapy offered to persons with aphasia (PWA) is the gold standard in aphasia rehabilitation and there is evidence for its efficacy in improving functional language, language comprehension and production (3). However, it is not clear how long these benefits last (3). In addition, positive therapeutic outcomes have generally been obtained in studies with longer hours of therapy or with an intensive therapy program (4–7). Moreover, PWA often do not fully recover and continue to suffer from a certain level of language difficulty even after therapy (5,8). These limitations highlight the need to complement and support speech and language therapy with other available techniques in aphasia rehabilitation.

Non-invasive brain stimulation (NIBS) techniques including transcranial direct current stimulation (tDCS) have recently been investigated as a potential complement to speech and language therapy. NIBS attempts to trigger neuromodulation of cortical activity associated with language processing. Using tDCS, depending on the montage of the two electrodes (anode and cathode), between which a weak current passes, a target region can be excited (anodal stimulation), inhibited (cathodal stimulation), or both (bihemispheric stimulation) (4). Previous research reported improvement in aphasic symptoms following excitation of the inferior frontal gyrus (IFG) in the lesioned left hemisphere through anodal tDCS (9–11) or inhibition of IFG in the intact right hemisphere through cathodal tDCS (12). Recent reviews also provided support for the effectiveness of tDCS in aphasia rehabilitation (13–15).

Despite the evidence supporting efficacy of tDCS in aphasia intervention, several studies provided little or no support for therapeutic benefits of tDCS in aphasia (16–19). Moreover, there is no agreement on the most ideal montage of the tDCS electrodes (14,20). Also, relatively limited number

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of studies directly compared bihemispheric stimulation of inferior frontal (Broca's area and its right-hemispheric homologue) and posterior temporal (Wernicke's area and its right-hemispheric homologue) sites within the same participant(s). Finally, to our knowledge, no previously published study investigated effectiveness of tDCS treatment in a PWA whose native language is Turkish, a language which is distinguished through its morphosyntactic differences (e.g., rich morphology, free word order) from English, in which most of this line of research was conducted. To fill this gap in the literature, the current study recruited a PWA suffering from chronic, post-stroke non-fluent aphasia, who underwent 5-week intervention encompassing two 5-day treatments of bihemispheric tDCS (to inferior frontal and posterior temporal sites) coupled with concurrent language therapy in addition to pre – and post-treatment assessments and follow-up assessments using a standardized language assessment test.

2. METHODS

Before commencing the study, approval was obtained from the Ethics Committee of Istanbul Medipol University. The participant provided oral consent and her custodian gave written informed consent prior to implementation.

2.1. Participant / Case History

The participant was an 81-year-old, right-handed woman with chronic aphasia following stroke in the left hemisphere 14 months prior to the commencement of the study. She suffered from hemiparesis affecting the right side of her body. She had received 8 years of formal schooling. Before the commencement of the present study, she reported having received speech and language therapy for aphasia for a period of 6 months with 2-3 sessions per week. Language assessment performed by an SLT (first author) using the Language Assessment Test for Aphasia (21) revealed severely impaired expressive skills (repetition and naming) while her receptive skills (auditory comprehension) were relatively spared consistent with non-fluent aphasia (please refer to 2.4.Language Assessments section and Table 1 for further details).

2.2. Study Design

A single-subject, crossover (ABACA) design was adopted. This study design involves a baseline where no treatment is provided (A), followed by a treatment (B), then by a return to the pretreatment baseline level (second A), then by another treatment condition (C), and finally a return to the baseline level again (third A) (22). This study design was adopted to compare two tDCS treatments by investigating the effects of their introduction and removal successively. Two tDCS treatments were coupled with a language therapy and administered to the patient in separate phases of the research. The language therapy was identical in the two treatments, while only the location of the tDCS stimulation differed between the treatments. As illustrated in Figure 1, a baseline language assessment was obtained one day before commencing Treatment 1. Treatment 1 was provided for five consecutive days during week 1. The second language assessment was performed on the next day of completion of Treatment 1, for which it served as a posttest. After a washout period of one week when no treatment was given, the third language assessment was conducted and this served as a follow-up for Treatment 1 and as a baseline for Treatment 2, which commenced on the day following the third assessment. Treatment 2 was administered for five consecutive days, and the fourth language assessment was carried out the day following completion of Treatment 2, for which it served as a posttest. Finally, the fifth language assessment was administered following a washout period of two weeks. This fifth assessment was originally planned one week after Treatment 2, as was the case for the follow-up of Treatment 1, but had to be postponed one week to accommodate the patient's availability. All treatment and assessment procedures were performed in the same setting (a quiet room) in the participant's home.

