Transcranial Direct Current Stimulation Improves Neurorehabilitation of Task-Specific Dystonia

A Pilot Study

Jaume Rosset-Llobet, MD, PhD, Sílvia Fàbregas-Molas, Phth, and Álvaro Pascual-Leone, MD, PhD

Sensory-motor retuning (SMR) can help the symptoms of task-specific focal hand dystonia. However, effects vary across patients and take many sessions. Here, we present proof of principle evidence that transcranial direct current stimulation (tDCS) can enhance these effects. We compared the effects of a combined tDCS-SMR protocol (n=4 patients) with the efficacy of SMR alone (n=30 patients). All 4 patients treated with the combined protocol showed greater improvement than those undergoing SMR alone. Results encourage a larger, parallel-group clinical trial with sham tDCS control. *Med Probl Perform Art* 2014; 29(1):16–18.

Task-specific focal hand dystonia leads to a loss of voluntary motor control during skilled tasks that can render affected individuals disabled. The etiology of task-specific focal dystonia remains poorly understood, though there appears to be alteration of motor cortical excitability and plasticity.[1,2]

Pharmacologic treatment (anticholinergic agents, botulinum toxin, etc) is often of limited efficacy and associated with side effects. Some patients can be helped with neurorehabilitation techniques, such as sensory motor retuning (SMR).[3] However, benefits vary across patients and require many months of treatment.[4]

Transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that delivers a weak electrical current (1–2 mA) through scalp electrodes. If appropriately applied, tDCS is safe, yet allows modulation of cortical excitability beyond the duration of the stimulation itself. Under the anode, cortical excitability is enhanced, while under the cathode it is suppressed.[5] Such neuromodulatory effects can induce behavioral effects and improve performance in a given task or the efficacy of an intervention.[6] For example, motor learning can be sped up by combining tDCS with physical motor practice in normal subjects[7] and in stroke patients.[8,9] The potential benefit of combining tDCS with other interventions has also been shown in visual rehabilitation[10] and pain treatment.[11]

Theoretically, tDCS seems that it might be a good tool for those patients affected by task-specific focal hand dystonia. Surprisingly, results in this field are sparse and contradictory.[12–15] We agree with Benninger[15] about the possibility that lack of results may be because tDCS is not changing neurological pathways but facilitating this kind of change. So, if tDCS is not followed by an effective neurorehabilitative protocol, no changes must be expected. Based on this hypothesis, in the present pilot study, we examined the potential enhancement effect of tDCS onto SMR for task-specific focal hand dystonia.

SUBJECTS

Four patients (study group) underwent treatment for task-specific focal hand dystonia with a combination of tDCS and SMR. Data from this group were compared with findings in 30 patients (18 guitarists and 12 pianists) affected with task-specific focal hand dystonia and consecutively treated with SMR in our center (control group). The epidemiologic characteristics of the patients are summarized in Table 1. None of the 4 patients in the study group, and none of the 30 in the control group, showed any signs or symptoms of neurological disorders other than the focal dystonia. None were undergoing pharmacological treatment or had any contraindications for tDCS.[16] All patients gave informed consent to the study, which was approved by the Institutional Ethical Research Committee and conducted in adherence to the Declaration of Helsinki.

PROTOCOL

All patients received daily 1-hour SMR sessions. Each session started with splint exercises: repetitive movements on the specific affected task using splints to change hand proprioception and thus facilitate the use of new motor programs. Compensatory fingers were alternatively splinted in seven different combinations. These combinations were not randomly decided but based on which fingers were affected and using therapist expertise to decide which can be the most effective ones for each patient (see more detail

Dr. Rosset-Llobet and Dr. Fàbregas-Molas are at the Institut de Fisiologia i Medicina de l'Art-Terrassa, and the Fundació Ciència i Art, Barcelona, Spain; and Dr. Pascual-Leone is at the Berenson-Allen Center for Noninvasive Brain Stimulation, Cognitive Neurology Unit, Department of Neurology, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA, and the Institut Guttmann de Neurorreabilitació, Universitat Autonoma, Barcelona, Spain.

Address correspondence to: Dr. Jaume Rosset-Llobet, Institut de Fisiologia i Medicina de l'Art-Terrassa, Ctra. de Montcada 668, 08222 Terrassa (Barcelona), Spain. Tel +34937844775. info@institutart.com.

