Acute effects of bi-hemispheric transcranial direct current stimulation on the neuromuscular function of patients with chronic stroke: A randomized controlled study

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Abstract

Background: Muscle weakness in patients with chronic stroke is due to neuromuscular disorders such as muscle atrophy, loss of voluntary activation or weak muscle contractile properties which are majored by the imbalance of interhemispheric inhibition following stroke. In patients with chronic stroke, unilateral transcranial direct current stimulation improved the maximal isometric strength of paretic knee extensors, but bilateral transcranial direct current stimulation failed to improve concentric strength. This study aimed to assess if a bilateral current stimulation improves isometric maximal strength, voluntary activation and contractile properties of knee extensors in patients with chronic stroke.

Methods: Thirteen patients with chronic stroke and eight young healthy individuals participated in this randomized, simple-blinded, crossover study that included two experimental sessions: one with sham bilateral transcranial direct current stimulation and another with effective bilateral transcranial direct current stimulation (20 min, 2 mA). In the stroke patients, the anode was placed over the primary motor cortex of the affected hemisphere and the cathode over the contralateral primary motor cortex. In healthy participants, the brain side targeted by the anode and the cathode was randomly assigned. In each session, participants performed three assessments of strength, voluntary activation and contractile properties: before, during and after effective/sham bilateral transcranial direct current stimulation.

Findings: bilateral transcranial direct current stimulation had no effect on any neuromuscular assessments in both groups (All P values>0.05, partial eta-squares varied from 0.02 to 0.06).

Interpretation: a single session of bilateral transcranial direct current stimulation did not compensate muscular weakness of knee extensors in patients with chronic stroke.

Key words: stroke, voluntary activation, tDCS, knee, MVC, contractile properties

Abbreviations:

- ANOVA Analysis of variance
- EMG electromyography
- HRT Half relaxation time
- iMVC isometric maximum voluntary contraction
- M1 primary motor cortex
- RF rectus femoris
- RMS Root Mean Square
- tDCS transcranial direct current stimulation
- Twpot Potentiated Twitch
- VA voluntary activation
- VL vastus lateralis

Introduction

Muscle weakness is one of the major symptoms after stroke (Teixeira-Salmela et al., 1999). The mechanisms underlying muscle weakness in patients with chronic stroke are generally attributed to muscle atrophy (Hunnicutt and Gregory, 2017), reduced ability to fully activate muscles during voluntary effort (i.e. voluntary activation, VA) (Miller et al., 2009) or changes in muscle contractile properties (Li et al., 2014). Consequently, clinical rehabilitation aims to strengthen patients' muscular function and, increasingly, to improve motor neural drive from supra-spinal (Nudo, 2013). The difficulty in inducing cortical adaptations in stroke patients is that, motor disorder is exaggerated by transcallinous asymmetry of interhemispheric inhibition, where the unaffected hemisphere excessively inhibits the affected hemisphere (Murase et al., 2004). The clinical challenge is therefore to develop new methods to improve the motor function of stroke patients. In this context, the use of cortical neuromodulation approaches, such as transcranial direct current stimulation (tDCS), could be of interest (Lindenberg et al., 2010).

