Stimulating Music: Combining Melodic Intonation Therapy with Transcranial DC Stimulation to Facilitate Speech Recovery after Stroke

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Summary. It may be strange to think that singing could help a stroke victim speak again, but this is the goal of Melodic Intonation Therapy (MIT), a speech therapy that emphasizes musical aspects of language. The positive effects of MIT on speech recovery may be mediated by a fronto-temporal brain network in the right hemisphere. We investigated the potential for a non-invasive brain stimulation technique, Transcranial Direct Current Stimulation (tDCS), to augment the benefits of MIT for patients with severe non-fluent aphasias. The tDCS was applied to the posterior inferior frontal gyrus (IFG) of the right hemisphere, under the assumption that the posterior IFG is a key region in the process of recovering from aphasia. The stimulation coincided with an MIT session, conducted by a trained therapist. Participants' language fluency improved significantly more with real tDCS + MIT, compared to sham tDCS + MIT. These results provide evidence that combining tDCS with MIT may enhance activity in a sensorimotor network for articulation in the right hemisphere, to compensate for damaged left-hemisphere language centers.

Key words. Melodic Intonation Therapy, Transcranial Direct Current Stimulation, tDCS, Stroke, Recovery, Neurorehabilitation, Singing, Music Therapy

1 Introduction

Approximately 20% of stroke victims suffer from aphasia, which is a loss of speech and language ability (Schlaug et al., 2008a). Though behavioral therapies for recovery from stroke can have a beneficial effect (Robey, 1994; Holland et al., 1996), recovery is most often incomplete, particularly for patients with large left-hemisphere strokes. Relatively few speech therapy techniques are available to help these patients. An intonation-based speech therapy, Melodic Intonation Therapy, may be particularly suited for patients who suffer from severe non-fluent aphasia (Schlaug et al., 2008a,b). Another line of research has recently emerged which shows that combining behavioral therapies with non-invasive brain-stimulation might enhance the potential for recovery (Schlaug, Renga, Nair, 2008). Indeed, the future of stroke-recovery therapy may lie in *combining* behavioral therapy with complimentary non-invasive brain stimulation to maximally engage brain areas that are important for recovery. We explored this promising frontier of rehabilitation by investigating the effects of combining non-invasive brain stimulation with a behavioral intonation-based speech therapy.

1.1 Aphasia and Music in the Brain

Because some language processes are largely lateralized to the left hemisphere, left-hemisphere damage can lead to devastating forms of aphasia. A stroke affecting the left frontal lobe can cause a non-fluent aphasia with relatively unimpaired comprehension – Broca's aphasia (Luria, 1970). Broca's aphasia hinders the ability to organize elements of speech (e.g., phonemes) into meaningful utterances. Previous research suggests that there are two neural pathways to recovery from Broca's aphasia. One pathway involves the re-activation of peri-lesional cortex in the left hemisphere; generally, this is only possible for patients who have smaller lesions that do not completely destroy Broca's area. The second pathway utilizes the right hemisphere, and may be the only option for patients with large left-hemisphere lesions (Blasi et al., 2002; Mimura et al., 1998; Pizzamiglio et al., 2001; Schlaug et al., 2008b; Thiel et al., 2001; Winhuisen et al., 2005). These studies provide evidence that language-capable centers in the right-hemisphere may compensate for damaged left-hemisphere "eloquent" areas to help patients recover language skill, particularly when damage to the left hemisphere is extensive.

An increasing number of studies point to common neural substrates for language and music (Maess et al., 2001; Koelsch et al., 2002; Patel et al., 1998, 2003). For example, neuroimaging techniques have revealed both overlapping as well as unique brain networks for speaking and singing (Ozdemir et al., 2006; Brown et al., 2004); though speaking tends to be lateralized to the left hemisphere and singing to the right (Jeffries et al., 2003; Riecker et al., 2000; Sparing et al., 2007), these two behaviors involve some of the same brain areas. In their fMRI study, Ozdemir and colleagues (2006) found that adding speech to melody engaged the right IFG. Singing, or intoned speaking, therefore, may provide a useful means for accessing language-capable brain areas in the right hemisphere for the purpose of facilitating language recovery (Racette et al., 2006).

