Table 1
Average Intensity of commonly experienced adverse events

Session Condition	Total Sessions	Tingling (SD, n)	Itching (SD, n)	Burning Sensation (SD, n)
2.0 mA Blinded	147	1.6 (0.8, 73)	2.2 (0.9, 35)	2.3 (1.3, 46)
2.0mA Open Label	94	1.8 (1.1, 36)	2.3 (1.2, 5)	2.2 (1.3, 28)
1.5mA Open Label	248	2.5 (2.2, 158)	2.0 (1.6, 65)	3.1 (2.1, 64)
Sham	135	2.4 (1.4, 40)	1.7 (0.9, 13)	1.4 (1.1, 15)

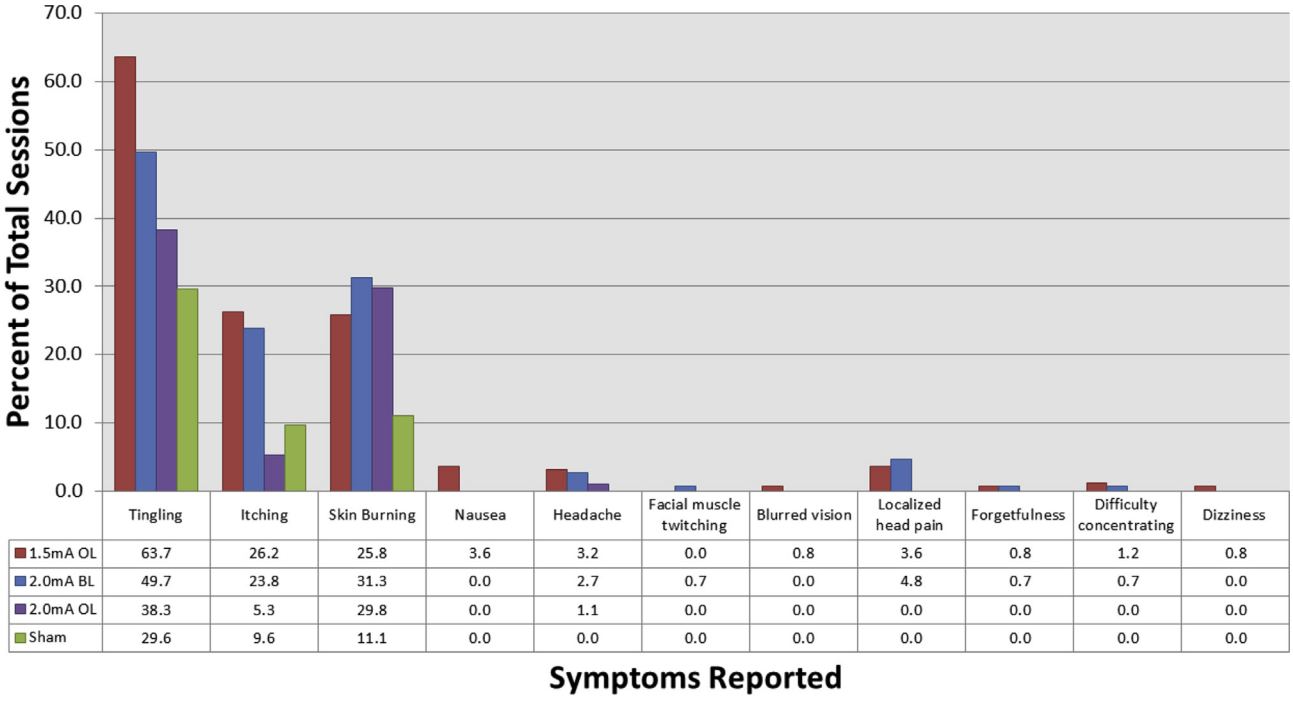

Fig. 1. Adverse events experienced with tDCS.

Discussion

The RS-tDCS protocol is safe and tolerable in both MS and PD participants, and continues to lead to high rates of compliance with treatment sessions. No serious adverse events have been reported. The most common side effects reported are skin tingling and itching.Of note, across conditions, the 1.5mA open label condition reported the highest rates of side effects. This may be accounted for by open-label treatment, where participants may have been more focused on potential effects of the stimulation. The 2.0mA open label condition may not be as comparable to the 1.5mA open label condition due to a smaller sample size in the 2.0mA condition.Overall, none of the adverse events were severe, with intensity below 3 on a visual analogue scale of 1-10. Both 1.5 and 2.0mA tDCS are safe and tolerable forms of treatment in both MS and PD, and may be generalizable for clinical study in a wide range of neurologic and psychiatric disorders.

