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The Effect of Two Weeks of Transcranial Direct Current Stimulation on Neurorehabilitation of Musician's Dystonia: A Follow Up

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Abstract

Background: We previously conducted a study where we combined a neurorehabilitation protocol for right hand task-specific focal dystonia with bi-parietal transcranial direct current stimulation (tDCS) with left-sided cathode. After two weeks, this protocol showed a significantly greater reduction of symptoms compared with the reduction observed in those musicians receiving neurorehabilitation combined with sham tDCS. After that, patients continued with the neurorehabilitation protocol without tDCS. As the whole rehabilitation process for these patients lasts more than a year, we wonder if this short period of tDCS stimulation is strong enough to change the outcome of the rehabilitation process in these patients.

Objective: Analyse whether, at the end of treatment, there is a higher proportion of cured musicians in the group of patients who received concomitant real tDCS during the first two weeks of the neurorehabilitation protocol, and whether this group recovered in a shorter period of time than those who received concomitant sham tDCS.

Method: Twenty-six musicians with right hand primary focal dystonia where followed during their neurorehabilitation process based on Sensory Motor Retuning therapy. During the first two weeks they also received either real or sham tDCS (cathode over left and anode over right parietal region) for the first 30 minutes of each 1-hour daily therapy session (total 10 sessions). After that, all patients continued with their daily rehabilitation sessions until complete recovery or until abandoning therapy due to lack of results. During the whole process, the therapist and the patients were blind to the initial tDCS condition. We compared proportions of cured patients and the time necessary to complete recovery in both groups.

Results: Of the 13 musicians who received active tDCS, 8 were cured of their dystonia whereas among the 13 who received sham tDCS, 9 were cured. This proportion is not statistically different (F=0.17; p=0.5; Risk Test=1.41). The patients of the active group who were cured took an average of 16.84±3.42 months to do so whereas those that received sham tDCS took an average of 17.38±4.26 months. The time taken was not statistically different between the two groups (U=33.5; p=0.82).

Conclusion: Although two weeks of bi-parietal tDCS can increase the effectiveness of rehabilitation in patients with task-specific focal hand dystonia, this short period of stimulation -mostly if we compare it with the average 17 months of duration of the entire process- do not produce any significant effect on the final therapy outcome. Future studies will be necessary to evaluate whether lengthening the stimulation period or maintaining it throughout the whole rehabilitation process can produce beneficial effects on the outcome of these patients.

Keywords: Task-specific dystonia; Neurorehabilitation; Transcranial direct current stimulation; Musician; Sensory motor retuning

Abbreviations

TSFHD: Task-Specific Focal Hand Dystonia; SMR: Sensory Motor Retuning; tDCS: transcranial Direct Current Stimulation; DES: Dystonia Evaluation Scale

Introduction

Musician's dystonia, one of the more frequent forms of task-specific focal hand dystonia (TSFHD), is a relatively frequent condition that is estimated to affect more than 1% of professional musicians. It

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Table 1: Summary of the Basic Clinical Data and Therapy Outcome.

Group	Patient	Gender	Age*(years)*	Instrument	Therapy outcome	Recovery time*(months)*
Active tDCS	*P1*	male	28	guitar	cured	10.29
	P2	male	25	guitar	cured	18.55
	P3	female	33	guitar	cured	16.71
	P4	male	37	guitar	partially recovered	
	P5	male	34	guitar	partially recovered	
	P6	male	31	guitar	cured	18.61
	P7	female	44	piano	cured	13.77
	P8	male	27	guitar	poor results	
	P9	male	31	piano	partially recovered	
	P10	female	54	piano	poor results	
	P11	male	27	guitar	cured	16.50
	P12	male	40	piano	cured	19.22
	P13	male	33	guitar	cured	21.03
Means (SD)			*34.15 (8.06)*			*16.84 (3.42)*
Sham tDCS	*P14*	male	32	piano	partially recovered	
	P15	male	33	guitar	poor results	
	P16	female	50	piano	cured	17.71
	P17	male	32	piano	cured	16.06
	P18	male	49	piano	cured	26.94
	P19	female	27	guitar	cured	11.97
	P20	male	44	guitar	poor results	
	P21	male	27	guitar	cured	17.61
	P22	male	41	guitar	cured	13.77
	P23	female	24	guitar	poor results	
	P24	male	32	piano	cured	17.36
	P25	male	41	piano	cured	19.65
	P26	male	34	guitar	cured	15.33
Means (SD)			*35.85 (8.39)*			*17.38 (4.28)*
Differences between groups		*Chi_{27}=0.00 p=0.68*	*t_{24}=-0.52 p=0.60*	*Chi_{27}=0.65 p=0.34*	*F=0.17 P=0.50*	*U=33.5 P=0.82*

