Transcranial Direct Current Stimulation Potentiates Improvements in Functional Ability in Patients With Chronic Stroke Receiving Constraint-Induced Movement Therapy

Krystian Figlewski, MD, PhD; Jakob Udby Blicher, MD, PhD; Jesper Mortensen, MSc; Kåre Eg Severinsen, MD, PhD; Jørgen Feldbæk Nielsen, MD, DMsc; Henning Andersen, MD, PhD, DMsc

**Background and Purpose**—Transcranial direct current stimulation may enhance effect of rehabilitation in patients with chronic stroke. The objective was to evaluate the efficacy of anodal transcranial direct current stimulation combined with constraint-induced movement therapy of the paretic upper limb.

**Methods**—A total of 44 patients with stroke were randomly allocated to receive 2 weeks of constraint-induced movement therapy with either anodal or sham transcranial direct current stimulation. The primary outcome measure, Wolf Motor Function Test, was assessed at baseline and after the intervention by blinded investigators.

**Results**—Both groups improved significantly on all Wolf Motor Function Test scores. Group comparison showed improvement on Wolf Motor Function Test in the anodal group compared with the sham group.

**Conclusions**—Anodal transcranial direct current stimulation combined with constraint-induced movement therapy resulted in improvement of functional ability of the paretic upper limb compared with constraint-induced movement therapy alone.

**Clinical Trial Registration**—URL: http://www.clinicaltrials.gov. Unique identifier: NCT01983319.

Key Words: anodal stimulation tDCS rehabilitation stroke transcranial direct current stimulation upper extremity
tDCS was applied at the beginning of each training day simultaneously with CIMT. Stimulation was delivered through 2 rubber electrodes (7×5 cm) placed in saline-soaked sponges. The anode was placed over the ipsilesional primary motor cortex (M1), using C3 or C4 position of the International 10 to 20 EEG System. The cathode was placed over the contralateral supraorbital region. Anodal tDCS was given for 30 minutes; current was ramped up from 0 to 1.5 mA during the initial 30-second period and remained constant thereafter. In the sham mode, current was ramped up to 1.5 mA in the initial 30-second period and immediately thereafter ramped down to 0. However, to ensure blinding in the sham mode, the tDCS device continued to display the time and impedance as with anodal stimulation.

**Outcome Measures**

Wolf motor function test (WMFT) consists of 15 function-based tasks and 2 strength tasks. The primary outcome measure was the Functional Ability Scale (WMFT-FAS; range, 0–75), which assess each of the 15 tasks on a 6-point scale, ranging from 0 (does not attempt with the involved arm) to 5 (normal movement). Secondary measures were performance time (WMFT TIME), grip strength (average of 3 trials) assessed with a Precision Dynamometer (Biometrics Ltd, Newport, UK), and arm strength assessed by lifting cuff weights strapped around forearm from a table onto a box on a table top. Baseline assessments were performed 4 to 5 days before CIMT, and postintervention assessments were performed immediately after the training. Blinded investigators recorded WMFT-TIME during the test and later on the same day assessed WMFT-FAS using a video recording of the test.

**Statistical Analyses**

The power calculation was based on WMFT scores from previous patients who had completed CIMT at our rehabilitation center. Assuming that anodal tDCS combined with CIMT would result in a 3-point improvement in WMFT-FAS change compared with sham combined with CIMT, 18 participants in both groups would be needed (power=80%, 2-sided significance level α=0.05). To account for nonadherence, we included 22 in both groups. The statistical software package STATA v13/IC was used for all analyses. WMFT-TIME was log transformed as previously suggested. For within- and between-group comparisons, t tests were used. Furthermore, the effect of tDCS on improvement in WMFT-FAS was analyzed using linear regression model with baseline WMFT-FAS, age, sex, and dominant hand as covariates.