References

1. Kasschau M, Sherman K, Haider L, et al. A Protocol for the Use of Remotely-Supervised Transcranial Direct Current Stimulation (tDCS) in Multiple Sclerosis (MS). Journal of visualized experiments : JoVE 2015:e53542.
2. Kasschau M, Reisner J, Sherman K, Bikson M, Datta A, Charvet LE. Transcranial Direct Current Stimulation Is Feasible for Remotely Supervised Home Delivery in Multiple Sclerosis. Neuromodulation : journal of the International Neuromodulation Society 2016.
3. Bikson M, Grossman P, Thomas C, et al. Safety of Transcranial Direct Current Stimulation: Evidence Based Update 2016. Brain stimulation 2016.

PROCEEDINGS #14. POSITIONAL ACCURACY OF SCALP ELECTRODES MOUNTED ON A READY-MADE BAND TARGETING MOTOR CORTEX

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1. Abstract

Proper electrode placement is an important aspect of effective transcranial electrical stimulation (tES). Traditional positioning methods rely on scalp measurements such as the 10-20 system, or physiological localization such as mapping of motor evoked potentials (MEPs) using transcranial magnetic stimulation (TMS). While effective, these methods can be laborious, and the relatively non-focal nature of tES due to spreading of current through the scalp, skull, and CSF suggests that faster or easier methods may achieve acceptably low error while facilitating research throughput.
The present paper presents a geometric analysis of a ready-made, one-size-fits-all flexible band design for targeting the primary motor cortex (M1) via a ready-made, non-custom flexible band design. Using established standards for head dimensions and head shape variability, we present data showing that the modelled design allows for consistent targeting of M1 over a wide range of head sizes and shapes.

2. Introduction

Transcranial electrical stimulation has been shown to modulate motor performance, both behaviorally and biologically [1-2]. While desirable

effects of tES have frequently been shown in laboratory studies as well as clinical trials, the safety profile and presumed mechanism of action for applications such as rehabilitation (i.e., incremental modulation of plasticity coupled with movement training or therapy activities) suggest that additional benefits may be obtained from scheduled use outside the lab or clinic [3].

One roadblock for applying this technology outside the clinic is the need to conveniently and accurately target the area(s) of interest, especially if the tES system is intended for non-expert users. In many motor-related tES studies, the area of interest is the left, right, or central M1 (C3, C4, Cz in the 10-20 system, [4]). Therefore, the current paper presents a method to effectively and easily target M1 without the need for traditional measurements, and presents accuracy data from a geometric analysis of the method.

3. Methods

Device model

The device model is based on the Halo Sport device (Halo Neuroscience, San Francisco, CA), a non-invasive electrical neurostimulator intended to target M1 including Cz, C3, and C4. The device provides a semi-rigid band onto which electrodes are mounted at three fixed points. The band is then placed over the bitragional coronal arc in the same manner that audio headphones are traditionally worn. Users are trained to center the band over the vertex of the head (Cz).

The band is modeled as three arc segments, each with a constant radius of curvature 8.59 cm spanning 40 degrees (60 mm arc length). The central segment is centered over Cz. The joints between arc segments are flexible in order to conform to the head. On each arc segment is mounted an electrode, each nominally 6 cm long and 4 cm wide. On each electrode is a 4x6 grid of flexible porous tips (10 mm in length) which act as sponges for delivery of current to the scalp. The model included realistic deformation of these tips to conform to the scalp.

Head models

The head model (Fig. 1) is based on the measurements reported in the HumanScale ergonomic dataset [5], with reference to Churchill *et al.* [6] for confirmation. This dataset shows mean and typical variation of key anthropometric parameters for men and women, including head breadth, coronal girth (i.e., distance between preauricular points in the 10-20 system), and distance from glabella to the top of the head.

