Published in final edited form as:
Brain Stimul. 2022 ; 15(5): 1026–1028. doi:10.1016/j.brs.2022.07.006.

Pre-frontal tDCS improves sustained attention and promotes artificial grammar learning in aphasia: An open-label study

Ellyn A. Riley, Ph.D., CCC-SLP[a], **Mikaella Verblaauw, B.S.**[a], **Hesham Masoud, M.D.**[b], **Leonardo Bonilha, M.D., Ph.D.**[c,1]

[a]Dept. of Communication Sciences & Disorders, Syracuse University, Syracuse, NY, USA

[b]Dept. of Neurology, SUNY Upstate Medical University, Syracuse, NY, USA

[c]Dept. of Neurology, Medical University of South Carolina, Charleston, SC, USA

Keywords

aphasia; tDCS; attention; artificial grammar; dorsolateral prefrontal cortex

Transcranial direct current stimulation (tDCS) is a potentially ground-breaking form of aphasia treatment, but questions remain related to stimulation targets and underlying cognitive benefits of tDCS. TDCS may be especially useful for increasing cost-effectiveness of aphasia therapy due to its relatively low cost and evidence that it may enhance certain types of therapy outcomes [1,2]. Many studies investigating tDCS in aphasia have used fMRI to locate active regions surrounding participants' lesions [2,3] then targeted for tDCS stimulation. This individualized approach has been very successful in achieving good response to treatment and is reasonable for a well-funded research study, but is less practical from a clinical perspective as the tools required to precisely locate perilesional targets are expensive and not readily available to most speech-language pathologists.

An alternative approach involves targeting stimulation to areas of the brain that are farther away from the damaged regions, but still involved in language processing. The few studies that have considered this approach in aphasia have primarily focused on stimulating the cerebellum [4,5] or the dorsolateral prefrontal cortex (DLPFC) [6]. Thus far, evidence suggests that non-perilesional tDCS stimulation targets have the potential to improve response to aphasia treatment (e.g., behavioral treatment that focuses on noun/verb retrieval or grammatical sentence production), but more research is needed to better understand the effects of stimulation on different aspects of language.

[*]**Corresponding author:** Ellyn A. Riley, Department of Communication Sciences and Disorders, Syracuse University; 621 Skytop Rd. Suite 1200 Syracuse, NY 13244, Tel: 315-443-9621; Fax: 315-443-4414; Mobile: 312-752-5075; earil100@syr.edu.
[1]Present address: Dept. of Neurology, Emory University, 12 Executive Park Dr NE, Atlanta, GA 30322 USA

Declarations of interest: Authors Riley and Bonilha report research funding from the National Institutes of Health and the NIH-funded National Center of Neuromodulation for Rehabilitation.

Prior presentations: This research was previously presented at the Brain Stimulation conference in Charleston, South Carolina in December, 2021.

Author Manuscript
Author Manuscript
Author Manuscript

Artificial grammar training [7] is a paradigm commonly used to study learning of information that requires specific sequential order (e.g., grammar). Studies in healthy controls have shown that tDCS paired with artificial grammar training can result in greater artificial grammar learning [8,9], suggesting that tDCS may also have the potential to enhance artificial grammar learning in aphasia. The objective of this study was to determine if administering anodal transcranial direct current stimulation (tDCS) to the left dorsolateral prefrontal cortex (DLPFC) and cathodal tDCS to right supraorbital region in conjunction with artificial grammar training would result in significant pre- to post-treatment change on a measure of sustained attention and successful artificial grammar learning. This was an open-label study designed to test the feasibility of our treatment protocol in this population and provide preliminary evidence that DLPFC is a reasonable tDCS target for improving attention and artificial grammar learning.