tDCS is a non-invasive technique based on neuromodulation of cortical excitability (Nitsche and Paulus, 2000), which has been used to improve motor function of lower limbs in patients with stroke (Lefaucheur, 2016). The modulation of excitability is related to the polarity of the applied current. When targeting the motor area, a cathodal current (cathodal tDCS) leads to reduced excitability of the neurons under the electrode, as revealed by the reduced motor evoked potential induced by transcranial magnetic stimulation. In contrast, increased motor evoked potential size under anodal current (anodal tDCS) highlights that anodal-tDCS increases excitability of neurons under the electrode (Nitsche and Paulus, 2000). When targeting the lower limb, for which cortical representation is deep and close to the interhemispheric fissure, anodal-tDCS effectively increases the cortical excitability of the lower limb cortical representation but cathodal-tDCS had minimal effect (Jeffery et al., 2007). The effects of tDCS are characterized by large inter-individual variability (Wiethoff et al., 2014). Furthermore, anodal-tDCS over leg representation of primary motor cortex (M1) in healthy participants and in stroke patients has demonstrated increased excitability of targeted M1 and a concomitant decreased excitability in the contralateral M1 (Madhavan and Stinear, 2010). As previously mentioned, motor deficit in stroke patients results in interhemispheric inhibition (Murase et al., 2004). To decrease the asymmetry of interhemispheric inhibition, bilateral-tDCS could be used to increase the excitability of the affected hemisphere and decrease the excitability of the unaffected hemisphere (Lefebvre and Liew, 2017). Some findings demonstrate that bilateral-tDCS induces a larger decrease in interhemispheric inhibition from the unaffected hemisphere to the affected hemisphere than unilateral tDCS (Tazoe et al., 2014).

In stroke patients, previous studies showed that tDCS may facilitate the motor performance of lower limbs (Elsner et al., 2013). Specifically, for lower limb strength, two studies reported an improvement in the isometric maximum voluntary contraction (iMVC) torque of knee extensors compared to the sham condition after 10 min at 2 mA of anodal-tDCS in patients with chronic stroke (Sohn et al., 2013; Tanaka et al., 2011). Based on the larger modification of interhemispheric inhibition after bilateral-tDCS compared to unilateral-tDCS and on the results of Tanaka et al, (2011), Montenegro et al., (2016) assessed the effects of 20 min at 2 mA of bilateral-tDCS on the torque during concentric maximum voluntary contraction (MVC) of knee extensors and knee flexors in patients with chronic sub-cortical stroke (Montenegro et al., 2016). While they found improved force steadiness for both muscle groups after bilateral-tDCS, they did not report changes in concentric MVC knee extensors. Montenegro et al., (2016) assumed that the dissimilarity between their results (no effect of tDCS) and those of Tanaka et al., (2011) (torque improvement with tDCS) may be attributed to different contraction modes (concentric vs isometric), given that the processes underlying these two types of contractions are different (Babault et al., 2006). Montenegro et al., (2016) indicated that concentric contraction could induce a hamstring stretch reflex exaggeration that could inhibit knee extensors, as previously observed in spastic paraparetic patients (Knutsson et al., 1997; Montenegro et al., 2016). This mechanism could explain why no maximal neuromuscular performance effect was observed in the Montenegro et al., (2016) study. However, these authors did not address outcomes for the neural and/or muscle mechanisms that underlie the maximal performance of the neuromuscular function in stroke patients.

The aim of this randomized sham-controlled study was to assess the effects of bilateral-tDCS on maximal isometric force production and muscle activation of knee extensors for the paretic leg of stroke patients. We therefore assessed iMVC torque, voluntary activation, EMG activity of knee extensors after, during, and before the application of bilateral-tDCS. We hypothesized that, compared with the sham condition, knee extensors iMVC and activation would increase during and after bilateral-tDCS. To assess whether potential bilateral-tDCS-related changes in neuromuscular performance are linked to stroke, a control group, including healthy participants was also included.

Methods

Subjects

The sample size for patients with chronic stroke was predetermined using the G*Power software (Universität Kiel, Kiel, Germany) and calculated based on the results of the study of Tanaka et al., (2011). For an expected increase in iMVC torque of 20%, a standard deviation (SD) of iMVC of 20%, a statistical power of 0.9, a required sample size of 11 patients with chronic stroke was obtained to

