

ONLINE SUPPLEMENT

Modulation of Training by Single Session tDCS to the Intact Motor Cortex Enhances Motor Skill Acquisition of the Paretic Hand

Máximo Zimmerman¹, MD; Kirstin F. Heise¹, MSc; Julia Hoppe¹, MD; Leonardo G. Cohen², MD;
Christian Gerloff¹, MD; Friedhelm C. Hummel¹, MD

¹ Brain Imaging and Neurostimulation (BINS) Labor, Department of Neurology University Medical Center Hamburg-Eppendorf, Hamburg, Germany

² Human Cortical Physiology and Stroke Neurorehabilitation Section, National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, USA.

Supplementary Methods

Motor skill acquisition task

The task consists of sequential pressing of a part five sequence on a four-button electronic keyboard performed with the paretic hand.¹ The fingers were numbered as follows: little finger=5; ring finger=4; middle finger=3 and index finger=2. Each block started with 5-second countdown displayed on the screen followed by a 'GO' signal, while the paretic hand was in the resting position (fingers over the keyboard), a 'STOP' signal appeared after 3 minutes followed by a 2-minute 'PAUSE' before the next countdown started. Subjects were instructed to perform the sequences as precisely and as quickly as possible according to the written instruction "Play as many accurate sequences as possible for a trial period of 3 min."² During the 2 minutes break they were instructed to place the hand outside of the keyboard. No feedback was given by the investigators during the task. The primary outcome measure was the number of correct sequences achieved per block. Additionally, the total numbers of performed sequences in each block were analysed. The rationale behind the present design consisted of an assessment of temporal components of motor skill acquisition (fast-online, slow on-line and off-line periods) for both interventions (tDCS or Sham).

Motor cortical excitability determined by TMS

TMS was delivered from two Magstim 200 magnetic stimulator connected via a Bistim module (Magstim Co., Whitland, UK) through a figure-of-eight shaped 70-mm coil. The coil was placed over the representation area of a hand muscle (first dorsal interosseus [FDI] muscle) of the paretic and the intact hand, with the handle in antero-posterior orientation, 45° angle to the interhemispheric line. Optimal scalp position to elicit consistently the largest MEPs in the FDI muscles of both hands was obtained with slight suprathreshold stimulator intensity (hot-spot) and marked with a skin-friendly pen. Resting motor threshold (RMT) was defined as the intensity of stimulator output to produce MEP amplitudes of at least 50 µV in 5 out of 10 consecutive trials in the relaxed FDI³. SICI was measured by subthreshold conditioning stimulus followed by a suprathreshold test stimulus with an interstimulus interval of 3 ms⁴. Conditioning stimulus was set at 80% of RMT⁵ and the test stimulus was adjusted to elicit unconditioned MEP amplitudes of ~1mV peak-to-peak. Each TMS block consisted of 15 single stimuli and 15 paired-pulse stimuli in each M1 (healthy and affected) applied in a pseudo-randomized order; the interval between stimulation was between 6 and 8 seconds (randomized). RMT were measured separately for each hemisphere after tDCS, as they did not change compared to the first values, it was not necessary to adjust the intensity of the stimulus.

EMG activity was recorded using disposable Ag/AgCl surface electrodes placed over the first dorsal interosseus muscle in a belly-tendon montage. EMG signals were amplified (*CED 1902 amplifier*, sampling rate 5 kHz) then bandpass filtered (50 Hz to 1 kHz), digitized and stored offsite. Data acquisition and processing was performed using Signal software 4.05 (*Cambridge Electronic Design, Cambridge, UK*).

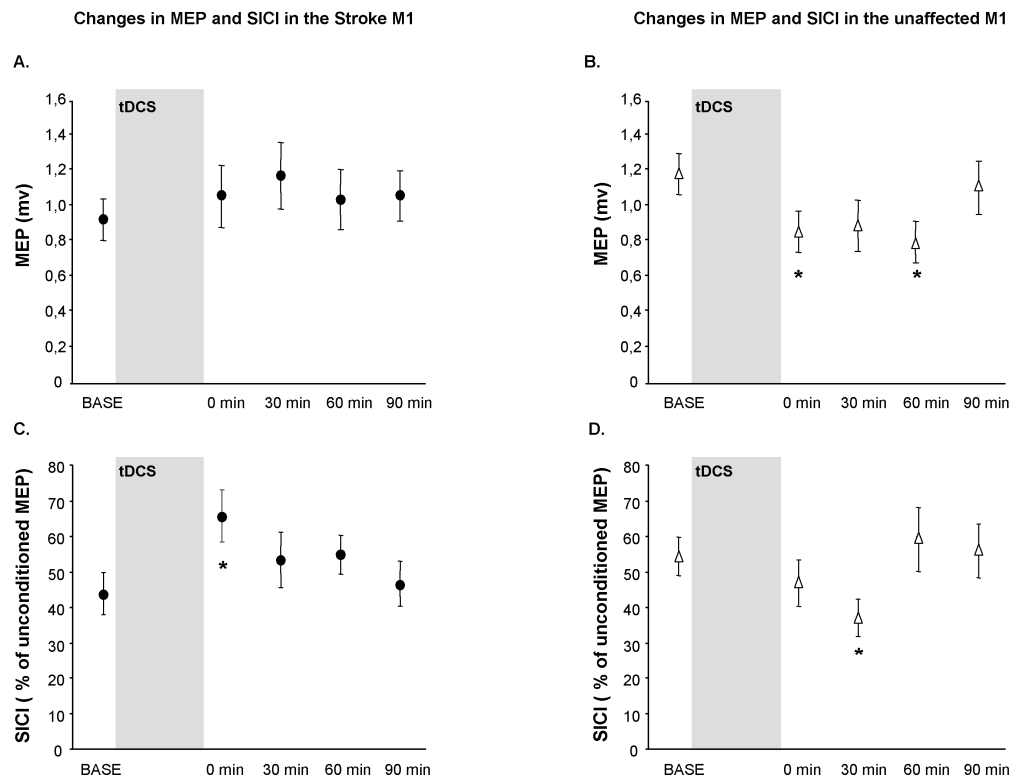
Supplementary table: Attention and fatigue measurements

