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LETTER TO THE EDITOR

Could dual-hemisphere transcranial direct current stimulation (tDCS) reduce spasticity after stroke?

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After providing informed consent, a 61-year-old chronic stroke female patient participated in a double-blind, randomised, placebo-controlled trial to test the potential of transcranial direct current stimulation (tDCS) to improve motor skill learning with the paretic hand. Two years before, she suffered from an ischaemic stroke in the territory of the deep right middle cerebral artery (Fig. 1), leading to left-sided hemiplegia (NIH Stroke Scale: 9). After discharge (modified Rankin Score: 4), she benefited from long-term neurorehabilitation. She recovered walking and partial control of the proximal left upper limb but she had no voluntary finger movements (mRS=3). She developed a severe left-sided spasticity, requiring the daily intake of baclofen 75 mg and tizanidine 4 mg. She was chronically on venlafaxin 75 mg, lorazepam 0.5 mg, aspirin, atorvastatin and ranitidine. The treatment was not modified during the whole experiment.

She participated in two experimental sessions separated by 2 weeks, each composed of two distinct parts. During the first part (Intervention session), she performed training on the circuit with dual-tDCS application (real or sham). Two versions (similar difficulty) of the circuit were used for the two Intervention sessions. During the second part (Recall session), which took place 1 week apart, the patient performed the same circuit as during the previous "Intervention session" to test the retention of the motor skill. The Recall session consisted of two evaluations (5 min apart) of the motor skill (duration: 5 min, alternating 30-s blocks of testing and rest).

She sat in front of a computer screen; the computer mouse was taped in her left hand. A circuit was displayed on the screen, she was instructed to move the cursor as fast as possible over the circuit, and as precisely as possible by keeping the cursor within the boundaries of the track [1].

During the Intervention session, training was provided during 30 min, alternating blocks of 30 s of practice and rest. Performance was evaluated before (Baseline), during, and up to 60 min after, and 1 week later (Recall). Velocity and accuracy were extracted to compute a performance index (PI) involving a speed/accuracy trade-off. The evolution of the PI from Baseline was expressed as a learning index (LI): $\mathrm{LI} = [(\mathrm{PI} - \mathrm{PI\ baseline})/\mathrm{PI\ baseline}] \times 100$. An increment of LI reflects a performance improvement relative to "Baseline" [1]. LI was computed on each circuit block.

Before training, she received a short familiarisation with a simple square circuit. During training, dual-tDCS was applied over both primary motor cortices (M1), with anodal stimulation over the ipsilesional M1 and cathodal stimulation over the contralesional M1. The M1 were located using the C3 and C4 positions of the 10-20 EEG system. Real (30 min) and sham (45 s) dual-tDCS were applied with an Eldith DC-Stimulator® (NeuroConn, Ilmenau, Germany) in a randomised, double-blind fashion. Dual-tDCS was delivered via two soaked (NaCl 0.9 %) electrodes (35 cm^2) at an intensity of 1 mA (fade in/out 8 s).

During the first experimental session, she was allocated to receive real dual-tDCS; motor performance and long-term retention of the motor skill markedly improved

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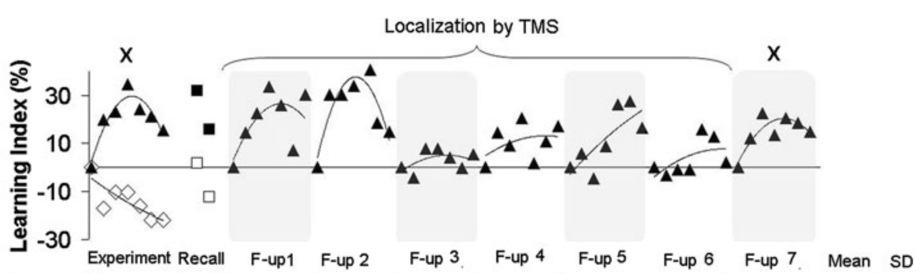
Fig. 1 The CT-scanner of the stroke patient demonstrated an ischaemic stroke in the deep territory of the right middle cerebral artery (MCA)

(Fig. 2). Spontaneously, she reported a noticeable reduction of spasticity in both the left upper and lower limbs, with a pleasant feeling of suppleness. Although there was no formal assessment of spasticity, several observations substantiated her report. First, after real dual-tDCS, she was able to easily open passively her left hand with the right hand, which was usually very difficult. Second, whereas she had a left spontaneous plantar extensor, her great toe spontaneously moved back to flexor. Third, her 5-year-old grand-daughter was used to play with her left spastic hand; she also reported an improved suppleness. Fourth, her physiotherapist reported a subjective reduction of spasticity. The spasticity reduction lasted approximately 1 week before fading progressively.

