Effect of Transcranial Direct Current Stimulation on Neurorehabilitation of Task-Specific Dystonia

A Double-Blind, Randomized Clinical Trial

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Task-specific focal hand dystonia can disable affected individuals. Although neurorehabilitation techniques such as sensory motor retuning can result in complete recovery in some patients, it requires many months of treatment. Combining transcranial direct current stimulation (tDCS) with neurorehabilitation is a new and promising approach that can help these patients. However, the results in different studies are contradictory. **OBJECTIVE:** Analyze whether delivering tDCS (cathode over left and anode over right parietal region) during the neurorehabilitation process for musicians with dystonia can increase the effectiveness of therapy. **METHOD:** A parallel double-blind randomized design was used to study 30 musicians with right-hand primary focal dystonia. All patients underwent a 2-week course of neurorehabilitation based on sensory motor retuning therapy coupled with either real or sham tDCS for the first 30 minutes of each daily 1-hour therapy session (total 10 sessions). The therapist and patient were blind to the tDCS condition. A dystonia severity score was obtained before and after the 2-week protocol. The therapist also rated the evolution of each patient. **RESULTS:** Both groups significantly improved their dystonia severity score during the 2 weeks. Score differences were 88.23 (±40.51) and 63.36 (±30.57) for the active and sham groups, respectively. The active group showed a statistically significant greater improvement. **CONCLUSIONS:** Biparietal tDCS with left-sided cathode is a safe technique that does not interfere with the neurorehabilitation procedure and can increase therapy effectiveness in rehabilitation patients with right-hand task-specific focal dystonia. *Med Probl Perform Art* 2015; 30(3):178–184.

Task-specific focal hand dystonia (TSFHD) leads to a loss of voluntary motor control during skilled tasks such as playing a musical instrument, writing or using a keyboard, or even practicing sports such as golf, tennis, table tennis, and darts. This condition can even disable affected individuals. Although the etiology of TSFHD remains poorly understood, there appears to be greater intensity of activation of the sensorimotor primary cerebral cortex, disruption of sensorimotor organization and integration, deficits in surrounding inhibition, and increased plasticity.[1,2]

Some patients can be helped with neurorehabilitation techniques such as sensory motor retuning (SMR).[3] SMR introduces proprioceptive changes in the affected area and enables the activation of nonaffected neurological networks when playing. These changes are obtained through the application of one or several splints on the compensatory fingers of the affected hand.[4,5] This kind of therapy not only relieves symptoms, but also promotes parallel brain reorganization.[6] However, benefits vary across patients and complete recovery requires many months of treatment.[5]

Transcranial direct current stimulation (tDCS) is a noninvasive brain stimulation technique that delivers a weak electrical current (1–2 mA) through scalp electrodes.[7] If appropriately applied, tDCS is safe, yet allows modulation of cortical excitability beyond the duration of the stimulation itself. Cortical excitability is enhanced under the anode and suppressed under the cathode.[8] Such neuromodulatory stimulation can induce behavioral effects and improve performance in a given task or the efficacy of an intervention.[9] For example, motor learning can be sped up by combining tDCS with physical motor practice in normal subjects[10] and in stroke patients.[11,12] The potential benefit of combining tDCS with other interventions also has been shown in visual rehabilitation[13] and pain treatment.[14]

As the average time for complete recovery using SMR is 15 months,[5] trying to speed up this process seems reasonable and even more so if, at the same time, we can modulate plasticity and reduce the greater intensity of activation of the primary sensorimotor cortex seen in these patients.

Trials examining the potential of tDCS to improve TSFHD symptoms or enhance retraining effects have failed to achieve significant results.[15–18] However, we hypothesized that these negative findings are due to the specific protocol used, and that a carefully designed, proof-of-principle, sham-controlled randomized trial of concurrent tDCS with SMR was warranted. Based on what we actually know about TSFHD pathophysiology, the most reasonable set-up would be to place the cathode on the contralateral parietal hemisphere of the affected hand (to reduce primary sensori-

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motor cortex activity) and the anode at the homolateral parietal side (to modulate plasticity). This setting has proven safe and effective in motor retraining.[11]

Our hypothesis was supported by a pilot study with four TSFHD patients in whom biparietal tDCS during SMR led to greater improvement than seen in patients undergoing SMR alone.[19] Interesting recent results from Furuya[20] also back up the importance of considering a biparietal cathode set-up and the importance of combining tDCS with concomitant retraining.