We generated a 9x9 matrix of test cases for each gender, including at the center the "overall typical" head, with median height, breadth, and coronal girth. The coronal section of each test head was modeled as a superellipse with parameter $r = 3.14$ (men) and $r = 3.36$ (women). The superellipse parameter r was necessary to appropriately model typical C3 and C4 locations (shapes with $r > 2.0$ become more convex here, with the extreme case $r \to \infty$ becoming a square).

Based on these data, the overall typical male head had width 15.5 cm, height from glabella to vertex 9.1 cm, and coronal girth 35.8 cm, with Cz-C3 arc length 7.16 cm. The overall typical female head had width 14.5 cm, height from glabella to vertex 8.6 cm, and coronal girth 34.0 cm, with Cz-C3 arc length 6.80 cm.

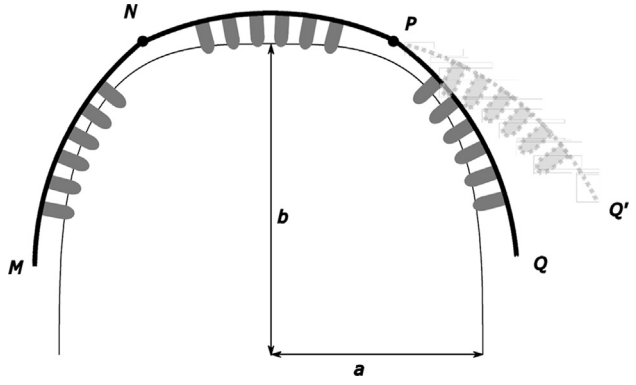

Fig. 1. Line drawing of the device/head mathematical model, representing a typical superelliptical ($r = 3.36$) coronal section of the head, as well as the segments of the electrode band. Measurements *a* and *b* represent the minor and major axes (based on the width and glabella-vertex height, respectively). Segments MN, NP, and PQ represent the bases of the three electrodes, with PQ shown at two different flexion angles.

4. Results

Results indicate that C3/C4 locations are well-approximated by the one-size-fits-all electrode band, with the center of the electrode deviating from the C3/C4 position by less than 0.6 cm for the great majority of users (Fig. 2), and by less than 1.4 cm for even the most extreme outliers across both men and women (Fig. 2). Of the parameters studied, positional accuracy is more sensitive to head height than head width.

5. Discussion and Conclusion

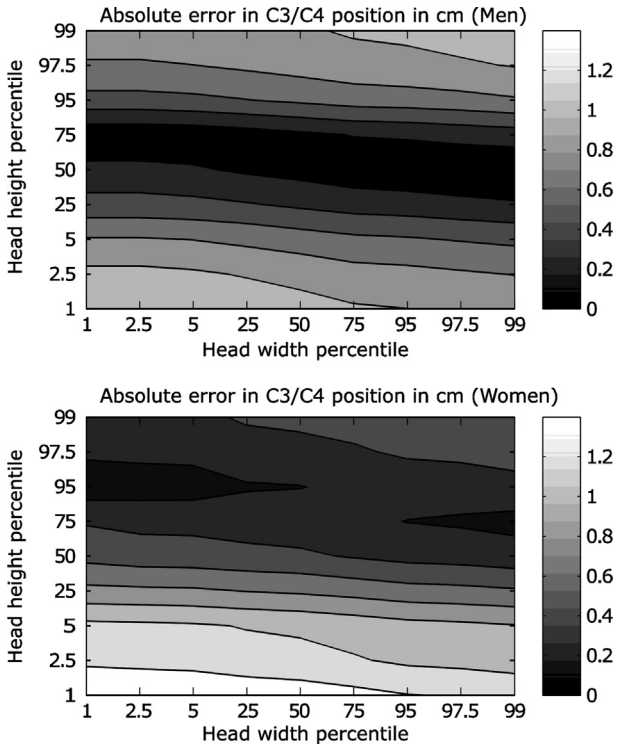

Fig. 2. Absolute difference between electrode center and C3/C4 position, measured across scalp arc for various head widths (abscissa) and heights (ordinate, showing glabella to vertex height) in men (upper panel) and women (lower panel).

The current paper presents mathematical modeling of how a tES device may effectively localize and target the motor cortex in humans using a ready-made, one-size-fits-all electrode band. As demonstrated above, by allowing the band to flex between semi-rigid electrodes and by providing flexible electrode tips, we achieve accurate positioning across virtually the entire plausible range of head sizes and shapes. Given the size of the electrode (6 cm x 4 cm), and the relatively nonfocal nature of tES due to skull, scalp, and CSF anatomy [2], error due to use of a ready-made band is small in comparison to the region of interest for neuromodulation.

