

Transient effects of a single transcranial direct current stimulation (tDCS) on gait performance in chronic hemiplegic patients.

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Abstract—

Transcortical direct current stimulation (tDCS) can be efficient to improve motor recovery in hemiplegic patients after stroke. Proofs of concepts are still needed regarding its potential use for gait recovery. This study evaluated the effect of a single session of stimulation of the primary motor cortex (M1) with tDCS versus placebo (SHAM) on the walking performance of hemiplegic patients at a chronic stage. It was a randomized, cross over and double-blind study. 18 chronic stroke patients (6 females, 12 men, average age 57 years) were included, with an initially complete hemiplegia. The post-stroke delay varied from 12 months to 11 years. Subjects participated to two randomly ordered sessions of stimulation: a session of anodal stimulation (2 mA, 20 min) of the lower limb ipsilesional M1 (STIM condition) and a SHAM session (20 min; SHAM condition). The primary endpoint was the six minute walking test (6MWT) and the secondary end point was the Wade test. These tests were performed 2 days before, during, after one hour, and 10 days after each session. Comparisons were based on the linearly corrected data of each patient. The comparison between the 6MWT under STIM versus SHAM conditions demonstrated a tendency for positive effect during the stimulation and significant difference (37.9 versus 13.2%) 1 hour after stimulation (Wilcoxon matched pairs, $p = 0.02$). There is no significant difference regarding the Wade test despite the increase 1 hour after stimulation. These results support a positive effect of a single session of anodal tDCS of the M1 ipsilesional area of the lower limb in chronic hemiplegic patients. This improvement is significant regarding the 6MWT.

Key words: tDCS, hemiplegia, stroke, walking.

INTRODUCTION

Those who survived stroke have persistent deficiencies(1). These damage or reduced performance represents a challenge for our world today. Indeed, it is important to help stroke survivors to have greater autonomy, ensuring good social participation. The discovery of new management methods has identified new avenues of research. In this sense, cortical stimulation remains an important tool for post-stroke management which provides meaningful results. This is an emerging therapeutic for the treatment of motor impairment after stroke(2). Two noninvasive cortical stimulation techniques are currently used: repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (tDCS). The latter, thanks to its advantages (low cost, few side effects) is of great interest for clinical research activities(3). tDCS modulates neuronal activity, modifying cortical excitability with effects beyond 30 minutes after the end of the stimulation(2). It has been shown that the anodal tDCS has an excitatory effect, while that is cathodal inhibitor; this resulting in an increase/decrease of the motor evoked potential (4). Several studies have used the anodal tDCS to improve functional recovery of upper limb after stroke (5,6). On the lower limb, some authors have demonstrated the ability to stimulate primary motor cortex(7) and an increase in the gripping force of the big toe of lower limb due to the use of anodal tDCS in post-stroke. However few studies have investigated the tDCS effects on functional recovery of the paretic lower limb. This study evaluated the effects of a single session of tDCS versus SHAM stimulation (placebo) on gait quantitative parameters (speed, endurance) for chronic hemiplegic patients (over 6 months).

METHODS

Study design

This pilot, randomized, cross-over, double-blind study was held in the Department of Adult Physical Medicine and Rehabilitation (MPR Adult) at Bellevue University Hospital and in the Interuniversity Laboratory of Biology of Motricity (LIBM) of Jean Monnet University in Saint Etienne (France). The protocol lasted 22 days after inclusion. It consisted in a velocity test (walking test, timed 5m with return) and an endurance test (6 minutes walking test (6MWT)). Both tests were carried out in the same order for all participants and performed during the five sessions allocated as following:

- **3 baseline evaluation sessions:** the subject performed the tests without stimulation. It took place at the inclusion session (V_0), 10 days (V_2) and 22 days later (V_4).

- **2 stimulation sessions** (2 and 11 days after the inclusion): during these sessions, the participants, under stimulation (STIM or SHAM randomized condition) performed the same tests. The patients were evaluated during the stimulation (V_1 and V_3) and one hour after (V_{1+1h} et V_{3+1h}). The measurements consisted in the walking speed for 10 m and the distance traveled in 6 minutes.