In our opinion, the study by Furuya also raises another important question. The paper shows how some parameters, including finger coordination measured on a MIDI keyboard, change during the intervention. We have concerns about the clinical significance of these kinds of measurements and their relevance for neurorehabilitation outcomes. They have the advantage that they are objective quantifications. But those who are familiar with musician's dystonia know that movement smoothness, finger coordination, and the number or degree of involuntary movements are not directly linked to performance difficulties. This is why, in this project, we have used more subjective evaluation tools which we think are more associated with the real task and thus can better inform us about the impact on TSFHD treatment.

Here we report the effects on dystonia symptoms in a parallel-group, double-blind clinical trial of a 2-week course of SMR combined with biparietal real or sham tDCS with the cathode over the left hemisphere.

MATERIAL AND METHODS

The design was a parallel, double-blind, randomized clinical trial. Participants were randomly assigned to one of two treatment groups according to a computer-generated, balanced randomization process. The patient allocation data were accessible by only the main researcher (JR-L) and locked in a password-blocked computer folder. The study took place at the Institut de Fisiologia i Medicina de l'Art-Terrassa (Barcelona), a medical center specialized in the diagnosis and treatment of performing artists with 20 years' expertise in this field. As this is one of the few centers in the world working in this field, patients came from abroad.

Participants

Thirty consecutive pianists and guitarists seeking treatment for their TSFHD affecting the right hand were included. Patients were visited and treated in a performing arts medicine clinic, in Terrassa (Barcelona, Spain) Their mean age was 35.43 ± 8.74 yrs; 7 were women and 23 men; 12 played the piano and 18 the guitar. All participants were first evaluated by the main author (JR-L), a physician with considerable 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 Ethical Research Committee and conducted in accordance with the Declaration of Helsinki.

Procedure

Sensory Motor Retuning (SMR): Each subject received daily SMR sessions[3,5] in the Institute by the same experienced SMR therapist (author SF-M), who was blinded to the tDCS group assignment of each subject throughout the study. Sessions were daily from Monday to Friday during 2 weeks.

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 splint was custom-made by the therapist. It had a thermoplastic band adapted and fitted to the hand, leaving freedom for normal finger movement. This band had a metal piece attached to the dorsal part with five holes, one for each finger, where a metallic cylindrical piece (3 mm in diameter) could be placed to fix the desired fingers in a slightly more extended position than the normal playing position (Fig. 1). The purpose was to change hand proprioception and thus allow the use of new motor programs. It is necessary to identify the dystonic and compensatori fingers. The dystonic finger is the one originally receiving the distorted command; it usually endures the highest tension and tends to bend toward the palm of the hand. The compensatory finger or fingers are the ones trying to help the dystonic finger to perform the correct movement.[4] The dystonic finger was never splinted. The musician had to perform basic technical movements on the instrument (scales, arpeggios, etc.) with the nonsplinted fingers.

Seven different exercises were designed for each musician based on how the dystonic finger interfered with the compensatory fingers.[5] Each exercise was performed during 3 minutes with 1 minute of rest between them.

This was followed by *task execution work*: 5 to 15 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 were adapted to avoid a dystonic response. So the total duration of each daily retraining session was 30 to 45 minutes.

Transcranial Direct Current Stimulation (tDCS): Stimulation was delivered by a battery-driven constant-current stimulator (Eldith Ltd, Illmenau, Germany) via two saline-soaked sponge electrodes (35 cm^2) placed on the scalp over the 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

FIGURE 1. Splint used for the SMR therapy. Compensatory fingers were splinted in a slightly more extended position than the normal playing position. The nonsplinted fingers were used to do the exercise.