Cured: no symptom of dystonia; Partially recovered: the musician is able to return to normal professional activity but still has some dystonia symptoms; Poor results: no improvement or some improvement but not able to return to professional activity.

is characterised by loss of coordination or motor control that affects specific tasks on the instrument. It can affect all kind of musicians and may severely compromise the career of the professional it affects. Although botulin toxin injections and neuro modulators have been used to reduce the symptoms, only neurorehabilitative techniques, such as Sensory Motor Retuning (SMR), have been able to completely revert the symptoms at the same time that it reprograms the brain [1]. However, these techniques require extremely long treatment times, rarely less than one year [2].

As Transcranial Direct Current Stimulation (tDCS) enables modulating cortical excitability and improves the efficacy of some neurorehabilitation processes [3-6] we hypothesised that this technique could also improve the efficacy of neurorehabilitation of musicians with dystonia, either by increasing the efficacy or accelerating the process. This is why we designed a study where we combined two weeks of SMR with real or sham tDCS. Using a dystonia evaluation scale, a structured test that included 15 items and that has been showed high correlation with objective measurements [1], we observed that both groups significantly reduced dystonia symptoms after these two weeks and the improvement was significantly greater in the SMR plus real tDCS stimulation group [7]. But the neurorehabilitation process in TSFHD patients requires months of retraining and there is still not enough scientific information about the effects and safety of tDCS if applied during more than two weeks. This is why these patients continued the retraining without tDCS stimulation until complete recovery or abandon of the therapy. In this second part of the study, we wanted to determine whether the enhancing effects of tDCS observed over the two weeks had any long term effect on these patients.

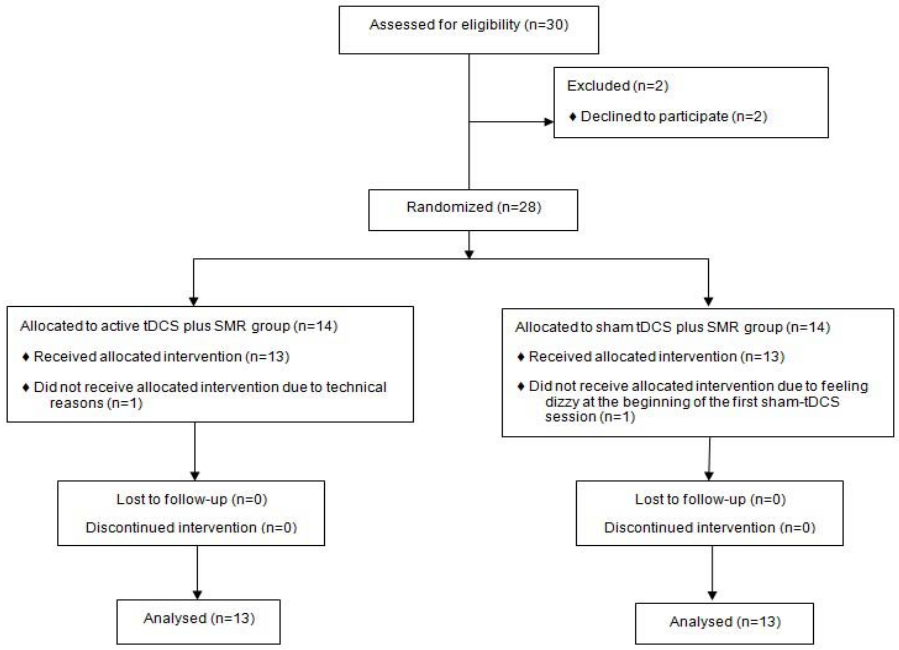


Figure 1: Flow diagram of the study.