This study was approved by the Syracuse University IRB and all participants provided written consent. Twelve participants (M_{age} = 63.7 years; 58.3% female) with mild/moderate aphasia ($M_{QAB[10]}$ = 7.5; 5 Broca's, 7 Anomic aphasia) were enrolled. Aphasia diagnosis was determined by a speech-language pathologist and left hemisphere stroke was confirmed by radiologist report ($M_{time\ post\text{-}onset}$ = 44.3 months).

All participants received tDCS using 5×5 cm electrodes (anode: left DLPFC [F3]; cathode: right supraorbital region [Fp2]); current was increased to 2.0 mA at the onset of training using a 1×1 tES device (Soterix Medical). This device was pre-programmed by the manufacturer to ramp the current up to the target (2.0 mA in this experiment) over the course of 30 seconds. Once the target current was reached, the timer on the device began counting down each minute of the stimulation session (20 minutes in this experiment) and at the end of the timer countdown, the device automatically ramped the current back down to 0.0 mA over the course of 30 seconds. During each of ten 30-minute training sessions, participants completed 20 minutes of simultaneous tDCS and artificial grammar training and 10 minutes of only artificial grammar training. During artificial grammar training, participants were presented with strings of shapes that followed specific rules of an artificial grammar and were asked to recall them in a matching task using laminated cards while the clinician provided auditory feedback regarding response accuracy.

Sustained attention was measured pre- and post-training using a Continuous Performance Task (CPT) and artificial grammar learning was measured post-training using a 2-choice grammaticality judgment task and an artificial grammar rules test. The CPT, 2-choice grammaticality judgment task, and artificial grammar training protocol were identical to those used during a prior pilot study we conducted in participants without aphasia [9]. The artificial grammar rules test was added to this study and asked participants open-ended questions about the artificial grammar rules they learned in training (e.g., which shapes can occur at the end of a sequence?); participants responded using picture cards.

Nonparametric statistics were used to compare pre- to post-training scores on the CPT and to compare probability-based pre-training scores to post-training scores on the two artificial grammar measures for 11 participants (1 participant withdrew after 5 treatment sessions and did not return for post-testing). Pre-training scores on the artificial grammar learning tasks were estimated based on the probability that a participant would provide an accurate response simply by chance (50% for grammaticality task; 21.5% for artificial grammar rules test). This procedure was used to generate non-zero pre-training scores for each participant using Excel to generate a random number for each participant that fit within the appropriate probability parameters. The post-training standard deviation of each artificial grammar learning task was used to estimate standard deviation.

Participants' sustained attention accuracy significantly increased following treatment (effect size $d = 0.55$); participants also demonstrated successful artificial grammar learning by significantly improving their ability to reject 'ungrammatical' structures (effect size $d = 2.98$) and by significantly improving their knowledge of implicitly learned rules of the artificial grammar (effect size $d = 11.87$). See Table 1 for additional detail. No participants reported adverse effects following tDCS, although most (10 of 12) participants reported feeling a mild burning or itching sensation at the start of each tDCS session.

In the current study, 12 participants with aphasia successfully completed multiple sessions of tDCS/artificial grammar training, and findings suggest that all three primary outcome measures significantly improved following training. Limitations of this study include its small sample size and the lack of a control treatment condition; the open-label design was intended to maximize the number of participants receiving treatment and avoid underpowering the study at this early stage. All participants were able to understand and complete the treatment task, regardless of aphasia type or severity, indicating that the artificial grammar training task is feasible to use with this target clinical population. Results suggest that active tDCS administered to left DLPFC and right supraorbital region may be beneficial for improving sustained attention during language training in persons with aphasia and this improvement may facilitate language learning. Future research should focus on comparing against a control (sham) condition to further investigate the role of tDCS in improving attention and language learning.

Acknowledgements:

The authors would like to thank Ying Wu for assistance with stimuli development, Caitlin Murphy and Alex Weiner for assistance with participant training and data collection, Stephanie Loveless for assistance with participant recruitment, and Ramani Voleti for assistance with participant testing.