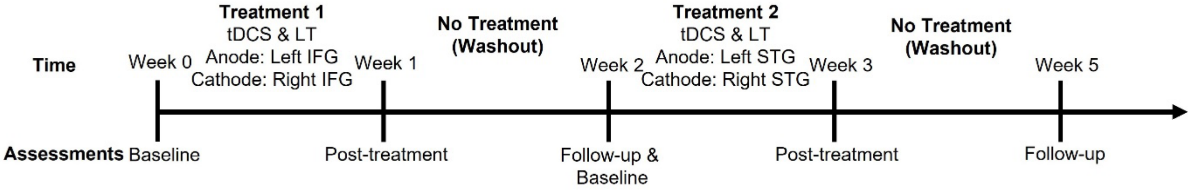

Figure 1. *Study design [LT: Language therapy].*

2.3. tDCS and Language Therapy

tDCS was delivered with a battery-driven direct current stimulator (neuroConn GmbH, Ilmenau, Germany) at 2mA using 5x7cm electrodes inside saline-soaked pads of 7x8cm. In Treatment 1, the anode was placed over Broca's area (left IFG) and the cathode over the homologous region in the right hemisphere (right IFG). In Treatment 2, on the other hand, the anode was placed over Wernicke's area (left posterior STG) and the cathode over its homologue in the right hemisphere (right posterior STG). The stimulation sites were determined using the international 10-20 system with an EEG electrode cap, as illustrated in Figure 2. Specifically, the midpoint of F7-FC5 and of F8-FC6 corresponded to the left IFG and the right IFG, respectively, while the electrodes CP5 and CP6 corresponded to the left posterior STG and the right posterior STG, respectively (15). Each tDCS treatment was administered with a daily dosage of 20 minutes for five consecutive days. The same tDCS parameters were used in Treatments 1 and 2 except for the stimulation sites. No adverse events were observed during or after the completion of the study.

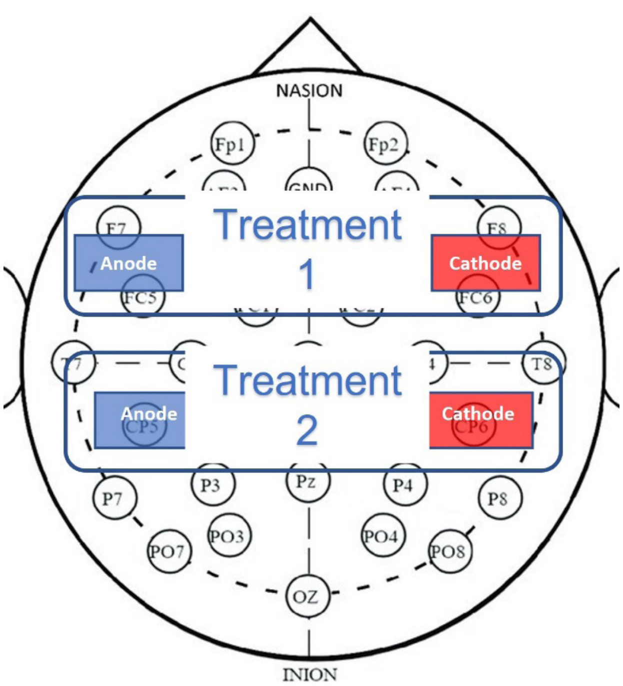

Figure 2. *tDCS montages used in Treatments 1 and 2.*

Language therapy was administered by a speech and language therapist (SLT, first author) to PWA. The therapy was primarily based on the semantic feature analysis approach, which aims to facilitate retrieval of conceptual information through access to semantic networks (23,24). To that end, visual and auditory cues were provided to PWA to support making associations with the relevant word. Specifically, PWA was trained in semantic categories (e.g., fruits, vegetables, furniture) using real-world photographs and drawings of the relevant items. The first 20 minutes of the 40-minute therapy session was provided concurrently with tDCS stimulation. Following completion of the tDCS phase of each therapy session, the electrodes were removed, and the therapy resumed until after forty minutes of therapy had been offered.