	Sham						tDCS						Statistics	
	Q1	Q2	Q3	Q4	Q5	Q6	Q1	Q2	Q3	Q4	Q5	Q6	ANOVA	RM
Attention (1-10)	8.3±0.6	7.9±0.6	8.1±0.5	7.6±0.5	8.5±0.4	8.2±0.8	8.6±0.4	7.8±0.5	8.4±0.4	7.9±0.8	8.5±0.4	8.0±0.6		ns
Fatigue (1-10)	3.1±0.8	3.2±0.7	3.3±0.8	3.5±0.8	2.7±0.5	2.9±0.4	3.5±0.6	3.8±0.7	2.8±0.7	3.6±0.7	2.9±0.7	3.4±0.8		ns
Hand fatigue (1-10)	0.3±0.2	2.1±0.8	1.8±0.4	2.3±0.9	1.7±0.5	3.5±0.8	0.5±0.3	1.7±0.8	1.3±0.2	2.4±0.8	0.9±0.6	3.7±0.8		ns

Attention and fatigue were assessed with VAS-questionnaire (Q₁₋₆). Attention scale (0-10; 0= no attention, 10= highest level of attention). Fatigue scale (0-10; 0= no fatigue, 10= highest level of fatigue). Hand fatigue scale (0-10; 0= no hand fatigue, 10= highest level of hand fatigue). All values were expressed at mean ± SE. ns = not significant.

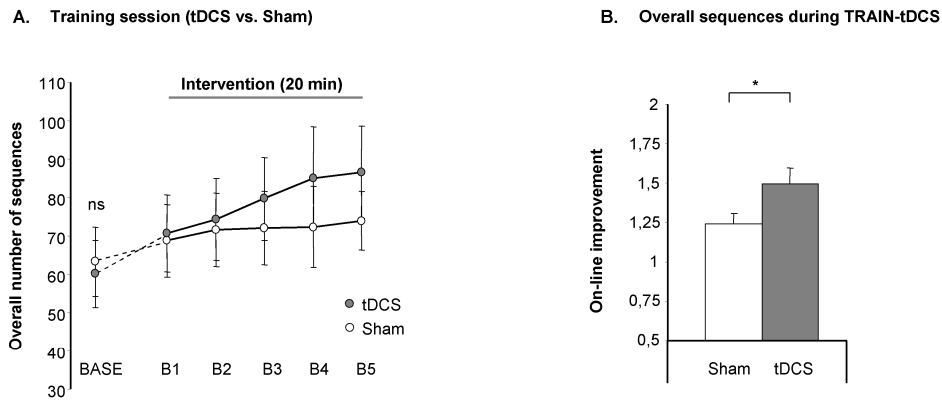
Supplementary Figures

S1



Motor cortex excitability changes. **A** and **B.** The values of MEPs (mV) were illustrated in this graphic for the stroke (black dots) and healthy (white triangle) hemisphere. **C** and **D.** these graphs represented the values of SICI in % of unconditioned MEP. An increase of SICI in the healthy motor cortex and a short-term decrease in the stroke hemisphere was observed after tDCS. Data were display as mean values, error bars=SEM; * Post-hoc significant values after correction).

S2



Overall sequences during TRAIN-tDCS. **A.** There were a significant difference in the overall sequences during the first training period. **B.** The on-line learning graphic bar shows a significant difference between tDCS and Sham stimulation

Supplementary References

1. Walker MP, Brakefield T, Hobson JA, Stickgold R. Dissociable stages of human memory consolidation and reconsolidation. *Nature*. 2003;425:616-620
2. Karni A, Meyer G, Rey-Hipolito C, Jezard P, Adams MM, Turner R, et al. The acquisition of skilled motor performance: Fast and slow experience-driven changes in primary motor cortex. *Proc Natl Acad Sci U S A*. 1998;95:861-868.
3. Rossini PM, Pauri F, Cicinelli P, Pasqualetti P, Traversa R, Tecchio F. Neuromagnetic recordings and magnetic brain stimulation in the evaluation of sensorimotor hand area interhemispheric differences: Normative, experimental and patients' data. *Electroencephalogr Clin Neurophysiol Suppl*. 1999;50:210-220
4. Kujirai T, Caramia MD, Rothwell JC, Day BL, Thompson PD, Ferbert A, et al. Corticocortical inhibition in human motor cortex. *J Physiol (Lond)*. 1993;471:501-519
5. Ziemann U, Rothwell JC, Ridding MC. Interaction between intracortical inhibition and facilitation in human motor cortex. *J Physiol (Lond)*. 1996;496:873-881