During the second experimental session, sham dual-tDCS was applied and her performance worsened dramatically during training, and there was no retention. This time, she reported a lack of the spasticity reduction she dearly expected.

Afterwards, she received seven follow-up sessions, every month, exclusively with real dual-tDCS while training with alternative versions of the circuit; no Recall was recorded. The M1 were located with transcranial magnetic stimulation (TMS), using a focal coil to evoke movements in the contralateral hand. The intensity of TMS was increased until a movement could be evoked in the hand, and could be repeated (typically 60–70 % of maximal stimulator output for the paretic hand, 50 % for the non-paretic hand). No target muscle was determined a priori since the size of the tDCS electrode would anyway preclude "focal" tDCS. We observed a 5 cm difference with the C3–C4 location for the ipsilesional hemisphere, in the direction of the premotor cortex. At every session, performance was enhanced and she reported the same lasting feeling of spasticity reduction as after the first session (Fig. 2). However, this improvement was limited to the left arm, with the noticeable exception of follow-up session 7. That time, TMS was unable to elicit movement in the paretic hand and the C3–C4 locations were used again for placing the tDCS electrodes. Remarkably, spasticity reduced in both the upper and lower limbs, as after



		Experiment	Recall	F-up1	F-up 2	F-up 3	F-up 4	F-up 5	F-up 6	F-up 7	Mean	SD
Real	LI max %	34	32	34	42	8	21	28	16	22	26	11
	LI end %	15	16	30	15	5	17	16	2	15	14	8
Sham	LI max %	-11	2									
	LI end %	-22	-13									

X Localization by EEG-system C3-C4

Fig. 2 Effect of tDCS on motor skill learning. Learning Index (LI) in % of improvement compared to baseline of each session, with the maximal improvement (LI max %) and the performance at the end of the session (LI end %). Note the improvement of motor performance during each session under real dual-tDCS (*black triangles*), with a worsening by the end of the session, and a retention of the motor skill 1 week later (*black squares*, Recall). During sham dual-tDCS (*white triangles*), performance worsened continuously, likely due to a fatigue effect, and there was no retention after 1 week (*white squares*, Recall). Experiment and Recall: dual-tDCS sessions performed in a double-blind fashion, with real dual-tDCS (*black*) and sham (*white*). *F-up* follow-up session 1–7. For each session, the *first triangles* reflect the baseline LI, each of the 6 next points referred to the mean of five consecutive LI across the 30 min of training.

the first session. In addition, in a recent follow-up session, the spasticity of the paretic upper limb was assessed before and after the dual-tDCS with the modified Arshworth Scale [2] (MAS) and the Tardieu scale [3] (TS). The MAS and the TS were reduced after dual-tDCS in both wrist flexor (MAS from 3 to 2; TS from 3 to 2) and finger flexors (MAS from 3 to 2; TS from 3 to 2+).

Thus, dual-tDCS improved on-line performance with the paretic hand, which translated into improved retention after 1 week, i.e. enhanced motor skill learning. Moreover, there was a dramatic, lasting and repeated reduction of spasticity. It is worth noting that, during the two sessions with dual-tDCS over C3–C4, spasticity reduction extended to the leg, whereas it was restricted to the arm when the more precise M1 localisation with focal TMS was used. This suggests that with the less precise C3–C4 localisation, the direct current modulated the cortical activity of areas neighbouring the M1 (e.g. premotor areas) and led to a more widespread improvement.

We felt worth reporting this unique observation as a hint to test the potential of dual-tDCS to reduce spasticity in patients with brain injuries. Whether dual-tDCS alone would lead to a similar result was not tested. However, we suggest that the combination of dual-tDCS with active training is a key factor for improving motor performance, motor skill learning and reducing spasticity as well in chronic stroke patients.

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