2.4. Language Assessments

The Language Assessment Test for Aphasia (ADD) (25) was used to aid diagnosis of the aphasia type and to obtain measures of linguistic performance throughout the study. ADD is a standardized, valid, and reliable language assessment tool commonly used in Turkey to aid diagnosis of aphasia and consists of eight subtests: spontaneous speech and language, auditory comprehension, repetition, naming, reading, grammar, speech acts (pragmatics), and writing (21). The assessment test was administered by the SLT who also provided the language therapy. The test was conducted at baseline, post-treatment and follow-up phases for Treatments 1 and 2, as illustrated in Figure 1. Except for the writing section, all subtests were conducted as part of the current study. However, the speech fluency subtest could not be completed at Times 2 and 3, and two parts of the auditory comprehension subtest could not be administered at Time 2.

The scores on each item of ADD were coded as follows. If the participant answered an item incorrectly or failed to provide an answer, it was coded as a zero. Partial/incomplete answers were coded as 1 if the answer was given using gestures and as 2 if it was given using speech. Likewise, correct answers were coded as 3 if it was given using gestures and as 4 if it was given using speech. The sum of the points taken from each subtest and tasks within each subtest are shown in Table 1 (for the raw data please refer to the online data repository).

2.5. Statistical Analyses

The items which could not be tested at one or more time points (the entire speech fluency subtest and two tasks within the auditory comprehension subtest) were excluded from the analyses. The results were visualized using graphs. In addition, inferential statistics were performed using nonparametric statistical tests, as the collected data were ordinal. The overall and subtest language scores obtained at the five assessment time points were subjected to Friedman tests to examine any differences in test scores across the assessment time points. Any significant effect was then followed up in post-hoc pairwise comparisons using Wilcoxon rank-sum tests with Bonferroni correction to identify specifically which time points differed significantly. Further Wilcoxon rank-sum tests were conducted to compare the change from the baseline to posttests for each treatment. The statistical analyses were conducted in R version 4.1.0 (26) using Friedman and Wilcoxon tests (the analysis code is available in the online data repository).

Table 1. Language assessment scores

Tests	Tasks	Time 1	Time 2	Time 3	Time 4	Time 5
		Pre-Tx1[1]	Post-Tx1	Tx1 Follow-up & Pre-Tx2[2]	Post-Tx2	Tx2 Follow-up
ADD[3] Subtests						
Speech fluency	Spontaneous language, speech and cognition	16/40	-	-	23/40	24/40
	Automatic speech and language	0/24	-	-	8/24	4/24
Auditory comprehension	Understanding commands	9/12	-	9/12	12/12	12/12
	Understanding yes-no questions	15/20	-	16/20	17/20	16/20
	Understanding objects	18/24	15/24	18/24	18/24	18/24
	Understanding categories	12/15	15/15	15/15	15/15	15/15
	Understanding details within categories	6/15	12/15	9/15	9/15	12/15
	Simple sentence-picture matching	9/12	12/12	12/12	9/12	12/12
	Complex sentence-picture matching	9/12	12/12	12/12	9/12	12/12
Repetition	Repetition of words, phrases and sentences	0/40	0/40	0/40	10/40	20/40
Naming	Spontaneous naming of words in a category	0/8	0/8	0/8	0/8	0/8
	Confrontation naming	0/40	2/40	6/40	4/40	10/40
	Naming in response to a question – nouns	6/20	3/20	3/20	3/20	9/20
	Naming in response to a question – verbs	6/20	0/20	0/20	0/20	2/20
Reading	Silent reading of commands	0/16	0/16	0/16	0/16	0/16
	Reading numbers and letters	0/20	0/20	6/20	4/20	12/20
	Reading words	0/20	0/20	0/20	0/20	0/20
	Word-picture matching	1/15	0/15	0/15	0/15	0/15
	Reading paragraphs	0/4	0/4	0/4	0/4	0/4
Grammar	Sentence completion	0/40	2/40	10/40	8/40	14/40
Pragmatics / Speech acts	Giving appropriate responses in context	0/40	0/40	0/40	6/40	12/40