Material and Methods

Design

This is the long-term follow up part of a previously published study [7]. The design was a parallel double-blind, randomized blocked clinical trial. Participants were randomly assigned to one of the two treatment groups according to a computer-generated, blocked (15 patients in each group) randomization process. As previous studies showed no influence of dystonia severity, age, sex, dystonia onset, instrument or other clinical or professional variables on the SMR treatment outcome, there was no balanced allocation for this aspect [8]. The patient allocation data were only accessible by the main researcher (JR-L) and locked in a password protected computer document. He was also responsible for setting the tDCS stimulator for each patient so participants, therapists, and data collectors did not know if the patient was treated with real or sham tDCS.

The study took place at the Institut de Fisiologia i Medicina de l'Art, Terrassa (Barcelona), a medical centre specialised in the diagnosis and treatment of performing artists and referral centre for TSFHD.

Participants

Thirty consecutive pianists and guitarists seeking treatment for their TSFHD affecting the right hand, between January and December 2012 were included. Of them, only twenty-six completed the previous study (Figure 1). The mean age was 35.00±8.11 years; 6 were women, and 20 men; 10 played the piano and 16 the guitar. All participants where first examined by the main author (JR-L), a physician with more than 25 years of experience in TSFHD to ensure the diagnosis and rule out other mental or physical problems. Exclusion criteria were bilateral TSFHD, secondary causes of TSFHD, generalized dystonia, other concurrent uncontrolled illnesses, pharmacological treatment of any kind, pregnancy, epilepsy, substance abuse, metal devices in the head, left handedness (assessed by the Edinburgh Handedness Inventory), and botulinum toxin injection within the last 15 weeks. All patients gave their informed consent to participate in the study, which was approved by the Institutional Research Ethics Committee, and conducted in accordance with the Declaration of Helsinki. This study was reviewed and approved by our IRB with identifier FCA-11/1.

Procedure

Sensory Motor Retuning (SMR): Each subject received daily SMR sessions [2,8] in the Institute, during two weeks, by the same experienced SMR therapist (author SF-M), who was blinded to the tDCS group assignment of each subject throughout the study. From that moment, each musician continued with the same routine at home and was seen for a follow up revision every 1-2 months. Each session started with splint exercises: repetitive movements on the specific affected task using splints that placed one or more fingers in a position slightly different from that used to play. The dystonic finger was never splinted. The purpose was to change hand proprioception and thus allow the use of new motor programs. The musician had to perform basic technical movements on the instrument (scales, arpeggios…) with the non-splinted fingers. Seven different exercises were designed for each musician based on how the dystonic finger interfered with the compensatory fingers [2]. Each exercise was performed during 3 minutes with one minute of rest between them. This was followed by task execution work: 5 to 60 minutes of repetition of the task (piano or guitar playing) without the splints. During each SMR session (splint exercises and task execution) the difficulty (in both parts of work) and the duration of the task execution work was adapted to avoid dystonic response and increased gradually. So the total duration of each daily retraining session was from 30, at the beginning, to 80 minutes at the end of the therapy (see Rosset-Llobet for more details) [7].

Transcranial direct current stimulation (tDCS): During the

first two weeks, patients received brain stimulation by a battery-driven constant-current stimulator (Eldith Ltd, Illmenau, Germany) via two saline soaked sponge electrodes (35 cm^2) placed on the scalp each one a parietal cortex (SM1; C3 according to the international 10-20 system). The cathode was placed in the homologous position of the hemisphere contralateral to the affected hand. As all patients had right hand dystonia, the cathode was placed on the left hemisphere. Current shunt between the electrodes over the scalp was minimized by carefully selecting the location of the electrodes so that the distance between the edges of the electrodes was at least 6 cm. The electrodes were held in place using an elastic skullcap. The device was set in advance by the main author (JR-L) to deliver either active or the sham stimulation, thus keeping both the patient and the therapist masked. The two treatment modalities were:

Active tDCS plus SMR: The stimulation intensity was set to 2 mA and applied over a 20-min period (fade-in/fade-out phases=10 seconds). During each treatment session, after five initial minutes of tDCS, the patients began the SMR protocol session. Patients underwent daily treatment (Monday to Friday) for 2 weeks (10 treatment sessions).