investigate potential bilateral-tDCS-related changes in maximal knee extensors performance. Then, it was decided to include 14 participants in the experiment, to account for potential dropouts. Initially, 14 patients were included but one patient did not complete all the study protocol. Finally, 13 patients with chronic stroke [2 women, 6 right hemiparesis, age: 57.3 (11.6) years, anteriority of stroke: 8.7 (5.1) years, mean (SD)] were included in this study. All characteristics of patients with chronic stroke are displayed in Table 1. Stroke patients were recruited during routine follow-up visits in the Physical Medicine and Rehabilitation department of the university teaching hospital. They were eligible for inclusion if: they had signed the information memorandum; were at least 18 years of age; were hemiplegia post-stroke for more than 6 months; were walking with or without technical assistance; were able to follow recommended guidelines. All patients with stroke gave their written consent prior to participation. The study was approved by the local Ethics Committee ("Comité de protection des personnes Ile de France IV"; reference number: 14025 / ClinicalTrials.gov: NCT02109796). In addition, a control group of 8 young healthy participants [3 women, age: 24.8 (2.3) years] was also included to this work. These participants have been evaluated prior to the beginning of this clinical trial. They also gave their written consent prior to participation. The study was performed in accordance with the ethical codes of the World Medical Association (Declaration of Helsinki, last update from October 2013).

--Table1—

Study design and experimental procedure

This study used a randomized, sham-controlled and simple blind crossover experimental method. The study design is available in Figure 1. Each subject participated in two randomized visits separated by at least 7 days: one with effective bilateral-tDCS and one with sham bilateral-tDCS. For each visit, a neuromuscular assessment of knee extensors was performed before (pre-stimulation), during (per-stimulation) and immediately (post-stimulation) after bilateral-tDCS. The knee extensors of the paretic limb were tested in stroke patients while the knee extensors of dominant or non-dominant limb (randomly assigned) were tested in healthy participants. A standardized warm-up including 5 submaximal isometric contractions was performed by each participant 5 minutes before the first neuromuscular assessment (pre-stimulation). Each neuromuscular assessment included 2 iMVCs without superimposed electrical nerve stimulation and then 2 iMVCs with electrical nerve stimulations during (superimposed twitch) and after (potentiated twitch). For each iMVC, participants were asked to contract their knee extensors as strong as possible, and to maintain the effort for 5 seconds (to observe a torque plateau when possible). A rest period of 30 seconds was included between each MVC. iMVCs with superimposed stimulation were performed to assess voluntary activation level using the "interpolation twitch technique" (Gandevia, 2001). This technique consists of superimposing

a percutaneous electric stimulation (a twitch) on the femoral nerve during the torque plateau phase of iMVC and three seconds after iMVC at rest (potentiated twitch) (Krishnan and Williams, 2010). iMVCs with superimposed stimulation were obtained in all healthy participants and only in 10 patients with chronic stroke. Indeed, for 3 patients with chronic stroke, electrical nerve stimulation induced too much discomfort (i.e. >5 on a 0-10 visual analogue scale, where 0 is no discomfort and 10 is an extremely important discomfort). The entire experiment, including data collection, was performed by the same operator.

-- Figure 1 --

Randomization

The randomization was performed at the hospital's Clinical Investigation Technological Innovation Centers. The allocation of the first visit (effective or sham tDCS) was concealed in sealed envelopes. The envelopes were opened by the investigator at the end of the pre-evaluation of the first visit.

Transcranial Direct Current Stimulation

Anodal-tDCS was administered through a pair of electrodes covered by saline-soaked sponges (7 cm× 5 cm, 35 cm2). The current was delivered by a constant-current stimulator (Eldith-DC, NeuroConn GmbH, Germany). In stroke patients, the anode was placed over M1 of the affected hemisphere and the cathode over M1 of the unaffected hemisphere, both with regard to the leg's cortical representation: laterally to Cz of the international electroencephalogram 10–20 system (Klem et al., 1999). In healthy participants, the placement of the anode and the cathode was randomized: the anode was placed either on the dominant hemisphere or on the non-dominant hemisphere (the cathode was placed contralaterally), also with regard to leg's cortical representation (Figure 2). During the effective bilateral-tDCS visit, the stimulation intensity was 2 mA and the duration of stimulation was 20 minutes, the current had a ramp time of 8 seconds at the beginning and at the end of stimulation. During the "sham" visit the electrodes were placed in the same way as the effective tDCS visit, but the current was only applied for 120 seconds to induce a pruritic sensation, as well as the effective bilateral-tDCS condition. As shown by Nitsche and Paulus (2000), this duration is not sufficient to induce changes in neuronal excitability , which would need the current to be applied for at least 3 minutes (Nitsche and Paulus, 2000).