Therefore, a device of this nature is likely to allow for sufficiently consistent location in the coronal arc without the need for the user to take precise measurements. While this is promising, we note several limitations to this model. We do not take into account the amount of force required to flex the band or foam tips; for optimal usability, a device of this nature must be designed such that these forces are appropriate for most head sizes, and so that the electrode band can easily and comfortably assume its optimal position. As well, this method does not currently replace functional localization of a specific portion of M1 using TMS. However, our results show that a device of this nature may reasonably be expected to facilitate reproduction - in a non-clinical environment - of the extensive history of results with M1 tES located using the 10-20 system.

References

[1] Kang N, Summers JJ, and Cauraugh JH. Transcranial direct current stimulation facilitates motor learning post-stroke: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry. 2015; 0: 1-11. Doi: 10.1136/jnnp-2015-311242

[2] Nitsche M A, Doemkes S, Karakose T, Antal A, Liebetanz D, Lang N, Tergau F, and Paulus W. Shaping the effects of transcranial direct current stimulation of the human motor cortex. J Neurophysiol 2007 97: 3109-3117 doi: 10.1152/jn.01312.2006

[3] Mortensen J, Figlewski K, and Andersen H. Combined transcranial direct current stimulation and home based occupational therapy for upper limb motor impairment following intracerebral hemorrhage: a double blind randomized controlled trial. *Disability and Rehabilitation* 2016; 38(7): 637-643. Doi: 10.3109/09638288.2015.1055379

[4] DaSilva AF, Volz MS, Bikson M, Fregni F. Electrode positioning and montage in transcranial direct current stimulation. J. Vis. Exp. 2011 (51), e2744, doi:10.3791/2744

[5] Diffrient N, Tilley AR, and Bardagjy, J. Humanscale 4/5/6. Book and access edition. Cambridge: MIT Press; 1981

[6] Churchill E, Kikta P, Churchill T. The AMRL Anthropometric Data Bank Library: Volume I-V, Technical Report AMRL-TR-77-1 (AD A047 314). AMRL, Wright-Patterson AFB, Ohio; 1977

PROCEEDINGS #15. FEASIBILITY AND SAFETY OF COMBINING RTMS WITH PHYSICAL THERAPY: PRELIMINARY DATA IN PARKINSON'S DISEASE.

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1. Introduction

Non-invasive brain stimulation can be used in combination with rehabilitative therapies or physical exercises to enhance or improve function [1-2]. It is believed that the combination of physical rehabilitation and brain stimulation may offer a greater or more sustained effect than either therapy alone [3]. The mechanisms underlying this potential synergistic effect are not fully known but may rely on associative plasticity [4]. It is known that task-specific training can induce task-specific neuronal changes based on use-dependent plasticity phenomena. However, training alone may produce a subliminal neural activation, resulting in only transient synaptic changes, whereas brain stimulation has been demonstrated effective to induce long-term potentiation (LTP)-like phenomena, presumably through Hebbian mechanisms [5]. In a previous study at our Lab, we demonstrated that repetitive transcranial magnetic stimulation (rTMS) could modulate motor memory in patients affected by Parkinson's disease (PD) [6]. Specifically, we showed that rTMS (and not sham), applied after the acquisition of a simple motor skill could increase motor skill retention. In our previous study, the effect of rTMS on skill retention was assessed through a visuomotor adaptation task consisting of a series of ballistic hand movements to reach a radially arrayed target by moving a cursor on a digitized tablet. Based on our promising results, we now plan to translate the paradigm into a clinical setting with the goal of improving functional restoration. To do so, we recently developed a novel non-invasive neuromodulation protocol pairing multiple, consecutive sessions of physical therapy (PT) for posture and gait rehabilitation back-to-back with rTMS sessions. Postural instability and gait disorders (PIGD) are the most important neurological risk factors for falls. In PD patients, PIGD are notoriously prevalent. Unfortunately, the available pharmacological treatments are scarcely effective, and PT is considered the standard of care [7]. The implementation of this translational study is primarily limited by its actual feasibility in everyday clinical settings. Here, we aimed to explore the feasibility of our protocol and its potential generalization in common clinical practice. This study is a collaborative effort between the Rusk Rehabilitation Institute and the Marlene and Paolo Fresco Institute for Parkinson's and Movement Disorders at NYU Langone Medical Center. We took advantage of a consolidated scientific partnership and a conveniently shared location in the same building to develop and test this new therapeutic paradigm.