Sham tDCS plus SMR: The stimulator was automatically and unnoticeably turned off after 30 seconds of stimulation. This ensured that patients could feel the initial itching sensation at the beginning of tDCS, a requisite for successful masking. See the previous publication for more details about the technique and procedure [7].

Outcomes

Patients were evaluated in the Institute every 1-2 months and followed up to 30 months by one of the authors (SF-M). In each control, patients completed a dystonia evaluation scale (DES), a structured test that included 15 items. This subjective measurement has been used previously and showed high correlation with objective measurements [1]. These items were specifically selected for each patient trying to find the most affected patterns. For instance, one item for a pianist might be to do a trill with index and middle fingers or to play the Sonata in D minor by Soler. The item for a guitarist might be a C major scale with index and middle fingers, an ascending arpeggio, or to play the Allegro solemne from Agustin Barrios' La Catedral. For each item, the musician was asked to gradually increase the execution speed up to their technical limit and to tell the therapist if they felt any symptom of dystonia during the execution. Items were therefore different between patients but the same for each patient during follow-up.

A patient was considered cured when they did not feel any symptom of dystonia in any of the 15 items of the DES during two or more controls. Patient was considered partially recovered when they felt dystonia symptoms in 3 items or less at the end of the follow up. We considered as poor results those patients that withdrew from therapy or felt dystonia symptoms in more than 3 items.

Recovery time was the number of days from the beginning of the therapy and the first control where the patient did not feel dystonia in any of the 15 items, expressed in months (calculated as number of days divided by 30).

Statistical analysis

All data were analyzed using SPSS version 13.0. The homogeneity of the characteristics of both samples was analyzed using the Fisher Exact Test, a non-parametric test for categorical variables. The Risk test was used to measure the strength of the association between the presence of a factor and the occurrence of an event. The Mann Whitney test for 2 independent samples of continuous variables was used to compare differences between groups. The confidence level used in all tests was 95%.

Data analysis was carried-out by an independent researcher who was blinded to the group allocation.

Results

Table 1 shows the descriptive data and the result of treatment for the study participants. There were no statistically significant differences between the two groups related to their clinical and demographic characteristics. Of the 13 musicians who received active tDCS, 8 were cured of their dystonia whereas among the 13 who received sham tDCS, 9 were cured. This proportion is not statistically different (F=0.17; p=0.5; Risk Test=1.41). The patients of the active group who were cured took an average of 16.84±3.42 months to do so whereas those that received sham tDCS took an average of 17.38±4.26 months. The time taken was not statistically different between the two groups (U=33.5; p=0.82).

Discussion

In spite of observing that tDCS increased the effectiveness of neurorehabilitation in patients with TSFHD [7] in the first part of this study, follow-up of these patients did not show any rehabilitation enhancing effect on the final result of the treatment. The patients who received two weeks of tDCS were not cured more quickly or in a greater proportion, in spite of being significantly better after the two weeks of treatment.

Given that tDCS has also proved useful in aiding rehabilitation of the TSFHD in the short term in other studies [9], the current results make us wonder why no differences can be appreciated at the end of the treatment.

The first thing to take into consideration is the fact that we are using a subjective measurement as the primary outcome and this may bias the results. But, since previous studies have shown that this subjective outcome is consistently correlated with the objective motor performance, we think that this may not be a remarkable source of error [8]. Another potential source of bias is how the tDCS was administered. We know that without neuro navigation assessment the effects on the motor cortex are highly variable [10].

As can be seen in the results, the process of neurorehabilitation of these patients lasts, on average, more than eighteen months. Although patients were regularly visited and adherence to the therapy checked at each control session, adherence to the therapy has not specifically been monitored in this study. This could be a source of bias and the cause of the lack of results. However, although all these facts can give some explanation to the lack of results, our main hypothesis is that the motive has been the short period of time of application of tDCS in relation to the long duration of the treatment. The enhancing effects, even though significant, are not strong enough to be able to mark differences over such a long term.

