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1 A single session of bihemispheric transcranial direct current stimulation does

2 not improve quadriceps muscle spasticity in people with chronic stroke.

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29 Cerebral lesions following stroke cause an interhemispheric competition in the brain 30 where the excitability of the affected hemisphere decreases and that of the unaffected 31 hemisphere increases. This leads to a reduction of inhibitory control of spinal networks by the 32 corticospinal tract of the affected side which in turn lead to the phenomenon of spasticity [1]. 33 It has been found that i) bihemispheric-transcranial direct current stimulation (bi-tDCS) may 34 reduce the interhemispheric imbalance in chronic stroke people (CSP) [2], and ii) anodal-tDCS 35 applied over the affected leg motor cortex can alter the excitability of some spinal circuits 36 involved in spasticity [3]. Although two studies have evaluated the acute effects of tDCS on spasticity of the upper limb [4,5], the effects of a single session of bi-tDCS on spasticity of 37 38 lower limb remain to be clarified. Accordingly, we examined whether a single session of bi-39 tDCS could improve quadriceps spasticity in CSP.

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41 Thirteen CSP (57±12 years) were included in this study. Inclusion and exclusion criteria
42 as well as characteristics of the patients are shown in the Supplemental Material.

This study used a randomized, sham-controlled and double-blind crossover experimental method. Each participant attended two experimental sessions one week apart: i) effective bi-tDCS, and ii) sham bi-tDCS. At the beginning of each session, participants performed 3 maximal isometric voluntary contractions (MVC). Then, an instrumental assessment of quadriceps spasticity was performed before effective/sham bi-tDCS, 10 minutes after the beginning of the effective/sham bi-tDCS (During), and immediately after the end of the effective/sham bi-tDCS.

For both bi-tDCS protocols the anode (7x5 cm) was placed over the leg motor cortex of the affected side with the medial border of the electrode placed laterally to Cz of the international electroencephalogram 10–20 system [6] (Fig.1A). The cathode was placed in the same position over the leg motor cortex of the unaffected side. For the effective bi-tDCS,

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current (intensity: 2 mA) was delivered for 20 minutes using a constant-current electrical
stimulator (Eldith DC-Stimulator, Germany). For the sham bi-tDCS, the same current was only
delivered during the first 2 minutes (18 minutes without stimulation).

As recommended, spasticity was assessed using an "objective" instrumental evaluation [7,8]. Each set of instrumental evaluations of spasticity consisted of 5 fast passive quadriceps stretches at an acceleration of ~ 500° .s⁻² (maximum speed of 240°.s⁻²).

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Figure 1. A. Schematic view of electrode placement for effective and sham current bihemispheric-transcranial direct stimulation (bi-tDCS). The right brain hemisphere and the left leg represent the affected sides while the left brain hemisphere and the right leg represent the unaffected sides. **B.** Schematic view of electrode placement for rectus femoris (RF) and vastus lateralis (VL) EMG recordings. C. Mean and standard deviation of the normalized torque (i). normalized work (ii), and normalized EMG of RF (iii) and VL (iv) signals during fast passive quadriceps stretches before ('B', white histograms), during ('D', blue histograms), and after ('A', red histograms) effective bitDCS ('bi-tDCS') and sham bi-tDCS ('sham tDCS'). * indicates significant difference with baseline assessment (before effective or sham bi-tDCS measurements).

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An isokinetic dynamometer (Biodex, Shirley Corporation, USA) was used to generate quadriceps stretches and to measure quadriceps torque of the affected limb. Participants were seated in the dynamometer chair with an 85° hip angle and the lower legs hanging over the edge

of the seat. The knee angle was set at 90° for the MVCs. Passive pain-free range of motion was
determined for each participant at the beginning of the first session and was used to set the
limits of motion for both sessions. EMG activity of the rectus femoris (RF) and the vastus
lateralis (VL) of the affected limb was recorded during both MVCs and quadriceps stretches.
Bipolar surface electrodes linked to their amplifier (Bagnoli-4, Delsys Inc., USA) were placed
on the skin, according to the SENIAM recommendations [9] (Fig.1B).

107 For each quadriceps stretching test, maximum resistive peak torque (MRPT, Nm) 108 produced was recorded, and work (J) was calculated by summing the area under the torque 109 curve (torque multiplied by angular displacement in radians). Then, the MRPT was expressed 110 as a percentage of the MVC torque to obtain the relative MRPT (rMRPT, %). The work (J.Nm⁻ ¹) was normalized by the MVC torque to obtain the relative work (a.u.). For each quadriceps 111 112 stretching test and muscle a RMS for the entire EMG signal during the stretching phase was 113 calculated and normalized to the RMS value obtained over a 0.5-s window around the MVC peak torque (relative EMG, %). For each spasticity parameter (rMRPT, relative work, and RF 114 115 and VL relative EMG) and assessment (before, during and after effective/sham bi-tDCS), a 116 mean of the 5 quadriceps stretching tests was used in the analysis.

To verify the effect of bi-tDCS on spasticity parameters, separate ANOVAs with factors
of time (×3: before/during/after) and stimulation (×2: effective/sham bi-tDCS) were used. *Post- hoc* analyses were performed using the Tukey-HSD comparisons.

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121 Statistical analysis revealed no main effect of "stimulation" on any spasticity parameter 122 but a main effect of "time" for rMRPT ($F_{(2,24)}=4.7$; P<0.05; Fig.1Ci) and relative work 123 ($F_{(2,24)}=4.4$; P<0.05; Fig.1Cii). No significant "time" effect was found for the RF ($F_{(2,24)}=2.5$; 124 P=0.14; Fig.1Ciii) and VL ($F_{(2,24)}=1.2$; P=0.31, Fig.1Civ) relative EMG. The lack of interaction

125 between the factors "stimulation" and "time" (All P-value>0.35) showed that the time effects 126 were not attributed to the effective bi-tDCS.

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128 Discussion

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The results showed that a single session of bi-tDCS does not alter quadriceps spasticity 130 either during or immediately after application.

131 Other than one case study [4], only Bradnam et al. [5] investigated the effects of a single 132 session of tDCS on upper limb spasticity. They found a reduction in spasticity according to the 133 modified Ashworth scale. Although their tDCS protocol (cathodal-tDCS over the unaffected 134 hemisphere) differed from the present study, our stimulation set-up also included the 135 application of a cathodal current over the unaffected hemisphere, thus should have had similar 136 effects to that of Bradnam et al. [5]. The differences in results suggest that neural structures 137 involved in lower limb spasticity do not respond to tDCS in the same way as those involved in 138 upper limb spasticity. Further studies are required to determine whether i) a single session of 139 bi-tDCS can modulate spinal networks excitability in spastic CSP, and ii) the lack of acute 140 effect of bi-tDCS on the spasticity of CSP is specific to the quadriceps or consistent for other 141 leg muscles (e.g. triceps surae). In addition, in contrast with studies reporting spasticity 142 improvement in CSP following a tDCS session and using a subjective spasticity assessment 143 (manual testing) [4,5], we used an objective instrumental spasticity assessment, which is more 144 sensitive to the degree of spasticity and is not operator-dependent [7,8].

145 The results of this study do not support the use of a single session of bi-tDCS to improve 146 quadriceps spasticity in CSP.

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148 **Conflict/declaration of interest**

149 None

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