Funding:

This work was supported by the NIH National Center of Neuromodulation for Rehabilitation [NC NM4R Collaboration Grant] and the National Institutes of Health [R21DC017787; PI: Riley].

References

[1]. Elsner B, Kugler J, Pohl M, Mehrholz J. Transcranial direct current stimulation (tDCS) for improving aphasia in adults with aphasia after stroke. Cochrane Database of Systematic Reviews 2019;2019. 10.1002/14651858.CD009760.pub4.

[2]. Fridriksson J, Rorden C, Elm J, Sen S, George MS, Bonilha L. Transcranial Direct Current Stimulation vs Sham Stimulation to Treat Aphasia After Stroke: A Randomized Clinical Trial. JAMA Neurol 2018;75:1470–6. 10.1001/jamaneurol.2018.2287. [PubMed: 30128538]

[3]. Shah-Basak PP, Norise C, Garcia G, Torres J, Faseyitan O, Hamilton RH. Individualized treatment with transcranial direct current stimulation in patients with chronic non-fluent aphasia due to stroke. Front Hum Neurosci 2015;9. 10.3389/fnhum.2015.00201.

[4]. Sebastian R, Kim JH, Brenowitz R, Tippett DC, Desmond JE, Celnik PA, et al. Cerebellar neuromodulation improves naming in post-stroke aphasia. Brain Communications 2020;2. 10.1093/braincomms/fcaa179.

[5]. Turkeltaub PE, Swears MK, D'Mello AM, Stoodley CJ. Cerebellar tDCS as a novel treatment for aphasia? Evidence from behavioral and resting-state functional connectivity data in healthy adults. Restor Neurol Neurosci 2016;34:491–505. 10.3233/RNN-150633. [PubMed: 27232953]

[6]. Pestalozzi MI, Di Pietro M, Martins Gaytanidis C, Spierer L, Schnider A, Chouiter L, et al. Effects of Prefrontal Transcranial Direct Current Stimulation on Lexical Access in Chronic Poststroke Aphasia. Neurorehabil Neural Repair 2018;32:913–23. 10.1177/1545968318801551. [PubMed: 30269644]

[7]. Reber AS. Implicit learning of artificial grammars. Journal of Verbal Learning and Verbal Behavior 1967;6:855–63. 10.1016/S0022-5371(67)80149-X.

[8]. de Vries MH, Barth ACRR, Maiworm S, Knecht S, Zwitserlood P, Flöel A. Electrical stimulation of Broca's area enhances implicit learning of an artificial grammar. J Cogn Neurosci 2010;22:2427–36. 10.1162/jocn.2009.21385. [PubMed: 19925194]

[9]. Riley EA, Wu Y. Brain Stimulation: Artificial grammar learning with transcranial direct current stimulation (tDCS): A pilot study. Brain Stimul 2019. 10.1016/j.brs.2019.07.002.

[10]. Wilson SM, Eriksson DK, Schneck SM, Lucanie JM. A quick aphasia battery for efficient, reliable, and multidimensional assessment of language function. PLoS One 2018;13:1–29. 10.1371/journal.pone.0192773.

Table 1.

Results of primary outcome measures.

	Primary Outcome Measures	Testing Session	Mean	Median	Std. Deviation	p-value	Test Statistic	Effect Size (Cohen's *d*)
Attention measure	CPT[a] Accuracy	Pre-Training	322.273	340.000	68.307			
		Post-Training	349.182	350.000	7.960	**0.005	55.0	0.553
Artificial Grammar Learning Measures	Accurate Rejection of Ungrammatical Structures	Pre-Training	8.183	8.021	0.984			
		Post-Training	14.455	15.000	2.806	**0.003	66.0	2.983
	Grammar Rule Knowledge Accuracy	Pre-Training	2.607	2.437	0.815			
		Post-Training	10.864	11.000	0.552	**0.003	66.0	11.867

** indicates p <.017 (adjusted p-value after Bonferroni correction)

[a] CPT = Continuous Performance Test