-- Figure 2 --

Data collection

Torque recordings

iMVCs were assessed by an isokinetic dynamometer (Biodex, Shirley Corporation, NY, USA; sampling frequency: 150Hz). The participants were sitting down on the isokinetic dynamometer chair with a hip angle of 85° (0°: complete hip extension) and a knee angle of 85° (0°: complete knee extension). To avoid muscular compensation of other parts of the body during the knee extensors assessment, the trunk and the assessed limb positions were maintained using straps placed around the chest, the waist and the thigh. The axis of the dynamometer arm was visually aligned with the articular center of the tested knee, defined by a line passing between the medial and lateral femoral epicondyles. The distal attachment of the lower limb with the arm of the dynamometer was set at 3 cm above the lateral malleolus.

Electrophysiological recordings

Participants were equipped with an electromyographic (EMG) analysis system composed of 2 surface electrodes (Bagnoli-4, Delsys Inc., Boston, USA; Sampling frequency: 2000Hz). The EMG activity of the rectus femoris (RF) and the vastus lateralis (VL) of the limb studied (paretic lower limb in stroke patients, dominant or non-dominant in healthy participants) was recorded during all assessments. The surface electrodes were placed on the participants' skin. The VL electrode was placed at the 2/3 point along the line from the great trochanter to the lateral side of the patella, the RF electrode was placed 5-10 cm above the patella to limit the stimulation artifact of the electrical stimulation (used to study the superimposed MVC) (Pierrot-Deseilligny and Burke, 2012).

Electrical stimulation

The electrical stimulation was manually delivered using a Digitimer DS7A (Digitimer Ltd; Hertfordshire, United Kingdom); the spherical cathode was placed above the femoral triangle and held in place by a bag of sand; the rectangular anode was placed under the thigh. A single rectangular pulse with a 1-ms duration was used and the stimulation intensity was set to induce the maximum peak-to-peak amplitude of compound action potential (M wave) (Fimland et al., 2011). Since the number of pulses (single vs. double pulse) does not affect the assessment of voluntary activation (Allen et al., 1998; Scaglioni and Martin, 2009), we chose to stimulate the nerve trunk using single pulse rather than multiple pulses to optimize the comfort of participants, especially that of patients with chronic stroke.

Data analysis

Throughout the analysis, we used data from the highest standard iMVC torque and highest superimposed iMVC torque. The iMVC torque was considered as the highest peak torque value

measured over each two standards and two superimposed trials. The voluntary activation level was estimated according to the following formula (Hureau et al., 2016; Strojnik and Komi, 1998):

$$VA\ (\%) = 100 - [\ d\ (Superimposed\ torque / Voluntary\ torque)\ /\ Potentiated\ twitch] * 100$$

Where *VA* means voluntary activation, *d* is the difference between superimposed torque and torque at stimulation artefact.

The Root Mean Square (RMS) of RF and VL EMG was calculated over a time interval of 500 ms around the maximum force value of MVC. The RMS value was then normalized to the corresponding M-wave (induced by the electrical stimulation at rest, after the contraction) for the RF ($RF_{EMG\text{-}RMS/M}$) and VL ($VL_{EMG\text{-}RMS/M}$). EMG-RMS is mainly influenced by central and peripheral factors whereas M-wave is influenced by peripheral factors (Rodriguez-Falces and Place, 2018). M-wave amplitude and duration were subsequently used to assess neuromuscular transmission (Rodriguez-Falces and Place, 2018) and EMG-RMS/M was used to assess central activation. Contractile properties were assessed by measuring potentiated twitch amplitude, contraction time and half-relaxation time (Miller et al., 1987).

