Transcranial Direct Current Stimulation and Aphasia Treatment: A Pilot Study of Anodal, Cathodal and Sham Stimulation

Abstract:

Transcranial direct current stimulation (tDCS) may potentially enhance language therapy outcomes in aphasia. We report behavioral results for twelve participants with chronic aphasia matched for severity and randomized to receive anodal, cathodal or sham stimulation to the left hemisphere, concurrent with intensive speech-language therapy. Importantly, tDCS (1mA for 13 minutes) given 5 days a week over a prolonged period of time (6 weeks) was found to be safe. There was an advantage of both anodal and cathodal stimulation over sham stimulation. Cathodal stimulation to the left hemisphere may be a viable option and should not be overlooked in future research.

Summary:

Methods that modulate cortical excitability have potential as adjuvant treatments for aphasia. Transcranial direct current stimulation (tDCS) is non-invasive with clinical advantages over other methods, in that it is portable, relatively simple and inexpensive to administer, with minimal side effects to participants. Furthermore, tDCS can be administered easily simultaneously with behavioral speech-language therapy (SLT).

With tDCS, constant weak electrical currents are delivered to the cortex via two electrodes placed on the scalp: an active electrode overlying the cortical target and a reference electrode usually placed over the contralateral supraorbital area. The nature of the effect depends on the polarity of the current. Generally, anodal tDCS has an excitatory effect believed to result from partial depolarizartion of superficial cortical axons; cathodal tDCS induces inhibition via presumed hyperpolarization.

Several studies have investigated the adjuvant effects of tDCS in acute (You et al, 2011) and chronic aphasia (Baker et al., 2010; Fiori et al., 2010; Fridriksson et al, 2011; Vines et al., 2011) administered simultaneously with SLT. These studies provided no more than 2 weeks of tDCS in combination with a range of treatments, from”traditional” SLT, to single word naming treatment, and MIT. Results varied and highlight the need for further exploratory investigations of tDCS in aphasia, especially with regard to preferred hemisphere, site of application and polarity (anodal vs cathodal) of the stimulation. Additionally, investigating longer periods of tDCS and in combination with different SLTs is warranted.

We report behavioral results from a Phase 1 single-blind placebo-controlled safety and feasibility trial that assessed tDCS in combination with SLT.

Method:

Study design
Twelve participants with chronic aphasia were randomized to receive anodal, cathodal or sham tDCS to the left hemisphere for six weeks, concurrent with the same intensive SLT. Assessments were conducted at three time points: pretreatment; post-treatment; and at six-weeks follow-up.

Subjects:
Demographic characteristics are presented in Table 1.

fMRI tasks:
Participants underwent fMRI on a Siemens 3.0 Tesla Trio Tim whole body system with a 32-channel head coil, before the six weeks of therapy. The pre-treatment scan was used to identify an individualized site for the tDCS electrode placement. Three speech-language tasks were performed during fMRI: a semantic categorization task; a task where a highlighted word within a sentence was read out loud; and imitation of consonant-vowel syllables. These tasks have been shown to activate overlapping areas of the brain (e.g., lateral premotor cortex, inferior prefrontal cortex) during word production. Intersection of activation between any two tasks was selected as the preferred site of stimulation.

Daily treatment:
Participants received 90 minutes of treatment a day, five days a week, for six weeks. This included 13 minutes of tDCS delivered by a battery-powered constant current stimulator (Dupel Iontophoresis System, Empi, MN) via an $8cm^2$ oblong saline soaked sponge electrode placed over the previously identified scalp location. A self-adhesive carbonized reference electrode (48 cm^2) was placed on the forehead above the contralateral orbit. Anodal and cathodal tDCS was the same current (1mA) and duration (13 minutes) but differed only in polarity. In the sham condition, the stimulation was turned off after 30 seconds.

SLT (90 minutes) was delivered via a computerized ”virtual therapist” and involved reading sentences aloud. The first 13 minutes of SLT was concurrent with the 13 minutes of tDCS.

Temperature, blood pressure and self-reported side effects were measured before and after stimulation and at the end of each treatment session. Self-reports were obtained using aphasia-friendly questionnaires. The same questionnaires were completed in weekly phone calls during the 6-week maintenance phase.

Outcome Measures:
The primary outcome measure was the Aphasia Quotient (AQ) of the WAB-R (Kertesz, 2006). The Language Quotient (LQ) of the WAB-R and the Communication Effectiveness Index (CETI) serving as secondary outcomes.