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.[21] The electrodes were held in place using an elastic skullcap (Fig. 2). The device was set in advance by the main author (JR-L) to deliver either active or sham stimulation, thus keeping both the patient and therapist masked.[22]

The two treatment modalities were:

1. ***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 sec). During each treatment session, after 5 initial minutes of tDCS, the patients began the SMR protocol session. Patients underwent daily treatment (Monday to Friday) for 2 weeks (10 treatment sessions).
2. ***Sham tDCS plus SMR:*** The stimulator was automatically and unnoticeably turned off after 30 sec of stimulation. This ensured that patients could feel the initial itching sensation at the beginning of tDCS, a requisite for successful masking.[22]

A questionnaire for the adverse effects of tDCS was administered at the end of each session.

Outcomes

Primary Outcome: Dystonia Severity Rating: The impact of the intervention was quantified by submitting all patients to a baseline evaluation using a structured test that included 15 items. Each item was a difficult motor task involving the affected activity (for instance, 1 item for a pianist might be to do a trill with the index and middle fingers or to play the D minor Sonata by Soler at 90 beats/min; the item for a guitarist might be a C major scale with the 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 follow the speed of the movements paced with a digital metronome. The speed was increased or decreased to a point where the patient did not feel dystonia and where the therapist did not see any abnormal (dystonic or compensatory) movement during that item. The execution speed was rated (in beats/min) and recorded for each item.

After testing the 15 items, the three most affected baseline items were selected to obtain three baseline scores for each patient. We considered the most affected items those where the execution speed was the slowest. These three items were again scored in the same way on the last day of therapy (final scores).

Secondary Outcome: Therapist's Evaluation: On the last day of treatment, the therapist (author SF-M) (blinded to treatment mode) was asked to say whether the evolution of each patient was better than or the same as expected. This evaluation was based on her experience treating TSFHD patients during 20 years. Evolution was considered better than expected if one or more of these aspects where present during SMR sessions: the learning process for the correct movement patterns was faster than expected, abnormal movements were less present than usual, or the degree of hand tension was lower than expected.

FIGURE 2. Electrodes were placed over both parietal cortex and held in place by an elastic skullcap.