1 Treatment 1
2 Treatment 2
3 Language Assessment Test for Aphasia
Tx1
Tx22

3. RESULTS

3.1. Comparison of Language Scores Across Assessment Times

The language scores obtained at the five time points of assessment are shown in Table 1 above. For illustration purposes, the percentage of the correct responses were calculated using the following formula: (points taken / maximum points possible) * 100 for the overall scores from the entire assessment test (Figure 3a) and for the subtest scores (Figure 3b).

A Friedman test was carried out to compare the overall language scores at the five assessment time points. As summarized in Table 2, the results revealed a significant difference among the overall scores across the five assessment time points, $p < .001$. Post-hoc analyses were conducted using Wilcoxon rank-sum tests with Bonferroni correction to compare each pair of the five time points, resulting in ten pairwise comparisons. Significant differences were found between Time 1 (M = 0.70, Mdn = 0) and Time 5 (M = 1.54, Mdn = 2), $p < .001$, Time 2 (M = 0.76, Mdn = 0) and Time 5, p = .002, while marginally significant differences were obtained between Time 3 (M = 0.95, Mdn = 0) and Time 5, p = .067. Time 4 (M = 0.99, Mdn = 0) did not differ significantly from any one of the other time points. None of the other pairwise comparisons produced significant results ($p > .104$).

Further Friedman tests were performed on the scores obtained from each subsection of the assessment test. As summarized in Table 2, the results showed that the scores obtained at the five time points differed significantly in the subsections of repetition ($p < .001$), naming (p = .029), grammar (p = .015) and pragmatics (p = .035), while the difference was marginally significant in the auditory comprehension subsection (p = .064). There was no significant difference between the scores of the reading subtest across the time points, p = .105. Post-hoc analyses were conducted using Wilcoxon rank-sum tests with Bonferroni correction to compare each pair of the five time points for each subtest. Significant differences were found only for the repetition subtest, where Time 5 (M = 2.0, Mdn = 2) was significantly greater than Time 1 (M = 0.0, Mdn = 0), Time 2 (M = 0.0, Mdn = 0) and Time 3 (M = 0.0, Mdn = 0), p = .004. None of the other comparisons yielded significant results ($p > .095$).

***Table 2**. Results of Friedman tests examining differences across the five assessment time points for overall and subtest language scores*

Language scores	Friedman tests
Overall language scores	**$\chi^2(4) = 54.879$, $p < .001$**
Subtest scores	
Auditory comprehension	$\chi^2(4) = 8.889$, $p = .064$
Repetition	**$\chi^2(4) = 25.857$, $p < .001$**
Naming	**$\chi^2(4) = 10.806$, $p = .029$**
Reading	$\chi^2(4) = 7.667$, $p = .105$
Grammar	**$\chi^2(4) = 12.421$, $p = .015$**
Pragmatics / Speech acts	**$\chi^2(4) = 10.341$, $p = .035$**

