Brain stimulation in aphasia

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**PROTOCOL FOR HUM00108213:** Brain stimulation in aphasia

## Research Design

### 5-1.1 Objective

This project will focus on treating aphasia with tDCS in conjunction with language therapy.

### 5-1.2 Specific Aim/Hypothesis

We are interested in determining if and how tDCS can be used as a tool to improve language ability in aphasic patients when used in conjunction with language therapy. We would like to assess the patient-specific parameters under which tDCS is effective: specifically, whether factors like lesion size and location, aphasia severity and type, and time post-stroke influence the efficacy of tDCS with language therapy.

### 5-1.3 Background Information

There has been research to support the idea that tDCS can have beneficial effects on aphasia when applied to the left hemisphere, typically around Broca's area (Aguiar, Paolazzi, & Miceli, 2015). These effects have been observed in studies with tDCS administered for ten minutes (Baker et al., 2010) to thirty minutes (Lee et al., 2013), over one session (Rosso et al., 2014) to ten sessions (Galletta & Vogel-Eyny, 2015; de Aguiar et al., 2015) with non-fluent (Campana, Caltagirone, & Marangolo, 2015; Shah-Basek et al., 2015) and fluent aphasics (Jung et al., 2011; Fridriksson et al., 2011). Although tDCS is often beneficial, there is a need for a targeted approach to assess the stimulation-specific and patient-specific parameters under which tDCS is a successful tool. Additionally, studies using tDCS in aphasic patients have not employed traditional language therapy in their sessions; instead, they often target one outcome like word retrieval (Baker et al., 2010; Floel et al., 2011; Fiori et al., 2011). Limited work has been done to determine whether stimulation can improve outcomes with traditional therapy.

### 5-1.5 Methodology

Subjects will be recruited from the University of Michigan Aphasia Program. In this clinical program, clients undergo intensive language therapy over four weeks which includes a combination of individual therapy (about 14 hours a week), group therapy (about 6 hours a week), and computer-based therapy (about 5 hours a week). This project will consist of tDCS sessions administered during the course of this clinical care. Subjects will receive up to 30 sessions of active tDCS over the left hemisphere while undergoing individual behavioral therapy. The standard numeric analogue scale used for pain in UMHS with the addition of faces on a scale of 1 to 10 will be placed in front of the client to allow them to communicate any discomfort they may feel and if they would like to stop the study.

### 5-1.6 Statistical Design

We will compare the baseline performance of subjects to their performance after tDCS in conjunction with language therapy, including specific measures of word fluency and naming. We have data collected from a group of 300 subjects who received the same type of therapy without tDCS which we can use as a "control group" to compare the effect of therapy alone to the effect of therapy with tDCS. We will also assess subject parameters as they relate to their performance, including age, time post-stroke, type and severity of aphasia, location and size of lesion, and other relevant variables. If possible, we will also have follow-up meetings with the subjects either 4 weeks post-therapy or 8 weeks post-therapy to see how long improvement is maintained.

## Participants

Recruitment: Clients who are participating in the University of Michigan Aphasia Program and meet study criteria will be invited to join this study. Clients who are identified by the Dr. Persad as a potential subject, will first be asked if they would like to hear about the study from a member of the research team. If the patient consents, then the member of the research team will meet with the patient and a family member if present to discuss the study. Only subjects with aphasia will participate in this study.

Inclusion criteria: Chronic receptive or expressive aphasia with or without apraxia.

Exclusion criteria: Any implanted devices or surgical instruments, history of severe mental illness or epilepsy, no active history of seizures (within three months). As the risks to pregnancy, are unknown, no pregnancy or plan to become pregnant during the study period will also be an exclusion criteria.

## tDCS

Parameters: All subjects will receive up to 30 sessions of active tDCS. Depending on the availability of the subject, the session number may vary from 15 to 30 sessions. Each session will begin with up to 20 minutes of active tDCS at 2mA in conjunction with the individual behavioral therapy. The anode electrode will be placed over the left hemisphere and the reference electrode will be placed on the contralateral frontopolar cortex. The specific montage will be determined based on individual patient characteristics.