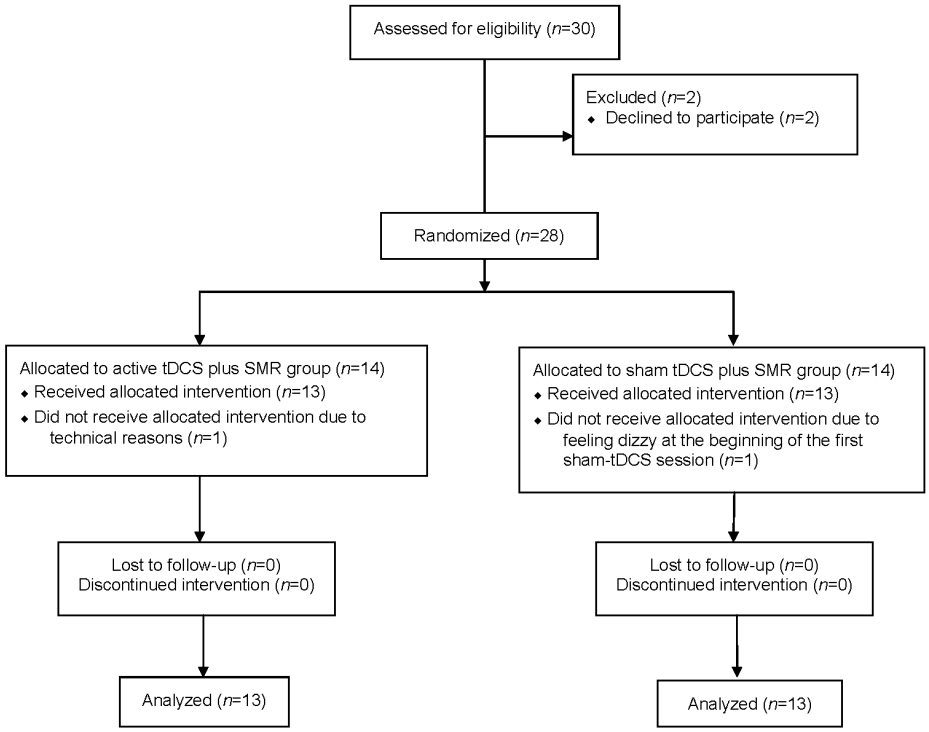

FIGURE 3. Flow diagram of the study.

Statistical Analysis

All data were analyzed using SPSS version 13.0 (IBM SPSS, Armonk, NY, USA). The Kolmogorov-Smirnov nonparametric test was used to test the normality of continuous variables. The homogeneity of the characteristics of both samples was analyzed using the chi-square parametric test for categorical variables, while Student's *t*-test for two independent samples was used for continuous variables. The concordance between the therapist's evaluation and treatment modality was analyzed using McNemar's test to confirm equal proportions and the chi-square parametric test to analyze the significance.

Any differences between the baseline and final score were tested using the Wilcoxon nonparametric test for paired samples. Differences were also compared within each group and between groups using Student's *t*-test for two independent samples. 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

Figure 3 shows the participant flow and, for each group, the number of participants who were randomly assigned, received intended treatment, and were analyzed for the primary and secondary outcomes. The diagram includes detailed information on the excluded participants. Patients were recruited between January 2012 and September 2014.

Table 1 summarizes the clinical and demographic data for all patients. There were no significant statistical differences between the two groups. None of the patients reported any discomfort or side effects when completing the side effect questionnaire administered after each session. All patients remained blinded to their tDCS condition, being a random guess when asked specifically. The same was true for the therapist. The application of tDCS did not interfere with the SMR sessions.

Table 2 shows the baseline Dystonia Severity Rating and final scores for each group. There were no statistical differences between groups in baseline scores (Z=–0.34; p=0.73). Final scores were statistically superior to baseline in both active (Z=–5.42; p=0.00) and sham (Z=–5.40; p=0.00) groups. Final scores were statistically superior in the active group (126.72±55.81) compared to the sham group (102.72±34.03) (Z=–2.38; p=0.02). Individual differences between final and baseline scores were statistically higher in the active (88.23±40.51) than in the sham group (63.36±30.57) (t=3.06; p=0.00).

The therapist's subjective clinical impressions are shown in Table 1. When the therapist was asked to rate patients as to whether the clinical course had been better than expected, 84.62% of those selected had received active tDCS, whereas 76.92% of the patients rated as having improved no more than expected had received sham tDCS (c^2_1=9.90, p=0.00).

DISCUSSION

Both groups had significantly better Dystonia Severity Rating scores after 2 weeks of retraining. This is in concordance with previous data.[3] However, those receiving concomitant real tDCS had a significantly greater improve-