Patients

18 stroke patients (who had a first ischemic stroke more than 6 months ago and no recurrence since then) took part in this study (Table I). A medical run-in has eliminated all patients having a metallic foreign body in the brain (surgical clips), or active medical devices in the body (pacemakers, defibrillators, neurological stimulators, implantable pump), being pregnant or having an uncontrolled epileptic disease. They showed no incapacitating comorbidities (renal failure, severe respiratory or cardiac progressive neoplastic disease,

neurological disease other than stroke). In addition to these criteria, they were able to walk on their own with or without technical assistance over at least 10 meters and to turn round while walking. They were affiliated to the social security system.

All participants gave their informed consent, 7 days after the run-in at the medical inclusion. This study has received permission from the Patient Protection Committee (CPP) of the University Hospital of Saint Etienne.

tDCS

Before the stimulation participant's hotspot was determined during the inclusion visit by TMS. The hotspot corresponds to the largest motor evoked potential (MEP) obtained for a stimulation of the primary motor cortex (M1). A monophasic device, Magstim 200 (*Magstim Company Limited, Whitland, UK*) and a conical coil were used. A variation of 30 to 60% of the stimulation intensity was performed in order to better target the motor point area. The best position of the coil corresponds to the cortical area which induces the most important MEP measured with EMG (EMG 8 canals, Medtronic, France) on the paretic quadriceps. Once the hotspot was found, its distance to nasion was measured, along the interhemispheric line.

The sessions of tDCS were achieved thanks to a type of medical device Eldith DC- Stimulator Over Neurconn Company (IImenau, Germany). Two (5 cm x 5 cm) sponge electrodes conducted current to stimulate the participant from the hotspot. The active electrode (anode) was placed on the scalp (hotspot) while the cathode was placed contralesional above the orbit. The apparatus has issued a 2mA current corresponding to a density of 0,08mA / cm² for anodale stimulation (STIM condition). As for the SHAM session (SHAM stimulation), it reproduces during the first and the last 30 seconds of the stimulation, tingling feelings due to current flow experienced during tDCS. In this way there is no possibility for the patient to recognize the difference between the real and the placebo stimulation (8). The order of stimulations (STIM or SHAM) was randomized with MATLAB Mathworks *Natick* software, USA. It was used to generate independently of the subjects and the experimenter, the codes of stimulation which insure the double blind condition. Thus, neither the patient nor the evaluator can distinguish the character and the order of the session of stimulation. The evaluator who generated the order of stimulations did not participate in the evaluation sessions. Each stimulation session lasted 20 minutes.

Statistical analysis

The MATLAB *Mathworks Natick* software, USA was used for statistical processing. The patient's performances were calibrated against the patient's maximum progression. As it is a cross-over study, the regular progression trend was subtracted to the data. Then stimulation effect was computed as the difference between the performance during or 1h after the stimulation session and the performance at the baseline session. The significance level was $p \leq 0.05$.

RESULTS

Independently of the conditions of stimulation a learning effect was observed, leading to a linear progression of participants on walking speed 20% versus and endurance in 6 minutes 21% (Figure 1).

The progression for the 6MWT between STIM and SHAM showed a non-significant increase during stimulation ($p < 0.05$) and a significant positive increase effect (37.9 versus 13.2%; $p = 0.02$) of anodal tDCS stimulation 1 hour after stimulation (Figure 2). However, the same comparison during the Wade test between STIM and SHAM were not significant ($p > 0.05$) despite the increase 1 hour after stimulation (Figure 3).

DISCUSSION

Comparing gait quantitative parameters (speed, endurance) for chronic stroke patients (over 6 months) with tDCS stimulation to that of SHAM stimulation (placebo), this study shows a significant positive effect of a single session of tDCS anodal stimulation of the area M1 ipsilesional lower limb. Endurance was improved (6MWT) but not the speed (Wade test). To date, the physiological effect of tDCS is not completely elucidated. Nevertheless, tDCS can increase balance, strength and motor control of the lower limb and can explain the positive effect of anodal stimulation on gait performance(9,10).