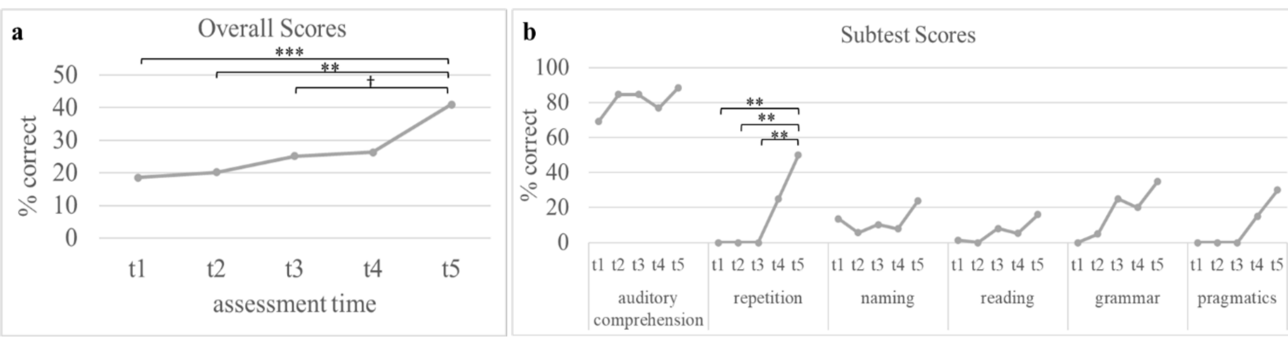

Figure 3.** Percentage of the correct responses at each assessment time for the entire assessment tool (a) and for each subtest (b) [Asterisks indicate statistical significance* (p < .001, ** p < .01, † p = .067)].

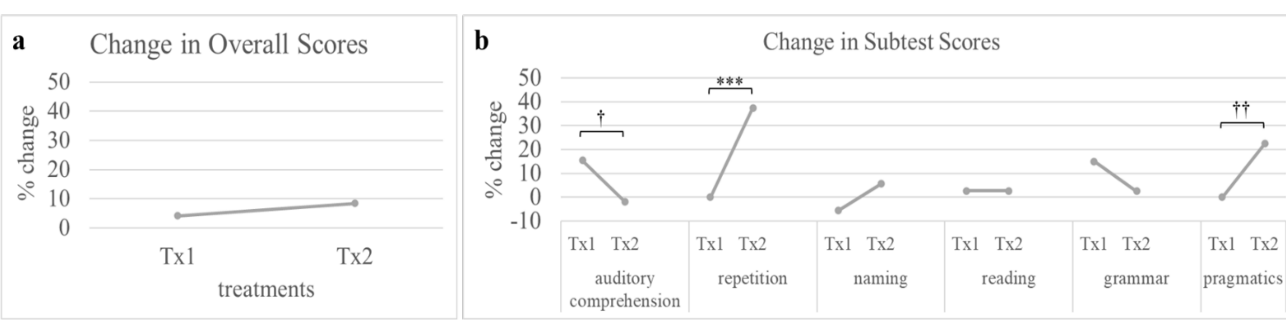

Figure 4.** Percentage of pre-to-post change in language scores associated with Treatments 1 and 2 for the entire assessment tool (a) and for each subtest (b)* [Asterisks indicate statistical significance (p < .001, † p = .063, †† p = .078)].

3.2. Comparison of Change in Scores Associated with Treatments

To directly compare the pre-to-post change or gain in language scores associated with Treatment 1 and Treatment 2, difference scores were calculated for each treatment using the following formula: Average of two posttest – pretest scores. In other words, the assessment scores at Time 1 (baseline) were subtracted from the average of the scores at Times 3 and 4 (posttests) to estimate the change in scores associated with Treatment 1, and the scores at Time 3 (baseline) were subtracted from the average of the scores at Times 4 and 5 (posttests) for Treatment 2. Therefore, for each treatment, the difference scores were obtained through comparison of the baseline and post-treatment assessment scores both for the overall scores from the entire assessment test (Figure 4a) and for the subtests (Figure 4b).

The analysis of the difference scores using a Wilcoxon rank-sum test did not produce a significant difference between the changes in the overall scores associated with Treatment 1 (M = 0.16, Mdn = 0) and Treatment 2 (M = 0.32, Mdn = 0), p = .12. Further Wilcoxon tests were conducted on the difference scores from the subtests of the assessment tool to compare the changes associated with the two treatments for different language skills. These analyses showed that the pre-to-post change for Treatment 2 (M = 1.50, Mdn = 1) was significantly greater than that for Treatment 1 (M = 0.0, Mdn = 0) in the repetition subtest (p < .001). Likewise, the change for Treatment 2 (M = 0.90, Mdn = 0) was greater than Treatment 1 (M = 0.0, Mdn = 0) in the pragmatics subset, albeit with marginal significance (p = .078). Also, the change in auditory comprehension following Treatment 1 (M = 0.50, Mdn = 0) was more than the change in the same domain after

Treatment 2 (M = – 0.06, Mdn = 0) with marginal significance (p = .063). The comparisons of the pre-to-post changes in the scores of the other subtests did not produce significant results (p > .13).