1.2 Melodic Intonation Therapy

Melodic Intonation Therapy (MIT) is a specialized speech therapy that emphasizes the melodic and rhythmic elements of speech. The technique was inspired by the common clinical observation that severely aphasic patients can sing the lyrics of a song better than they can speak them (Goldstein, 1942; Gerstman, 1964; Geschwind, 1971; Keith & Aronson, 1975; Kinsella et al., 1988; Hebert et al., 2003). MIT uses a simplified and exaggerated prosody in which high probability words and phrases are intoned and tapped out syllable by syllable, with gradually increasing complexity as the patient progresses through levels of difficulty. Research has found MIT to be effective in facilitating significant improvements in language production (Albert et al., 1973; Bonakdarpour et al., 2000; Laughlin et al., 1979; Schlaug et al., 2008a; Sparks et al., 1974; Wilson et al., 2006). MIT's efficacy may be due to its unique potential to engage language-competent brain regions in both hemispheres, and in the right hemisphere in particular (Albert et al., 1973; Schlaug et al., 2008a; Sparks et al., 1974). It is still unknown which brain regions could potentially drive the therapeutic effect of MIT. However, the posterior IFG very likely plays a critical role in the network underlying recovery. It is possible to test the unique contributions of different brain regions by either temporarily blocking them or by enhancing their activity using non-invasive brain-stimulation.

1.3 Transcranial Direct Current Stimulation

Transcranial Direct Current Stimulation (tDCS) is a non-invasive brain stimulation technique that has been shown to influence excitability in a targeted brain region by modulating the spontaneous firing rate of neurons (Priori et al., 1998; Nitsche and Paulus, 2000). Research suggests that the polarity of the current determines the effects of tDCS – anodal tDCS increases cortical excitability and cathodal tDCS decreases excitability. TDCS effects may be mediated by activity in sodium and calcium ion channels as well as by the efficacy of NMDA receptors (Liebetanz et al., 2002; Nitsche et al., 2003a). Anodal tDCS can improve cognitive and behavioral performance on tasks involving the stimulated brain area (Antal et al., 2004; Fregni et al., 2005; Boggio et al., 2006; Kincses et al., 2004; Nitsche et al., 2003b; Vines et al., 2006a). For example, Iyer and colleagues (2005) found that applying anodal tDCS to the left prefrontal cortex significantly improved verbal fluency in healthy participants. Is it possible that tDCS could be used to improve verbal fluency for stroke patients as well?

Transcranial direct current stimulation is an ideal non-invasive brain stimulation technique for use in treatment therapies because it is portable, relatively inexpensive, and safe. Though tDCS does not have the temporal or spatial acuity of Transcranial Magnetic Stimulation (TMS), it is possible to stimulate a larger area of cortex using the technique, and to easily combine tDCS with simultaneous behavioral therapy; this is ideal for modulating cortical activity in a network of related brain areas that is relevant to stroke recovery. The results of studies investigating whether tDCS can be used to improve stroke victims' motor skill have been encouraging (Hesse et al., 2007; Hummel et al., 2005; Hummel et al., 2006; Hummel & Cohen, 2005; Nair et al., 2008; Schlaug et al., 2008c,d). At least one study has investigated the potential for tDCS to facilitate recovery from non-fluent aphasia, with promising results (Monti et al., 2008).

The present study compared the effects of two tDCS conditions (anodal and sham) when applied over right IFG during MIT sessions. We hypothesized that, compared to sham, applying anodal tDCS in coordination with MIT would significantly augment the positive effects of therapy on language production by recruiting music processing in the brain to facilitate speech recovery.

2. Materials and Methods

2.1. Participants

Six adult non-fluent stroke patients participated in the study after giving their informed, written consent following protocol approved by the Beth Israel Deaconess Medical Center IRB. For all participants, at least one year had elapsed since their first ischemic stroke. The participants suffered from

Broca's aphasia due to a stroke affecting the left frontal lobe including the inferior frontal gyrus, with relatively unimpaired comprehension. Prior to this study, they each underwent 75 sessions of Melodic Intonation Therapy as part of a different experimental protocol in the laboratory. The ages of the patient participants ranged between 30 and 81 years. All participants were right handed, except for one who was mixed-handed with a dominant left hand. One of the six participants was bi-lingual - a native Russian speaker with some knowledge of English; the other participants were native English speaking.