The modulation of cortical excitability is one of the mechanisms which could explain this progression by changing potential membrane cell polarization and enhances recruitment of neuronal population. This depolarization of the neuronal membrane with anodal stimulation is mediated with the activation of sodium or calcium depending channels or the growing expression of NMDA receptors. Then, an increasing excitability of the affected corticospinal tract is also observed and could explain the better activity in the innervated lower limb muscles(11)

These results correlate with previous study which evaluate the positive effect of the tDCS on the primary motor cortex of the lower limb(9,10). It would therefore be possible to achieve therapeutic walking training protocol under iterative tDCS stimulation for hemiplegic patients.

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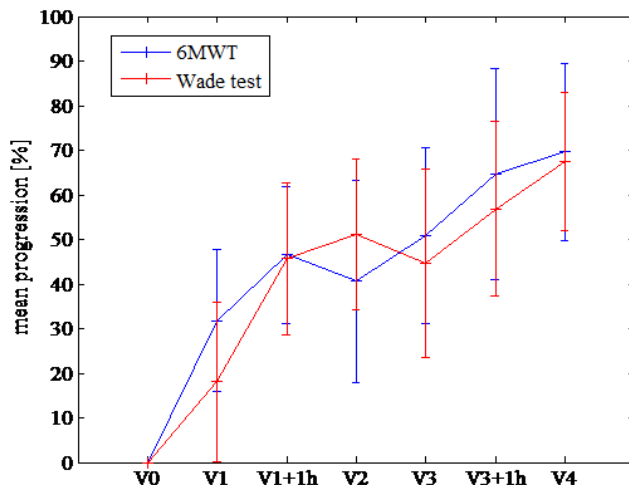


Figure 1: progression of participants during sessions

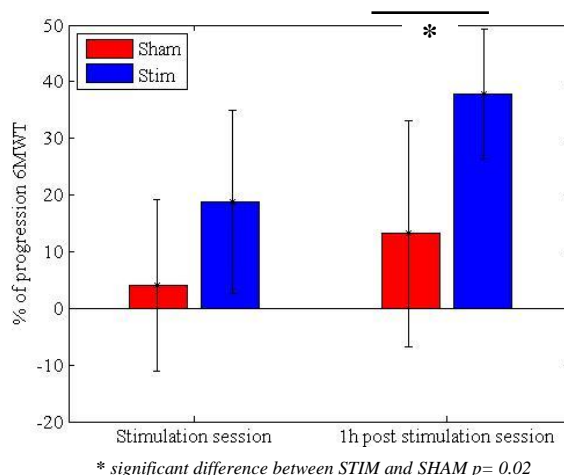


Figure 2: comparison of the progression for the 6MWT between STIM and SHAM

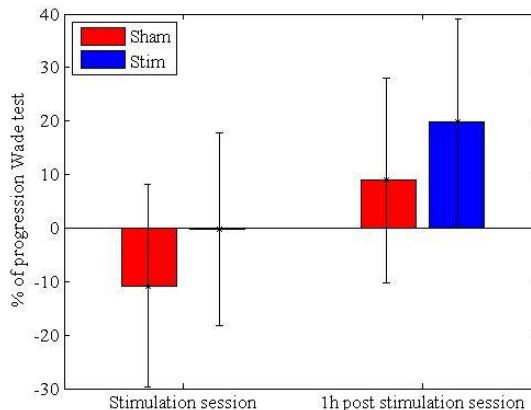


Figure 3: comparison of the progression for the Wade test between STIM and SHAM

Table I: Population

	Participants	Range
Age(years)*	57.1 ± 7.7	45-74
Time since stroke (months)*	43.4 ± 35.4	12-123
Gender (M/F)	12/6	NA
Nature of stroke (ischemic/hemorrhagic)	14/4	NA
Hemiparesis side (right/left)	8/10	NA

* Mean ± SD (Standard deviation)

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