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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
37 spasticity of the upper limb [4,5], the effects of a single session of bi-tDCS on spasticity of
38 lower limb remain to be clarified. Accordingly, we examined whether a single session of bi-
39 tDCS could improve quadriceps spasticity in CSP.

40

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.

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

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

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

57 As recommended, spasticity was assessed using an “objective” instrumental evaluation
 58 [7,8]. Each set of instrumental evaluations of spasticity consisted of 5 fast passive quadriceps
 59 stretches at an acceleration of $\sim 500^{\circ} \cdot s^{-2}$ (maximum speed of $240^{\circ} \cdot s^{-2}$).

60

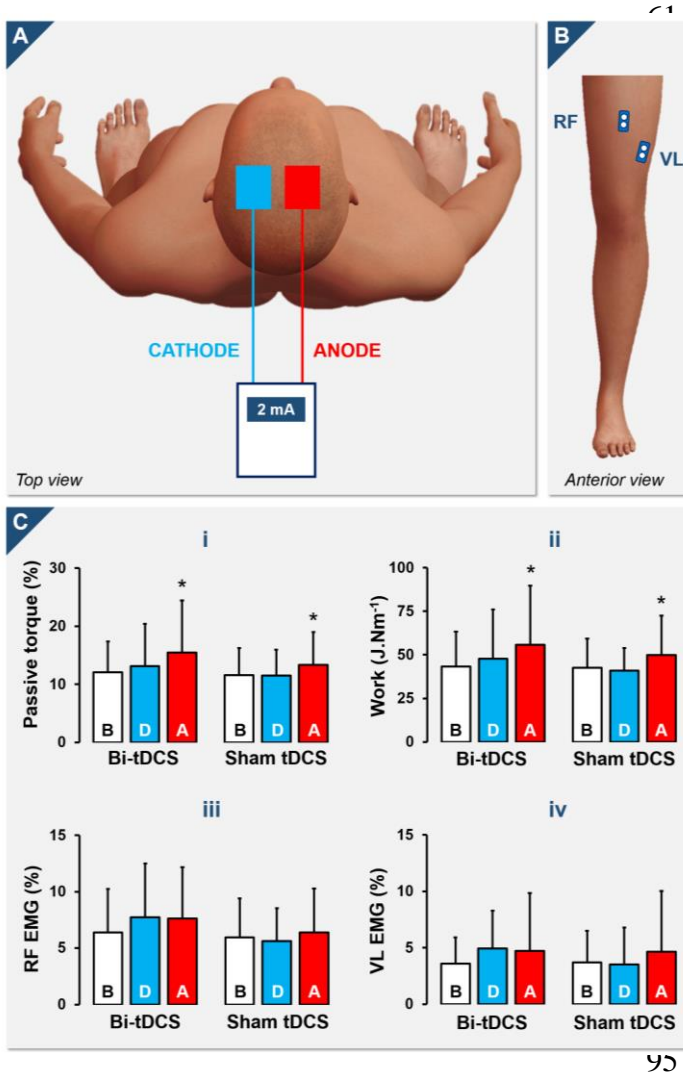


Figure 1. A. Schematic view of electrode placement for effective and sham bihemispheric-transcranial direct current stimulation (bi-tDCS). The right brain hemisphere and the left leg represent the affected sides while the left brain hemisphere and the right leg represent the unaffected sides. B. Schematic 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 bi-tDCS ('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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97

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

101 of the seat. The knee angle was set at 90° for the MVCs. Passive pain-free range of motion was
102 determined for each participant at the beginning of the first session and was used to set the
103 limits of motion for both sessions. EMG activity of the rectus femoris (RF) and the vastus
104 lateralis (VL) of the affected limb was recorded during both MVCs and quadriceps stretches.
105 Bipolar surface electrodes linked to their amplifier (Bagnoli-4, Delsys Inc., USA) were placed
106 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)
111 was normalized by the MVC torque to obtain the relative work (a.u.). For each quadriceps
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
114 peak torque (relative EMG, %). For each spasticity parameter (rMRPT, relative work, and RF
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.

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

120

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.

127

128 **Discussion**

129 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.

147

148 **Conflict/declaration of interest**

149 None

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153

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