4. DISCUSSION

The present study compared efficacy of two bihemispheric tDCS treatments with frontal versus posterior montages paired with language therapy. We observed a significant increase in overall language outcomes following both treatments, particularly in the repetition subtest. However, the rehabilitative effect was greater for Treatment 2 with the posterior montage, and some differences were observed between the two treatments in terms of the subset scores. These findings suggest that bihemispheric tDCS treatment combined with language therapy is effective in remediating language performance in non-fluent aphasia, and that treatment gains in particular linguistic subskills may vary depending on the montage used.

We found that combining language therapy with tDCS resulted in improvement of language performance by a non-fluent PWA. This improvement was observed in the overall language scores measured in the final follow-up assessment (Time 5) when compared to the first baseline measurement (Time 1) as well as the second and third assessment times. This finding is consistent with a large body of research on the use of brain stimulation including tDCS and repetitive transcranial magnetic stimulation in rehabilitation of aphasia, which has shown promising, positive effects (4,13–15,27,28). However, in contrast with these previous studies and the findings of the present study, several studies failed to show a significant effect of tDCS on language outcomes in aphasia, or showed only weak evidence for its efficacy (16,18,29,30). The inconsistent findings might be related to variable stimulation parameters including electrode montage (anodal only, cathodal only, or bihemispheric), number and length of stimulation sessions, language outcomes assessed, as well as patient characteristics (e.g., aphasia type, severity, lesion location). Indeed, a recent meta-analyses of randomized controlled trials utilizing non-invasive brain stimulation interventions found differences among tDCS electrode montages, with the bihemispheric tDCS outperforming only anodal and only cathodal montages in terms of naming and repetition gains (28). Utilizing bihemispheric tDCS montages, our study also yielded similar findings. That is, although examination of the subset scores showed a tendency for all subtest scores (auditory comprehension, repetition, naming, reading, grammar, pragmatics) to increase from the initial tests to the final assessment; we found that only the increase with treatment in the repetition subtest remained significant after correction for multiple comparisons. This indicates that the gain in the outcomes across the treatments was more robust in the repetition task. This finding is consistent with previous research implicating tDCS treatment with improvement in performance of PWA in repetition (28,31–34).

To investigate any differences between the two tDCS montages, the pre-to-post change in language scores associated with each treatment was compared. Although Treatment 2 with the posterior temporal montage was associated with numerically greater overall gain in language performance than Treatment 1 with the inferior frontal montage, this difference was not statistically significant. This suggests that the two different montages adopted in the present study did not differ to a great extent in terms of the overall language outcomes. However, certain differences were observed between the two treatments in terms of the subset scores. In particular, the analyses of the subset scores showed that Treatment 2 brought about significantly greater pre-to-post change than Treatment 1 in the repetition subtest. Although Treatment 2 was also associated with numerically greater improvement in the naming and pragmatics subtests, this difference did not reach statistical significance. Finally, the change following Treatment 1 was numerically, but not significantly, greater than that following Treatment 2 in the auditory comprehension and grammar subsections. Overall, the greater improvement in language outcomes was observed in Treatment 2 compared to Treatment 1 in terms of the repetition performance. These findings suggest that therapy gains in particular language subskills may vary as a function of the specific montage used. In parallel with these findings, several previous studies associated excitation of the left posterior temporal cortex or inhibition of the right posterior temporal cortex with improved outcomes in aphasia (35–37). However, a few other studies failed to reveal significant improvement in language outcomes following stimulation of posterior compared to frontal sites (9,10). These differences might stem from differences across studies in terms of participant characteristics and stimulation parameters, as suggested in the preceding paragraph.