TABLE 1. Summary of the Clinical Data and Therapist's Evaluation

Group	Gender	Age (yrs)	Age Beginning Studies	Age Dystonia Onset	Dystonia Evolution	Years Playing	Instrument	Practice (hr/day)	Dystonic Finger	Therapist Evaluation
Active tDCS										
P1	M	28	16	22	6	6	Guitar	4	Ring	Better
P2	M	25	6	22	3	16	Guitar	4	Middle	Better
P3	F	33	7	31	2	24	Guitar	8	Index	Better
P4	M	37	11	34	3	23	Guitar	8	Middle	No change
P5	M	34	14	28	6	18	Guitar	6	Middle	Better
P6	M	31	9	29	2	20	Guitar	6	Ring	No change
P7	F	44	5	43	1	38	Piano	7	Middle	Better
P8	M	27	11	21	6	10	Guitar	2	Middle	Better
P9	M	31	15	27	4	12	Piano	6	Middle	Better
P10	F	54	26	50	4	24	Piano	5	Index	Better
P11	M	27	8	26	1	19	Guitar	5	Middle	Better
P12	M	40	12	24	16	25	Piano	4	Middle	Better
P13	M	33	11	29	4	21	Guitar	5	Index	Better
Means (SD)		34.15 (8.06)	11.62 (5.49)	29.69 (8.47)	4.56 (3.89)	19.69 (8.01)		5.38 (1.71)		
Sham tDCS										
P14	M	32	13	19	13	6	Piano	4	Middle	No change
P15	M	33	10	32	1	22	Guitar	5	Middle	No change
P16	F	50	5	40	10	35	Piano	4	Middle	No change
P17	M	32	19	26	6	7	Piano	6	Index	No change
P18	M	49	18	47	2	29	Piano	4	Middle	Better
P19	F	27	14	26	1	12	Guitar	5	Middle	Better
P20	M	44	7	39	5	32	Guitar	5	Middle	No change
P21	M	27	21	25	2	4	Guitar	6	Middle	No change
P22	M	41	17	40	1	23	Guitar	5	Ring	No change
P23	F	24	8	22	2	14	Guitar	5	Middle	No change
P24	M	32	12	30	2	8	Piano	2	Middle	No change
P25	M	41	7	31	10	30	Piano	8	Ring	No change
P26	M	34	9	24	10	22	Guitar	7	Middle	Better
Means (SD)		35.85 (8.39)	12.31 (5.19)	30.85 (8.38)	5.00 (4.32)	18.77 (10.85)		5.08 (1.50)		
Differences between groups	χ_{27}=0.00 p=0.68	t_{24}=-.52 p=0.60	t_{24}=–.33 p=0.74	t_{24}=–.35 p=0.73	t_{24}=–.33 p=0.74	t_{24}=.25 p=0.81	χ_{27}=.65 p=0.34	t_{24}=.49 p=0.63	χ_{28}=1.22 p=0.54	χ_{1}=9.90 p=0.00

ment. The therapist's evaluation also confirmed the beneficial effects of this tDCS set-up on retraining. None of the patients reported any side effect of the therapy. These findings, taken as a whole, demonstrate that cathodal biparietal tDCS is a safe technique that enhances the improvement induced by neurorehabilitation on TSFHD and makes retraining easier, thus supporting the preliminary data of our earlier pilot study.[19]

tDCS may prime central somatosensory pathways, promote their plasticity, and facilitate surrounding inhibition in the hyperactive areas rendering them more responsive to neurorehabilitation.[7,23] tDCS may also act by means of a rise in consolidation mechanisms or facilitate performance during training, e.g., through reduction of inhibition.[24,25] But tDCS alone, without being coupled with an effective retraining protocol, does not improve dystonia symptoms.[15] Therefore, no direct effect of tDCS on neurorehabilitation should be expected, but rather an additive or modulating one as we have seen in this study. Furthermore, it seems logical to assume that, although tDCS can simplify TSFHD retraining, this technique will not make an ineffective rehabilitation procedure work. Even more, each brain disorder has its own physiopathology; each neurorehabilitation protocol and tDCS montage has its specific neuronal effects. Therefore, it is highly improbable that all montages will equally help one specific neurorehabilitation technique.[17,26–31] Many variables seem to determine effectiveness and a lot of them are still insufficiently known. For instance, Giacobbe et al.[32] demonstrated the importance of applying tDCS at the right time; while a motor improvement in stroke patients was seen if tDCS was applied before neurorehabilitation, a worsening was observed if it was administered during or after training.[32] All these aspects could explain why there are contradictory results about the effectiveness of tDCS for TSFHD neurorehabilitation.