2.2. Procedure

Participants underwent two series of three therapy sessions – one session per day - in which tDCS was applied to the right-posterior IFG with an angle towards the temporal lobe during twenty-minutes of MIT administered by a trained therapist. The therapist tailored each MIT session to the level of skill of the participant. For one three-day therapy series, anodal tDCS was applied, and for the other, sham tDCS. The ordering of the two stimulation conditions was counterbalanced across participants such that half of them received the sham tDCS series first. The tDCS was applied for 20-minutes, with the active electrode positioned over participants' right IFG, centered approximately 2.5 centimeters posterior to F8 of the 10-20 International EEG system. The correspondence between F8 and the right IFG has been confirmed by neuroimaging studies (Homan et al., 1987; Okamoto et al., 2004), including our own pilot study using high resolution structural MRI (N=5). We chose to position the active electrode slightly posterior to F8 based upon our pilot study investigating the location of the analogue to Broca's area in the right hemisphere. A number of TMS and tDCS studies have used the 10-20 EEG system to identify the location of brain structures for stimulation (Fregni et al., 2005; Iyer et al., 2005; Kincses et al., 2003; Rogalewski et al., 2004, Vines et al., 2006a,b, 2008a,b). Due to the size of the active electrode (area = 16.3 cm^2), the stimulation may have extended into anterior temporal cortex and ventral premotor cortex, which make up the network of fronto-temporal regions thought to underlie MIT's therapeutic effect. The reference electrode (area = 30 cm^2) was positioned over the left supraorbital region, contralateral to the targeted hemisphere. This location for the reference electrode was functionally ineffective in the experimental design (Nitsche et al., 2003b).

A battery-driven, constant current stimulator (Phoresor, Iomed Inc., Salt Lake City, UT) delivered 1.2 mA of electrical current to a participant's scalp by means of the saline-dampened electrodes. For anodal stimulation, the tDCS current ramped up over the first few seconds, and then remained on for the remainder of the 20-minute stimulation period. The sham control was identical to the anodal stimulation, except that the experimenter reduced the current to zero after it ramped up for 30 seconds; the current then stayed at zero for the remaining time period. Participants reported a tingly or itchy sensation at the start of the stimulation, which typically faded away after a few seconds. This sensation was present for both real and sham tDCS. Gandiga et al. (2006) found that naive participants were not able to distinguish between real and sham tDCS, as employed in a manner similar to the present study. The application of tDCS began five minutes after the start of MIT, and continued five minutes after the end of the MIT session. During the five-minute break after the end of MIT and before the end of the stimulation, the patients rested before completing the verbal fluency tasks.

2.3. Task

Participants were tested on a combined measure of verbal fluency comparing performance on a test-battery before and after each stimulation session. The tasks included automatic production of verbal sequences (e.g., counting from one to twenty-one, pronouncing the days of the week/months of the year, reciting the United States pledge of allegiance, and describing flash-card scenes), as well as picture naming. The flash-card scenes were taken from drawings published with the MIT intervention (Helm-Estabrooks & Albert, 1991). Pictures were drawn from the Snodgrass inventory and the Boston Diagnostic Aphasia Examination (BDAE 2nd edition; Goodglass & Kaplan, 1983). The automatic response items were conducted in the same order for each testing session. Pictures were shown in a new random order for each testing session. The number of items (automatic production and picture naming) depended upon the ability of the participant, and were chosen such that the testing session did not exceed 30 minutes to avoid excessive fatigue for the patients. Patients were instructed to always try their best during each testing session, both pre- and post-therapy; they were blind as to whether they were receiving sham or anodal stimulation.