TABLE 1. Demographic Data and Scores for Patients Receiving Combined tDCS+SMR Treatment

Case	Age (yrs)	Gender	Task	Affected Finger	Evolution Time (yrs)	Protocol	Baseline Score	10d score	20d score
1	35	male	piano	right middle	3	10 days: tDCS+SMR + 10 days: SMR	97.69	76.51	70.21
2	32	female	piano	left index	1	20 days: tDCS+SMR	97.65	83.12	73.24
3	30	male	electric guitar	right index	7	10 days: tDCS+SMR + 10 days: SMR	97.95	85.12	78.38
4	45	male	piano	right index	2	20 days: tDCS+SMR	99.34	86.24	71.02
Study group mean (SD)	35.50 (6.66)				3.25 (2.63)	tDCS+SMR	98.16 (0.80)	82.75 (4.36)	73.21 (3.68)
Control group mean	34.40 (4.78)				3.26 (1.92)	SMR	96.33 (2.96)	89.02 (5.45)	85.38 (5.37)
p-value	0.681				0.993		0.233	0.015	0.001

Note that patients 1 and 3 underwent tDCS+SMR during 10 days followed by 10 days of SMR alone, while patients 2 and 4 had combined tDCS+SMR for 20 days. No statistical differences were found on baseline, 10d, and 20d scores between these two pairs of patients (p=1.000, 0.667, and 1.000, respectively).

about the therapy on Rosset-Llobet and Fàbregas-Molas' work[17]). Exercises were done in two equal series each, one including 3 minutes of each combination with 1 rest minute between them. These two series were followed by task execution work: 5 to 15 minutes of repetition of the task without the splints. During each SMR session (splint exercises and task execution), the difficulty of the task was adapted to avoid dystonic response. Treatment was delivered by a very experienced SMR therapist.

In the four patients undergoing tDCS, stimulation was delivered with a battery-driven, constant-current stimulator (Phoresor II, IOMED Inc., Salt Lake City, USA) via two saline-soaked sponge electrodes (35 cm^2) placed on the scalp, each one over one of the sensorimotor 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. 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 5 initial minutes of tDCS, the patients began the 1-hour SMR protocol session. Patients underwent daily treatment session (Monday to Friday) for 2 to 4 weeks (10 to 20 treatment sessions).

To quantify the impact of the intervention, all patients were evaluated at baseline using a structured test that included 15 items. Each item was a difficult motor task involving the affected activity (for instance, a pianist might be asked to do a trill with index and middle fingers at 100 beats/min and to play the D minor Sonata from Soler at 90 beats/min). After performing each item, patients were asked to rate the severity of their dystonic symptoms (with 0 meaning no difficulty/no dystonia sensation and 100 indicating impossible to perform the task/maximal dystonia sensation). We calculated an average score for all tested items (baseline score). Patients repeated the same test after the 10th (10d score) and 20th day of retraining (20d score).

Means were compared between groups using the Mann-Whitney nonparametric test. All calculated p-values were two-sided, and $p< 0.05$ was considered statistically significant. There were no statistical differences between groups' ages or time of dystonia.

RESULTS

All patients in the study group, combining tDCS with SMR, tolerated the intervention without adverse or side effects. Combination therapy was easy to apply and did not interfere with the SMR interventions.

There was no statistical difference in baseline scores between groups, but the study group had statistically significant lower day 10 and 20 scores. Table 1 and Figure 1 summarize the results in all patients (study group and controls).

DISCUSSION

These data suggest that multisession tDCS can enhance the efficacy of SMR in task-specific focal hand dystonia neurorehabilitation. It is unclear whether this enhancement is due to speeding up of the benefit or actually increasing efficacy. tDCS may prime central somatosensory pathways, promote their plasticity, and facilitate surrounding inhibition in the hyperactive areas rendering them more responsive to SMR.[5] tDCs may also act by means of a rise in consolidation mechanisms.[18] Future neurophysiologic or neuroimaging studies may help clarify this further and offer mechanistic insights.

Two of our patients had only 10 days of combined tDCS+SMR intervention followed by 10 days of SMR alone. The efficacy in these two cases was similar to that of

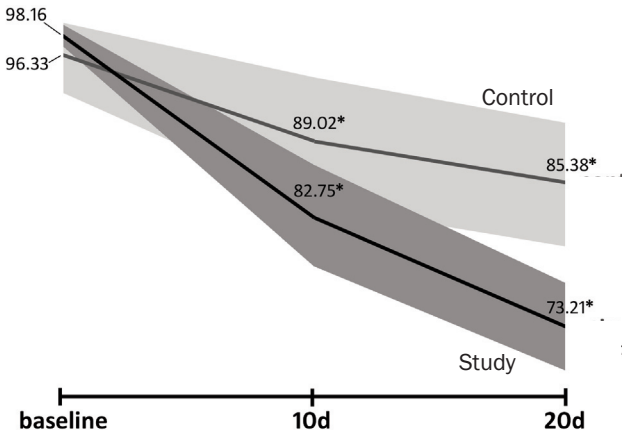

FIGURE 1. Mean scores ± SD for control (*light gray*) and study groups (*dark gray*). Asterisks identify statistically different means.

the 20-day course of combined intervention. Future studies with larger sample sizes need to address the optimal treatment regimen, timing of the tDCS combination, and other related factors.