Our study has some limitations. The first is the fact that we have not tested the effects of tDCS alone. We decided not to include this condition because there are studies showing that tDCS alone does not significantly change fine motor control in TSFHD.[15,16,20] As our center is a private clinic where musicians come from abroad looking for an effective therapy for their condition and time for them

TABLE 2. Dystonia Severity Rating for Each Patient

	Active tDCS				Sham tDCS		
	Basal	Final	Difference		Basal	Final	Difference
P1	142	287	145	P14	80	132	52
	139	285	146		2	90	88
	63	236	173		10	129	119
P2	28	154	126	P15	15	96	81
	28	175	147		11	92	81
	32	185	153		8	92	84
P3	65	155	90	P16	20	126	106
	69	160	91		11	125	114
	61	185	124		34	177	143
P4	0	79	79	P17	121	189	68
	20	100	80		44	124	80
	25	114	89		49	129	80
P5	40	106	66	P18	35	101	66
	32	104	72		33	100	67
	34	107	73		25	99	74
P6	45	19	–26	P19	80	111	31
	44	22	–22		80	118	38
	52	93	41		74	124	50
P7	46	112	66	P20	15	69	54
	47	115	68		10	67	57
	35	113	78		9	69	60
P8	30	108	78	P21	102	175	73
	35	114	79		14	111	97
	28	107	79		11	112	101
P9	0	79	79	P22	28	25	–3
	1	82	81		34	86	52
	0	81	81		31	88	57
P10	10	99	89	P23	6	9	3
	12	102	90		21	77	56
	51	152	101		29	90	61
P11	18	128	110	P24	41	89	48
	25	140	115		39	93	54
	33	85	52		65	108	43
P12	49	139	90	P25	44	80	36
	52	162	110		20	75	55
	15	133	118		33	100	67
P13	11	135	124	P26	105	115	10
	41	80	39		68	110	42
	43	110	67		89	115	26
Means (SD)	38.49 (30.25)	126.72 (55.81)	88.23 (40.51)		40.46 (31.15)	102.72 (34.03)	63.36 (30.57)

is extremely important, we thought it unethical to waste their time and money on a procedure that we know will not be useful for them.

We know that the outcome measurements used in this project are not really objective, and this is another limitation. However, being able to play is a subjective evaluation, made by each musician himself, of his particular situation. When observing normal musicians playing, abnormal movements, like those detected when evaluating musicians with dystonia, can be seen. And the music they produce is fine and they do not feel constrained by these dystonia-like movements. So, when planning the protocol of this study, we discussed the dilemma of using objective measurements that are not completely linked to musical execution or using more subjective outcomes that provide more information about the musician's ability to play. As what we want to achieve with the neurorehabilitation process is to restore the ability to play, we decided to test, as objectively as possible, the ease of playing.

Another limitation of this study was that we did not have measurements about what happens after the 2 weeks of treatment. Once the intensive 2 weeks work in our center was completed, patients continued the daily retraining routine at home. Given that there are no studies demonstrating the safety and effects of tDCS when applied over long periods, we decided to discontinue stimulation when the in-clinic protocol ended. In addition, the design of the study did not allow us to measure whether the differences between the two groups were maintained or changed after these 2 weeks. Some studies showed how improvements in motor learning remained 4 weeks after the end of stimulation, but we do not have any data refer-

ring to longer periods.[33] New studies will have to clarify if this also happens in TSFHD patients and explore whether there are more beneficial effects when tDCS is continued over a longer period, repeated at intervals, or even used throughout the whole retraining process.

In our protocol, tDCS was administered by the same therapist who administered the SMR sessions. She was not previously trained in noninvasive brain stimulation techniques and a short training session was enough to enable her to apply the procedure properly. No side effects or problems were reported during this study. For all these reasons and also because this is a cheap tool needing no specific setting or administration in a hospital, we believe that it could be used in any kind of medical center treating musicians having TSFHD using a retraining protocol.

In conclusion, we demonstrated that cathodal bilateral tDCS enhances the effectiveness of SMR in TSFHD and can be safely and easily applied during this kind of retraining. Patients receiving real tDCS not only showed greater improvement, but the retraining was much easier and more effective. More precise knowledge is needed to take full advantage of this technique and to determine its advantages when used in a therapy lasting many months.

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