2.4. Data Analysis

We calculated the dependent variable as the percentage of change in the sum duration of fluency measures from before the first of three stimulation sessions to after the last of three stimulation sessions. This calculation produced two values for each participant: 1. (post anodal series – pre anodal series)/(pre anodal series), 2. (post sham series – pre sham series)/(pre sham series). To ensure equality for all four time-points of interest (pre-anodal, post-anodal, pre-sham, post-sham), the calculation of the dependent variable only included durations for fluency items, or portions there-of, that were intact at all of these time-points. For example, on the task of counting from 1 to 21, if a participant made it to 21 at all measurement points excepting one for which the participant only made it to 18, the duration for counting from 1 to only 18 was used at all time-points. Similarly, only pictures that a participant was able to name at all four time-points of interest were used. Doing this ensured that the material at each time-point was identical in terms of content, or what was actually uttered. The dependent variable, therefore, was not sensitive to changes in the amount of verbal production, but in the rate of verbal production - how quickly the participant was able to speak. The measure reflects fluency, with regard to ease of speech production. The percentage of change found for anodal and sham combined with MIT was compared using a planned two-tailed paired-samples *t*-test.

3 Results

All six participants completed the experimental procedure. Data for the effects of anodal and sham stimulation, combined with MIT, are shown in Figure 1. The *t*-test comparing the effects of anodal and sham tDCS yielded a significant result ($t(5) = 3.22, p = .02$). This result was not due to a significant difference in the pre-stimulation therapy performance. A paired samples *t*-test comparing the pre-anodal duration to the pre-sham duration for each patient did not support abandoning the null hypothesis that the pre-stimulation values were equal in mean ($t(5) = -.31, p = .77$); there was no difference in the pre-stimulation scores for sham and anodal tDCS. Compared to sham tDCS, applying anodal tDCS to the right IFG during MIT produced a significantly greater improvement in verbal fluency.

4 Discussion

The results of this study provide evidence that applying real tDCS during MIT augments the beneficial effects of MIT. By increasing excitability in the right IFG, the anodal tDCS may have increased plasticity in brain areas that are engaged by MIT. We posit that increasing excitability in the right IFG with tDCS enabled greater recruitment of that area of the brain, to facilitate verbal output and fluency.

Future research will investigate whether the positive effects of tDCS were due to the particular placement of the anodal electrode over the right IFG, or if anodal stimulation over other brain areas, such as the right anterior temporal cortex could also improve the beneficial effects of MIT. Additionally, it remains unknown whether tDCS, as applied in this study, exerts a positive influence on language recovery only in combination with a behavioral speech therapy, or if tDCS can be used on its own to improve verbal fluency for stroke patients. Because neural plasticity that facilitates language recovery after stroke may involve the development of neural connections that are latent in the undamaged brain, it is possible that modulating cortical excitability with non-invasive brain stimulation will have its greatest impact when a behavioral therapy is used to induce neuroplastic changes.

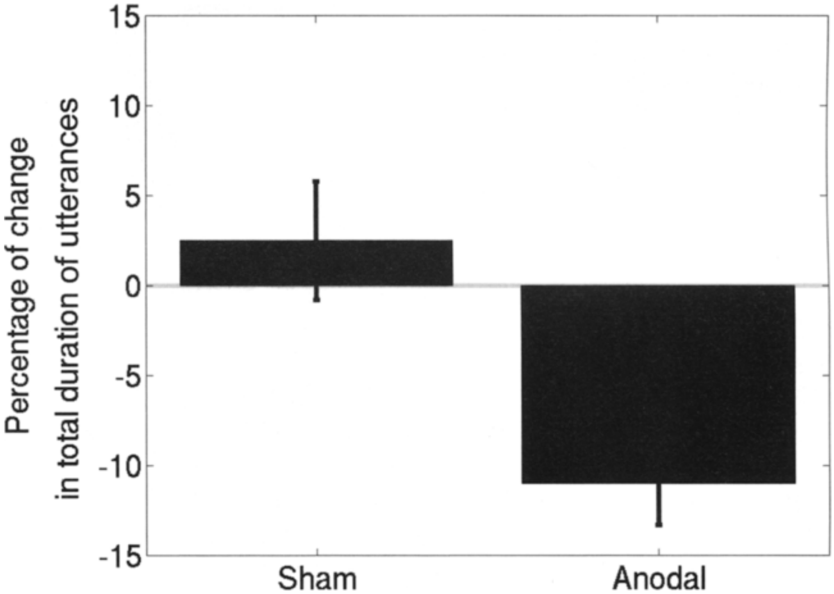

Fig. 1. Data for six Broca's aphasia patient participants. Note that a decrease in the total duration signifies an improvement in verbal fluency. Anodal tDCS led to a significantly greater improvement compared to sham tDCS.

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