In any case, our results force us to consider the possibility of

extending the enhancing effects of tDCS on neurorehabilitation and how this should be done. At first, the most logical option seems to be to maintain tDCS, either with the same frequency or with sessions more spaced apart over a longer period of time, or even during the whole treatment.

There are studies that lead us to believe that this possibility is not pure fantasy. They show how the technique can maintain its efficacy and safety over long periods of time. But these are studies that only include isolated cases and which only concentrate on the control of psychiatric symptoms or chronic pain [11-14].

There are numerous questions to be answered before being able to extend the period of stimulation with tDCS in patients enrolled in a neurorehabilitation program for TSFHD. One of the first things to be defined is the stimulation protocol to be used. We know that the current dosage, interval between sessions, and timing of stimulation in relation to rehabilitation protocol are factors critical to the effectiveness of the technique [15]. There are few studies available and the doses and the application intervals they use are normally selected in an arbitrary or intuitive way. All of them include an initial intensive stimulation period (of up to two sessions a day) that usually lasts one or two weeks to achieve the required therapeutic benefits. But after this point the strategies do not follow any clear pattern. Whereas some studies maintain two sessions a day over many months [11], others continue with one session a week [13] or month [12]. There are even studies that established the sessions on demand of the patient [14].

On the other hand, we know that the effects are not linear. This leads us to consider whether, in the same way that increasing the intensity or the application time might shift the direction of excitability alterations [16], this type of change in the effects could also be observed if the stimulation is repeated over many consecutive days. Furthermore, a recently published paper about evidence-based guidelines for the therapeutic use of tDCS in dystonia did not find enough evidence to be able to recommend this particular application [17]. Moreover, the safety of the doses of this technique has only been studied in depth in animal models and short treatments [18].

There are also practical aspects regarding delivery that should be resolved. As patients with TSFHD continue the neurorehabilitation process at home, with controls every one or two months in reference centres, consideration could be given to a domiciliary stimulation protocol. This would complicate the process even further as correct administration would have to be ensured. There are some proposals along these lines that are based on telemedicine and attempt to resolve the problems represented by domiciliary tDCS [19,20]. It has been proved that self-administered domiciliary tDCS can be safe and feasible and gives outcome results similar to in-hospital delivery [21]. But, even after correct training of patients, many subjects reported difficulty applying tDCS and this was associated with a high dropout rate (41%) [22].

As musicians with TSFHD are usually young people, without mental or physical disabilities other than the task specific dystonia, they would probably not have any great difficulty in correctly applying self-administered tDCS. However a structured protocol is obviously needed to identify subjects who are appropriate candidates for domiciliary treatment and to ensure that they are adequately trained. The devices we are actually using for research are probably not the best machines for domiciliary administration. So, specific tDCS devices will be required for this new purpose. The literature includes some interesting proposals about the guidelines and kind of devices to be used [23].

One strength of this study is the inclusion of a very homogeneous patient group with respect to the kind of TSFHD and the task affected. Strength is the low patient dropout rate even after a relatively long follow up. One important limitation is the fact that DES is a subjective outcome measure. We chose this type of measurement because we believe that the most important thing for the musician, as a patient, is whether he or she is or not able to play at a high level, and this is completely subjective. In addition, previous studies have shown that there is a high correlation between this subjective measure and the objective measurement of the smoothness and coordination of finger movements [1]. As the patients in this study come from different countries (some of them quite far away) it was very difficult to be able to visit them exactly when desired. Although controls have been close enough to make it possible to determine when they could be considered cured or not, it has prevented us from obtaining exact information on precisely when the two groups ceased to evolve differently from each other. This information would enable more efficient design of any future interventions.

In conclusion, in spite of the first phase of this study demonstrating that tDCS was capable of improving the efficacy of neurorehabilitation in patients with TSFHD after two weeks of stimulation, we found that this does not imply any significant change in the long term. We think that this is probably due to the short duration of the tDCS stimulation compared to the long duration of the training. So, in treatments of conditions like TSFHD, if we want to take advantage of the synergic effect between tDCS and neurorehabilitation, more prolonged stimulation protocols should be considered.

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Conflicts of Interest and Source of Funding

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