We relied on subjectively reports by the patients and qualitative evaluations by clinicians. Future studies will require more objective outcome measures, as well as a parallel group and sham-controlled interventions (e.g., sham tDCS combined with SMR).

Nonetheless, we believe that these pilot findings are interesting and warrant reporting, as they do establish the feasibility of the approach and the results encourage a well-powered, properly controlled clinical trial.

REFERENCES

1. Pujol J, Roset-Llobet J, Rosinés-Cubells D, et al. Brain cortical activation during guitar-induced hand dystonia studied by functional MRI. Neuroimage 2000;12:257–267.
2. Hallett M. Pathophysiology of dystonia. J Neural Transm Suppl 2006;70:485–488.
3. Candia V, Schäfer T, Taub E, et al. Sensory motor retuning: a behavioral treatment for focal hand dystonia of pianists and guitarists. Arch Phys Med Rehabil 2002;83:1342–1348.
4. Rosset-Llobet J, Fàbregas-Molas S. What should be done when there are symptoms of dystonia. In: Rosset-Llobet J, Fàbregas-Molas S, eds. *Musician's Dystonia: A Practical Manual to Understand and Take Care of the Disorder that Affect the Ability to Play Music*. Rome: Panamir; 2010: pp193–228.
5. Nitsche MA, Paulus W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. J Physiol 2000;527:633–639.
6. Antal A, Terney D, Poreisz C, et al. Towards unravelling task-related modulations of neuroplastic changes induced in the human motor cortex. Eur J Neurosci 2007;26:2687–2691.
7. Matsuo A, Maeoka H, Hiyamizu M, et al. Enhancement of precise hand movement by transcranial direct current stimulation. Neuroreport 2011;22:78–82.
8. Boggio PS, Nunes A, Rigonatti, SP, et al. Repeated sessions of noninvasive brain DC stimulation is associated with motor function improvement in stroke patients. Restor Neurol Neurosci 2007;25:123–129.
9. Edwards DJ, Krebs HI, Rykman A, et al. Raised corticomotor excitability of M1 forearm area following anodal tDCS is sustained during robotic wrist therapy in chronic stroke. Restor Neurol Neurosci 2009;27:199–207.
10. Plow EB, Obretenova SN, Fregni F, et al. Comparison of visual field training for hemianopia with active versus sham transcranial direct cortical stimulation. Neurorehabil Neural Repair 2012;26:616–626.
11. Soler MD, Kumru H, Pelayo R, et al. Effectiveness of transcranial direct current stimulation and visual illusion on neuropathic pain in spinal cord injury. Brain 2013;133:2565–2577.
12. Buttkus F, Weidenmüller M, Schneider S, et al. Failure of cathodal direct current stimulation to improve fine motor control in musician's dystonia. Mov Disord 2010;25:389–394.
13. Buttkus F, Baur V, Jabusch HC, et al. Single-session tDCS-supported retraining does not improve fine motor control in musician's dystonia. Restor Neurol Neurosci 2011;29:85–90.
14. Buttkus F, Baur V, Jabusch HC, et al. Retraining and transcranial direct current stimulation in musician's dystonia–a case report. Mov Disord 2010;25:1758–1760.
15. Benninger DH, Lomarev M, Lopez G, et al. Transcranial direct current stimulation for the treatment of focal hand dystonia. Mov Disord 2011;26:1698–702.
16. Nitsche MA, Cohen LG, Wassermann EM, et al. Transcranial direct current stimulation: state of the art 2008. Brain Stimul 2008;1:206–223.
17. Rosset-Llobet J, Fàbregas-Molas S. Diagnostic du doigt dystonique et du doigt compensatory. In: Rosset-Llobet J, Fàbregas-Molas S, eds. *La Dystonie du Musician*. Montauvan: Alexitère editions; 2013: pp63–83.
18. Reis J, Schambra HM, Cohen LG, et al. Noninvasive cortical stimulation enhances motor skill acquisition over multiple days through an effect on consolidation. Proc Natl Acad Sci USA 2009;106:1590–1595.