Statistical Analyses

All statistical analyses were carried out using the Statistica ® version 7.1 software. The level of statistical significance was set at $p < 0.05$.

Separate analysis of variance tests (ANOVAs) were performed on the amplitudes for iMVC, voluntary activation, EMG activities and contractile properties; with group (×2: healthy participants vs. patients with stroke) as the between-participants factor, and stimulation condition (×2: Sham vs. Effective) and time (×3: Pre vs. Per vs. Post) as the within-participants factor. Post hoc comparisons were performed using Tukey test. Effect sizes for each ANOVA were calculated as partial eta squares (n_p^2).

Results

All data from stroke patients and healthy participants are available in Table 2 and Table 3, respectively. In the result section, only crucial results as the interaction between condition, time and group or between only time and group will be presented. All the group effects are available as supplementary material.

Mechanical properties

The Figure 3 show the individual response to effective and sham tDCS on iMVC torque in patients with chronic stroke. There was no interaction between condition, time and group on iMVC ($F=0.32$, $df=2$, $p=0.72$, $n_p^2=0.02$). The repeated measures ANOVA revealed no effects of interactions between

condition, time and group on voluntary activation (F=0.68, df=2, p=0.51, n_p^2=0.06). There was no interaction between condition, time and group on the potentiated twitch (F=0.42, df=2, p=0.65, n_p^2=0.03). There was no interaction between condition, time and group on contraction time (F=0.77, df=2, p=0.47, n_p^2=0.05). A significant interaction between time and group was observed for the half-relaxation time (F=5.50, df=2, p=0.01, n_p^2=0.31). The Tukey test showed that, in stroke patients, half-relaxation time increased over time and was higher than in healthy participants. There was no interaction between condition, time and group on the half-relaxation time (F=0.007, df=2, p=0.99, n_p^2<0.01).

Electrophysiological properties

There was no interaction between condition, time and group on the $RF_{EMG\text{-}RMS/M}$ (F=0.70, df=2, p=0.50, n_p^2=0.07) and on the $VL_{EMG\text{-}RMS/M}$ (F=0.95, df=2, p=0.41, n_p^2=0.13). The repeated measures ANOVA revealed no effects of group, time or condition, and no interaction between these factors on the M amplitude and duration of RF (respectively F=2.45, df=2, p=0.11, n_p^2=0.21 and F=2.81, df=2, p=0.07, n_p^2=0.15) and VL (respectively F=1.30, df=2, p= 0.30, n_p^2=0.12 and F=0.99, df=2, p=0.37, n_p^2=0.06).

--Table 2 --

-- Table 3 --

-- Figure 3 --

Discussion

The aim of this study was to assess the acute effects of bilateral-tDCS on maximum voluntary strength and activation of paretic knee extensors in patients with chronic stroke compared to healthy participants. No significant improvement of isometric knee extensors performance was found during and after bilateral-tDCS in both groups. This novel observation added to the work of Montenegro et al., (2016) (for concentric contractions) highlights the limits for the use of bilateral-tDCS as an acute treatment for improving neuromuscular function of lower limb in patients with chronic stroke, regardless of muscle contraction mode (isometric and concentric). In this discussion, only the main results will be discussed, however we also performed a comparison of our data with data in the literature such as maximal strength and voluntary activation of healthy participants and patients with stroke in other studies which is available as supplementary material.