2. Methods

This is a double-blind, randomized, sham-controlled protocol for PD patients referred to PIGD-oriented rehabilitation. Inclusion criteria: age 35-89, diagnosis of PD, recent referral for PIGD-oriented PT at our institution's rehabilitation facilities, Hoehn and Yahr 2 through 4. Referred patients have been pre-screened for eligibility, including potential TMS contraindications, e.g. the presence of implanted devices or history of seizures. Prescreened subjects underwent formal screenings to assess eligibility. All patients provided written, informed consent. PT was delivered by an expert physical therapist on a one-to-one basis and specifically addressed PIGD rehabilitation. The experimental treatment was designed to follow the PT session without interfering with PT standard of care. Pre-established time window limit was 40 minutes maximum and session's frequency were matching PT (1 to 2 times weekly). Following each PT session, patients were immediately directed to our TMS lab to randomly receive rTMS or sham. TMS mapping and motor thresholds were performed at the first session. Clinical outcomes measures were obtained at baseline and following the final PT session. Both patients and PT providers were blinded to the TMS intervention. Preliminary data of feasibility, safety and adherence to the protocol were analyzed.

3. Results

Nine patients were consecutively referred to PIGD-oriented PT from August to November 2016 from our Institute. Among these, 7 subjects were telephonically prescreened for the study and were invited to participate (2 were not reached prior to starting initial PT session). Five subjects (71%) were screened and enrolled (1 patient refused participation, and one patient received PT from another provider). The mean age of the sample was 74 ±8.6 years (4 males). The mean disease duration was 9±4.6 years. The mean UPDRS-(III) score was 44.2 ±10.5. The H&Y stages at screening were 2 (n=1) and 3(n=4). One subject withdrew consent, citing lack of motivation. In this case, the clinical severity of PIGD was very mild (Mini BESTest=26/28). The duration of each TMS or sham session was 20 minutes. The mean resting motor thresholds of the sample was 38%±9.8. The average time lapse between PT and TMS/sham delivery during the first session was 23 minutes (min: 10 minutes and max: 40 minutes). At the following sessions, the average time lapse between PT and TMS/sham was 13.5 minutes (min: 5 minutes and max: 25 minutes). There was 1 adverse event; the subject reported mild neck pain after one of the TMS/sham sessions. There were no severe adverse events. There were no PT sessions without being followed by the experimental TMS/sham stimulation. A total of 28 paired sessions were completed with 100% compliance.

4. Discussion and Conclusion

Our protocol was originally developed and tested in PD participants, but designed to be appropriate for more generalized use. Recently, it has been emphasized how the control of the temporal aspect between motor training and none-invasive brain stimulation is crucial for successful associative plasticity, as the latter is a time-dependent phenomenon [8]. Task execution (or motor training) and brain stimulation should therefore be coupled with proper timing to maximize the possibility of harnessing adequate long-term plastic changes. However, in order to pair rTMS with multiple PT sessions in clinical practice, some practical issues need to be preliminarily addressed. First, the rehabilitation setting where PT is performed should have, or be located near the TMS device. Furthermore, administering TMS after a PT session can present an additional burden for PD patients, whose tolerance and endurance may be limited by comorbid factors including chronic pain, anxiety, apathy and depression. Therefore, the possibility of drop-outs needs to be considered and appreciated. We designed our study so that administration of TMS pulses could promptly follow each PT session within a standardized temporal window of 40 minutes. Such a limited interval implies adequate logistics to ensure an effective, standardized and reproducible work flow. According to our preliminary data, systematic TMS adjuvancy in conjunction with multiple sessions of standard-of-care PT represents a feasible and safe paradigm with good adherence. Limitations of our current work include: small sample size that prevents comprehensive analysis on the efficacy of this paradigm for PIGD, and lack of available data for the paradigm with a wider temporal window.. The latter could challenge the further applicability of