Risks: tDCS is generally considered safe with no more than minimum risk. In a meta-analysis of over 200 tDCS studies conducted from 1998 to 2010, 56% of studies mentioned adverse events (Brunoni et al., 2011). The available evidence suggests that it is safe. However, it is investigational in nature, which means that we are doing these studies to learn more about tDCS. The most common side effects associated with tDCS based on the available scientific data are:

Sensations under the electrode: These sensations usually stop shortly after tDCS begins but can sometimes continue throughout and for a brief period after tDCS.

• Mild tingling • Light itching • Slight burning sensation • Discomfort

Effects reported that occur ONLY during tDCS:

• Visual sensation during switching on and off the stimulation

Other effects that can occur both during and after tDCS include:

• Fatigue,

• Skin redness

• Headache

• Changes in concentration, memory, or other cognitive abilities. This is partially what we will be testing.

Additionally the following rare side effects have been described in previous studies that used tDCS:

• Nausea

• Nervousness

• It is also possible that the electric current can cause a burn on your skin. This is unlikely because we are using a smaller dose than what is known to cause burns and because we use saline or gel to reduce electrical resistance that leads to burns.

• A shock-like sensation at the initiation of tDCS was reported in one participant.

• Changes in the activity of the prefrontal region (front of the head) have the potential to induce sudden changes in your mood. Hypomania has been reported in a few patients receiving tDCS for bipolar disorder and depression but never in normal controls.

Subjects with a history of bipolar disorder will be excluded from the study. At this time, tDCS has never been reported to cause a seizure in any patient population. Seizures are, however, theoretically possible and a seizure plan is in place for such an unlikely event. Importantly, the majority of the above side effects have been also reported in association with sham (fake) tDCS, even with similar rates. The table below comes from a recent review of tDCS safety and shows the percentage of studies reporting these common sensations (Brunoni et al., 2011) These data suggest that other factors may cause these sensations, such as your expectations or the pressure of head straps or caps.

**Table 3.** Frequency of adverse effects in 117 (active group) and 82 (sham group) experiments. We considered the presence of adverse effect if the study reported its occurrence in at least one patient

| Sensation | Active group | Sham group |
|---|---|---|
| Itching | 46 (39.3%) | 27 (32.9%) |
| Tingling | 26 (22.2%) | 15 (18.3%) |
| Headache | 17 (14.8%) | 13 (16.2%) |
| Burning | 10 (8.7%) | 8 (10%) |
| Discomfort | 12 (10.4%) | 11 (13.4%) |
| Total | 117 studies | 82 studies |

Due to the investigational nature of this study, there may be risks, discomforts or side effects that are not yet known.

We will follow current safety guidelines for tDCS and will use a current strength of up to 2mA and a duration of up to 20 minutes. Few, if any, side effects are reported with these parameters (Nitsche & Paulus, 2011). We will also monitor subjects for discomfort during and after each session. During the session, we will verbally ask the subject if they are experiencing discomfort. The Speech-Language Pathologists will be in the room while the stimulation is being applied and will consequently be available to assist the patients in communicating any side effects they may be experiencing. After the sessions, subjects will complete the following post-tDCS questionnaire:

tDCS Adverse Effects Questionnaire – Session _____

| Do you experience any of the following symptoms or side-effects? | Enter a value (1–4) in the space below (1, absent; 2, mild; 3, moderate; 4, severe) | If present: Is this related to tDCS? (1, none; 2, remote; 3, possible; 4, probable; 5, definite) | Notes |
|---|---|---|---|
| Headache | | | |
| Neck pain | | | |
| Scalp pain | | | |
| Tingling | | | |
| Itching | | | |
| Burning sensation | | | |
| Skin redness | | | |
| Sleepiness | | | |
| Trouble concentrating | | | |
| Acute mood change | | | |
| Others (specify) | | | |

## Data Monitoring

Once a year, a review of participant recruitment procedures and consent forms as well as any adverse events will be conducted by a member of Dr. Hampstead's research team, who is not part of this study.