**Results**

Table 1 presents demographic and clinical characteristics. Of the 22 patients in the anodal group, 19 completed all sessions with CIMT and tDCS. One patient missed 2 days of CIMT because of a flu, 1 patient missed ≥6 hours of CIMT because of excessive fatigue, and 1 did not receive tDCS for 2 consecutive days because of technical issues. In the sham group, 21 patients completed all sessions with CIMT and sham tDCS.
patients completed all days of CIMT and sham tDCS. One did not receive tDCS for 2 days because of technical issues. All patients completed postintervention assessment.

Both groups improved significantly on all outcome measures after training (Table 2). Unadjusted between-group comparison showed that the anodal tDCS group gained 2.9 (95% confidence interval, 0.25–5.57; \(P=0.03\)) points more on WMFT-FAS when compared with the sham group. After adjustment for WMFT-FAS baseline scores, age, sex, and dominant hand, the between-group difference was still significant (coefficient of \(\beta=2.8; 95\%\) confidence interval, 0.05–5.5; \(P=0.046\)). Coefficients for the other variables in the model were not significant: WMFT-FAS baseline score (\(\beta=0.09; P=0.2\)), age (\(\beta=0.1; P=0.15\)), sex (\(\beta=−0.72; P=0.6\)), and dominant hand (\(\beta=1.4; P=0.3\)).

No significant differences were found for the secondary outcome measures. tDCS was well tolerated with only minor adverse events including tingling (16 anodal/13 sham), headache (4 anodal/3 sham), light flashes (1 anodal/1 sham), and a transient mild burning sensation under the electrodes (5 anodal/7 sham).

### Discussion

The main finding of the study was that anodal tDCS enhanced the effect of CIMT and lead to clinical important improvement in the quality of the paretic upper limb movements (WMFT FAS) compared with CIMT with sham tDCS.

Previous studies incorporating tDCS in various rehabilitation regimes have reported promising results. However, results of trials exploring the combination of tDCS with CIMT are equivocal. In a study of 14 patients with chronic stroke receiving 2 weeks of CIMT with either active or sham tDCS, active tDCS improved motor function. However, 5 patients from this study did not complete postintervention assessments, and interpretation of the results should be made with caution. In another randomized trial, 5 days of CIMT and bilateral tDCS in patients with acute stroke did not lead to any additional significant improvements.

Our study provides evidence, showing that anodal tDCS leads to additional clinical benefit of CIMT, as measured with the quality of upper limb movement. This benefit is remarkable, as it was achieved by adding only 30 minutes of noninvasive brain stimulation to 6-hour CIMT regime, which is as stand-alone intervention one of the most effective evidence-based treatments in stroke rehabilitation. However, the present study is limited by a lack of long-term follow-up. Thus, it remains unknown whether the functional gains induced by combined tDCS-CIMT regime are long-lasting.

### Conclusions

This study demonstrates that anodal tDCS of the affected primary motor cortex given for 30 minutes daily as add-on therapy to CIMT improves functional ability of the paretic upper limb in patients with chronic stroke compared with CIMT alone. Further research is warranted to identify patients with the greatest potential for an effect of tDCS and to evaluate the long-term benefits.

### Sources of Funding

This study was funded by the Bevica Foundation and supported by a scholarship from the Health Research Fund of Central Denmark Region.

### Disclosures

None.

### References


Transcranial Direct Current Stimulation Potentiates Improvements in Functional Ability in Patients With Chronic Stroke Receiving Constraint-Induced Movement Therapy

Krystian Figlewski, Jakob Udby Blicher, Jesper Mortensen, Kåre Eg Severinsen, Jørgen Feldbæk Nielsen and Henning Andersen

*Stroke*. 2017;48:229-232; originally published online November 29, 2016; doi: 10.1161/STROKEAHA.116.014988

*Stroke* is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2016 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/48/1/229

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in *Stroke* can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to *Stroke* is online at:
http://stroke.ahajournals.org/subscriptions/