Language probes (oral reading of 10 trained and 10 untrained sentences) were taken at baseline and weekly during the treatment period. Each word of the sentence was scored on a 5-point scale for accuracy. Rate (words per minute) was calculated using recognizable words.

Results:

No adverse events were reported. Blood pressure, heart rate, and temperature remained stable and within normal limits for all participants during the 6-week treatment and 6-week maintenance periods.

Behavioral Measures - Standardized Tests:

Table 2 shows the mean gain for each group from pretreatment to posttreatment and pretreatment to follow-up.

Both anodal and cathodal groups demonstrated clinically significant improvements for the WAB AQ (>5 point gain) and CETI (> than 12 point gain) from pretreatment to post-treatment and pretreatment to follow-up. For the LQ, the anodal group demonstrated clinically significant changes (> 5 point gain) for both time intervals; the cathodal group demonstrated clinically significant changes from pretreatment to follow-up. The sham group did not meet the criteria for clinical significant gains for the AQ, LQ or CETI for either time interval. It is noteworthy that mean performance improved during the maintenance period for the anodal and cathodal groups whereas it decreased during maintenance for the sham group.

Behavioral Measures - Treatment Probes:

Figure 1 illustrates mean performance of each group on the probes. Improvements occurred for all groups, with overlap across treatment groups. The trajectory of change (slope during treatment) appeared the greatest for the cathodal group.

Table 3 shows percent gain from baseline for accuracy and rate. Percent gain for the anodal and cathodal groups was greater than for the sham group for all time intervals except baseline to follow-up for accuracy.

Discussion and Significance:

Prolonged tDCS to the left hemisphere (1mA for 13 minutes, given 5 days a week for 6 weeks), in combination with SLT, was safe. Six weeks duration of tDCS was longer than any previous study in aphasia where the maximum duration has been two weeks.

Participants received intensive SLT; therefore we expected some language improvement for all participants. Beyond this, results indicate that participants receiving either cathodal or anodal tDCS performed better on standardized testing and treatment probes than participants receiving sham tDCS, and these results were consistent with reported observations on the CETI.

There was persistence of the treatment effect during the six-week maintenance period with continued improvements on some measures following the conclusion of treatment. Such gains have been noted in other aphasia studies following epidural cortical stimulation (Cherney et al., 2010) and rTMS (Barwood et al., 2011; Naeser et al., 2005a,b; Hamilton et al., 2010). Evidence suggests that enhanced neural plasticity with more robust long-term learning and reorganisation of neural circuits plays a role in the improvements in language function associated with the delivery of tDCS (Fritsch et al., 2010).

Participants differed on many uncontrollable variables. Although tDCS parameters were kept constant (1mA for 13 minutes), differences in head anatomy, including skull thickness, lesion size and location, complicate comparisons across participants.

Generalization of findings is limited, given only four participants received each type of tDCS. However, results are compelling – six weeks of tDCS combined with SLT is safe and has the potential to enhance outcomes. Furthermore, cathodal stimulation to the left hemisphere may be a viable option and should not be overlooked in future research on tDCS and aphasia.

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Table 1. Demographic and language characteristics of study participants

Participant	Age (years)	Gender	Lesion size (mL)	TPO (months)	Education (years)	WAB AQ	WAB LQ	WAB CQ	Treatment
AQ > 55									
JONRA	46.1	M	66.9	6.3	16	70.3	64.0	70.90	ANODAL
SHAER	51.5	M	80.3	29.2	16	61.3	61.90	69.73	ANODAL
LEELO	57.1	F	92.8	38.9	17	74.3	74.80	76.18	CATHODAL
TONMA	57.8	F	94.7	50.9	16	63.9	71.10	73.52	CATHODAL
PEACA	55.3	F	76.6	155.7	12	70.1	65.10	69.80	SHAM
PIWTO	61.4	M	155.8	53.3	13	75.3	65.80	70.32	SHAM
AQ < 55									
ANDJA	54.4	M	118.6	35.6	12	45.2	46.4	54.18	ANODAL
HOWSH	55.7	F	136.4	9.2	17	47.1	37.40	42.17	ANODAL
KARYA	58.8	M	46.5	6.2	16	38.7	37.60	45.83	CATHODAL
TRAWI	64.9	M	83.3	18.6	18	44.0	58.0	61.57	CATHODAL
KANJO	71.1	M	24.5	6.2	16	54.3	60.30	65.63	SHAM
BUTFR	54.7	M	56.1	7.3	18	22.3	30.0	38.42	SHAM
MEAN (SD)	**57.4 (6.4)**			**34.78 (41.98)**	**15.6 (2.1)**	**55.57 (16.45)**			

