Methods that modulate cortical excitability have potential as adjuvant treatments for aphasia rehabilitation. Transcranial direct current stimulation (tDCS) is a non-invasive method of stimulation 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 on the site 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. In general, anodal tDCS has an excitatory effect believed to result from the 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) provided simultaneously with SLT. These studies provided no more than 2 weeks of tDCS in combination with SLT that included a range of treatments, from"traditional" SLT, to single word naming treatment, and MIT. Results are varied and highlight the need for further exploratory investigations of tDCS in aphasia, especially with regard to preferred side and site of application and polarity (anodal vs cathodal) of the stimulation. Additionally, investigating tDCS administered for longer treatment periods and in combination with different SLTs is warranted.

We compared behavioral and imaging results from two participants with chronic aphasia, who received tDCS to the left hemisphere over a period of six weeks, concurrent with the same intensive SLT targeting sentence level production. The tDCS was of the same current (1mA) and length of stimulation (13 minutes). However, polarity of the electrical current (anode vs cathode) differed between the two participants.

Method:

Subjects:
Demographic characteristics are presented in Table 1. Both participants (1M, 1F) were right-handed Caucasians, with non-fluent aphasia following a single stroke. Both spoke English as their native language and were similar in years of education. Initial severity of aphasia as measured by the Aphasia Quotient of the Western Aphasia Battery-Revised (WAB AQ) (Kertesz, 2007) was similar (74.3 and 70.0).

fMRI tasks:
Participants underwent fMRI on a Siemens 3.0 Tesla Trio Tim whole body system with a 32-channel head coil, before and after the six weeks of therapy. The pre-treatment scan determined eligibility, establish baseline of brain activity during functional language tasks and identify the site for the tDCS. The post-therapy scan assessed physiological changes associated with therapy. 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.

During the 13 minutes of tDCS, participants completed sentence production tasks (Oral Reading for Language in Aphasia - ORLA) delivered via a computerized "virtual therapist". Then participants continued with computerized therapy tasks for an additional 77 minutes. Temperature, blood pressure and self-reported side effects were measured three times during a session to ensure safety: before and after stimulation and at the end of treatment. Self-reports were obtained using aphasia-friendly questionnaires.

Outcome Measures:
The WAB-R was administered before and after the 6 weeks of treatment, and at 6 weeks following the end of treatment. The primary outcome measure was the Language Quotient (LQ), with the Aphasia Quotient and Cortical Quotient (CQ) serving as secondary outcomes.

Additionally, language probes were taken at each assessment and weekly during the treatment period. Language probes included oral reading of 10 trained and 10 untrained sentences. Each word of the sentence was scored on a 5 -point scale for accuracy. Rate (words per minute) was calculated using recognizable words. Effect sizes for trained and untrained probes were calculated by dividing the difference between the mean of three baseline probes and the mean of three post-treatment probes by the standard deviation for the baseline scores (Beeson & Robey, 2006).

fMRI scans were compared pre- and post-treatment and perilesional activated volumes on the left hemisphere were compared.

Results:

Tables 2 and 3 show results of behavioral testing and probe date for each subject. Both participants improved approximately three points on the WAB LQ from pre-treatment to post-treatment, with continued changes occurring during the 6 week maintenance phase, resulting in a change of more than 5 points from pretreatment to maintenance. Improved writing skills contributed to the WAB LQ change for the participant receiving cathodal stimulation, whereas for the participant receiving anodal stimulation, improved oral expression skills (as evidenced by the WAB AQ) and reading skills contributed to this change.

Effect sizes from pretreatment to post-treatment were larger for the subject receiving anodal tDCS. For both subjects, as expected, effect sizes were larger for trained than untrained probes.

Imaging data showed that the number of activated voxels in perilesional areas from pre-treatment to post-treatment varied by task. See Table 4. In general, there tended to be a decrease/consolidation of activity with anodal tDCS and an increase of activity with cathodal

tDCS. An example of the pre-post scans is included in Figure 1 (participant receiving cathodal stimulation, imitation task). Further analyses are currently underway.

Discussion:

Our comparison of anodal vs. cathodal tDCS to the left hemisphere in conjunction with intensive speech-language therapy over a 6 week period of time in two participants matched for type and severity of aphasia, indicates a slight advantage of anodal stimulation. These findings are consistent with some but not all previous studies. Reported differences in the polarity-specific effects of tDCS complicate our understanding of the neurophysiologic and behavioral effects of tDCS in aphasia, and indicates the need for additional investigations.

Several variables of tDCS may impact efficacy including current strength, application time of each tDCS session, and overall length of the treatment period. While we kept these constant across the two subjects, and standardized the type and amount of SLT, other variables could not be controlled. These include size and location of the lesion, and time post-onset. While both participants presented with chronic aphasia of similar severity, the subject receiving anodal stimulation was 6 months post-onset as compared to 3+ years for the other participant. Possibly this difference alone could account for the different behavioral responses. Therefore results must be interpreted cautiously.

tDCS remains a novel treatment for aphasia, with many unanswered questions about safety, administration, and efficacy. Importantly, this study shows that tDCS given over a prolonged period of time (6 weeks) is safe. Research with larger numbers of subjects is warranted to confirm these findings.

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Table 1 – Demographic Information

Participant	tDCS	Time Post Onset (months)	Type of Aphasia	WAB AQ (severity of aphasia)	Age (years)	Education (years)	Gender
1.	Cathodal	38.9	Nonfluent	74.3	57	17	F
2.	Anodal	6.3	Nonfluent	70.0	46	16	M

Table 2 – Western Aphasia Battery Results

	session #	WAB LQ	WAB AQ	WAB Rdg	WAB Wtg	WAB CQ
Participant 1 Cathodal tDCS	1-pre-testing	74.8	74.3	73	71.5	76.18
	2-post-testing	77.4	77.7	80	66	78.98
	3- maintenance	79.6	75.5	77	85.5	79.83
Participant 2 Anodal tDCS	1- pre-testing	64.0	70.3	66	38.5	70.90
	2-post-testing	67.8	76.6	66	38	75.77
	3-maintenance	69.7	77.1	76	42	76.67

Table 3. - Effect Sizes of Weekly Probes from Pre-treatment to Post-Treatment

	Oral Reading - Trained Sentences		Oral Reading - Untrained Sentences	
	% accuracy	Words/Minutes	% accuracy	Words/Minutes
Participant 1 Cathodal tDCS	2.3	2.4	0.2	-1.4
Participant 2 Anodal tDCS	5.2	7.3	1.2	5.2

Table 4. Number of perilesional activated voxels for each fMRI task before and after treatment

Participant	Category Task Pre	Category Task Post	Oral Reading Pre	Oral Reading Post	Imitation Pre	Imitation Post
Participant 1 Cathodal tDCS	1402	1150	78	2893	383	9774
Participant 2 Anodal tDCS	724	485	378	223	616	810

Figure 1. Example of Imaging data: Pre- and Post-treatment scans for Participant 1 (cathodal treatment) on a consonant-vowel syllable imitation task