The present finding that bihemispheric tDCS with excitatory anodal stimulation of left-hemispheric language centers and inhibitory cathodal stimulation of their right-hemispheric homologues is associated with improvement in aphasic symptoms is consistent with the interhemispheric inhibition framework (4,8,38–40). Within this framework, while normally the left and the right cerebral hemispheres strike a desirable balance through mutual inhibition, this balance may be lost through a neurologic insult to the typically language-dominant left hemisphere, which may result in decreased inhibition of the right hemisphere and, hence, maladaptive overcompensation of the latter in linguistic functions. Arguably, this imbalance can be modulated either through excitation of the intact, language-related areas in the left hemisphere or through inhibition of their homologues in the right hemisphere, or both. The present study has provided evidence that combining language therapy with bihemispheric tDCS to simultaneously excite the left-hemispheric language-related areas and inhibit the homotopic regions in the right hemisphere facilitates improvement in language outcomes in chronic, non-fluent aphasia.

Although the current study allowed us to test effectiveness of tDCS coupled with language therapy in aphasia rehabilitation and to compare two different bihemispheric montages, several limitations need to be kept in mind while interpreting the results. First, although initially planned, we could not include a sham control condition in the study since the participant declined it. Inclusion of a sham control condition with a similar tDCS setup but without therapeutic stimulation could have minimized potential confounds due to a placebo effect. However, we believe that a placebo effect alone cannot explain the current results, because the participant did not exhibit a steady increase in assessment scores throughout the study phases, and, instead, there were differences between the gains associated with the two tDCS treatments. Moreover, these differences in gains between the treatments were not uniform across different subtests. A second limitation concerns the design and sample size. Since only a single subject was included in the present pilot study, it is difficult to make strong conclusions regarding generalizability of the study findings. However, there are certain advantages of using a within-subject, crossover design over between-subject, case-control designs, as the former reduces heterogeneity (e.g., differences in language symptoms and other participant characteristics) (14). Nevertheless, to establish causality between tDCS intervention and improvement in aphasic symptoms, randomized controlled trials that also consider participant characteristics and differences are needed. Third, in the current study, tDCS treatments were coupled with language therapy; therefore, it is not possible to attribute the improvement observed following the treatments solely to tDCS. However, since we found a difference between the two tDCS treatments, which comprised identical language therapy, tDCS appears to have provided unique contribution to the improvement in language outcomes. More importantly, we do not consider this as a limitation, since speech and language therapy remains to be the gold standard in aphasia rehabilitation (3) and tDCS may serve as an inexpensive and convenient complementary, adjuvant tool for speech and language therapy (4,36).

5. CONCLUSION

The current study investigated efficacy of two bihemispheric tDCS treatments coupled with language therapy, one targeting the inferior frontal cortex (Treatment 1) and the other targeting the posterior temporal cortex (Treatment 2). In both treatments, the left-hemispheric, language-related areas were excited through anodal tDCS while simultaneously inhibiting their right-hemispheric homologues through cathodal tDCS. The findings revealed an increase in overall language outcomes following the treatments, most markedly in the repetition subtest. This therapeutic effect was greater for Treatment 2 with a posterior montage. Since the rehabilitative effect was observed following anodal, excitatory stimulation in the lesioned left hemisphere with simultaneous cathodal, inhibitory stimulation of the corresponding regions within the intact right hemisphere, the findings support the interhemispheric inhibition account of neuromodulation in aphasia. Overall, the findings suggest that tDCS may be a convenient adjuvant tool that can support speech and language therapies in aphasia rehabilitation.

Data Availability Statement: *The data and statistical analysis codes that support the findings of this study are openly available in the online data repository at https://doi.org/10.17605/OSF.IO/ANCUX.*

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Author Contributions:

Research idea: DGA, TB

Design of the study: DGA, TB, ÇK

Acquisition of data for the study: DGA

Analysis of data for the study: TB

Interpretation of data for the study: DGA, TB, ÇK

Drafting the manuscript: DGA, TB, ÇK

Revising it critically for important intellectual content: DGA, TB, ÇK

Final approval of the version to be published: DGA, TB, ÇK

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