Table 2. Mean (Std Dev) Gain on Testing from Pretreatment to Post-Treatment and 6-weeks follow-up on the Western Aphasia Battery-Revised (WAB) Aphasia Quotient (AQ) and Language Quotient (LQ) and the Communication Effectiveness Index (CETI)

Group	WAB-R AQ		WAB-R LQ		CETI - Caregiver	
	Pre - Post	Pre – F/Up	Pre - Post	Pre – F/Up	Pre - Post	Pre – F/Up
Anodal	5.2 (1.70)	7.38 (2.15)	5.68 (1.80)	6.57 (1.42)	13.93 (13.28)	14.52 (17.59)
Cathodal	5.4 (2.45)	5.68 (5.64)	3.7 (2.49)	6.23 (2.63)	17.16 (2.34)	20.81 (2.09)
Sham	4.83 (7.69)	3.12 (8.43)	4.6 (2.20)	3.33 (3.97)	7.24 (6.27)	10.02 (8.03)

Pre-Tx = Pretreatment; Post-Tx = Post treatment; F/Up = Follow Up. NA = not available

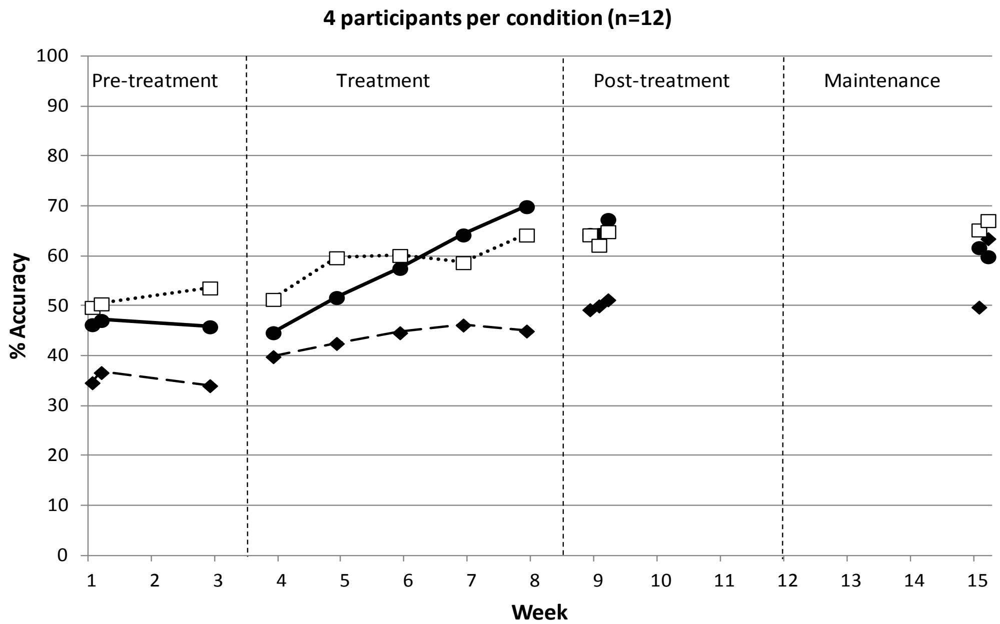
Table 3. Group mean percent gain (std dev) for treatment probes from pretreatment to post-treatment and follow-up

Group	Treatment	Accuracy		Rate	
		Baseline to Post-Tx	**Baseline to F/Up**	**Baseline to Post-Tx**	**Baseline to F/Up**
Group Mean (std dev)	ANODAL	47.3 (34.7)	25.7 (0.64)*	63.2 (62.8)	120.7 (74.3)*
Group Mean (std dev)	CATHODAL	47.6 (37.5)	30.2 (47.3)	43.7 (53.4)	140.4 (96.3)
Group Mean (std dev)	SHAM	19.9 (22.8)	32.5 (12.7)	21.4 (55.2)	15.8 (41.6)

Percent gain calculated as the (mean of 3 post-treatment probes or mean of 2 6-week follow-up probes minus mean of 3 baseline probes) divided by the mean of 3 baseline probes.

Figure 1. Mean Performance on trained probes (oral reading of sentences)

Accuracy (% Accuracy)



Rate (Words per minute)