Our results showed that iMVC torque was not statistically improved by bilateral-tDCS, neither the mechanical properties, nor the electrophysiological properties in both groups. In healthy participants,

these results are in accordance with Montenegro et al., (2015) and with the review of Angius et al., (2017) who reported no improvement on neuromuscular performance in healthy participants after tDCS (Angius et al., 2017; Montenegro et al., 2015). In patients with chronic stroke, the absence of significant effects of bilateral-tDCS treatment is also in accordance with a previous study. Montenegro et al., (2016) found no significant improvement in patients with chronic sub-cortical stroke on concentric MVC torque of knee extensors after 20 min at 2 mA of bilateral-tDCS over both M1 (Montenegro et al., 2016). Montenegro et al., (2016) assumed that this lack of effect was due to the concentric contraction mode, but the present study also failed to observed bilateral-tDCS-effects on maximal motor performance with isometric contractions. Our results are in contrast not in agreement with Tanaka et al., (2011) who found an improvement of iMVC torque of knee extensors in patients with chronic stroke after anodal-tDCS (Tanaka et al., 2011). While the contraction mode appears not to be involved in the absence of a bilateral-tDCS-related effect on maximal motor performance, this kind of stimulation deserves to be questioned: is it the use of bilateral-tDCS instead of unilateral-tDCS that leads to an absence of effects? Indeed, Vines et al., (2008) observed that bilateral-tDCS is more efficient than unilateral-tDCS in improving motor learning of the non-dominant hand in healthy participants (Vines et al., 2008). Bilateral-tDCS may also improve motor learning (Lefebvre et al., 2012) and motor recovery in the paretic hand in stroke patients (Lindenberg et al., 2010). Motor learning and motor recovery are closely related processes (Krakauer, 2006) whose responses to tDCS are not identical to the maximal motor performance responses to tDCS (Karok et al., 2017). Thus, perhaps bilateral-tDCS should preferentially be used to improve motor learning rather than maximal motor performance. A final explanation for the absence of significant effects of bilateral-tDCS on motor performance could be the inter-individual variability in response to tDCS. Wiethoff et al., (2014) showed that in 53 healthy participants, approximately 50% of the participants showed only a minor response or even no response to tDCS (Wiethoff et al., 2014). Furthermore, in anodal conditions about 25% of participants showed an inhibition of cortical excitability and in cathodal conditions about 40% showed an excitation (Wiethoff et al., 2014). Thus, it can be assumed that the participants in our study presented no or low sensitivity to bilateral-tDCS. In this regard, the assessment of cortical excitability under bilateral-tDCS could help us predict the real effects of bilateral-tDCS for each participant.

In the current study, we only focused on the acute effects of bilateral-tDCS on knee extensor performance. Therefore, possible effects for chronic application of bilateral-tDCS (repeated sessions) cannot be thus discarded based on our work. The chronic effects of tDCS on maximal muscle strength has been poorly investigated. Khedr et al., (2013) has shown a small effect of 6 consecutive sessions of anodal and cathodal tDCS cathodal-tDCS (25 min at 2 mA) on muscle strength (hand grip, shoulder abduction, toes dorsiflexion, and hip flexion) in patients with acute stroke (Khedr et al., 2013). In

contrast, a recent meta-analysis showed that tDCS (6 studies with an anodal setup and 2 studies with cathodal setup) does not significantly improve the upper extremity impairment of patients with acute, sub-acute or chronic stroke (Tedesco Triccas et al., 2016). Danzl et al., (2013) also found no effect of 12 sessions (3 sessions per week for 4 weeks) of anodal tDCS anodal-tDCS (20 min at 2 mA) combined with robotic gait orthosis on several functional assessments (e.g., the timed up and go test and the berg balance scale) in patients with chronic stroke. Taken together, these few studies highlight the low efficacy of repeated tDCS sessions to improve motor function of patients with stroke

Limitations

This study has several limitations. The first limitation is that we did not investigate the cortical excitability of M1 across visits and time, so we cannot be sure that bilateral-tDCS modulated the cortical excitability as expected. The second limitation is that the VA standard deviation of stroke patients was larger than the standard deviation for healthy participants, which may obscure potential differences in VA between groups or during the experiment. The variability of the measure for stroke patients may therefore be a limiting factor for VA comparisons. The third limitation is that the sample of patients was heterogenic, unlike Montenegro et al., (2016) who recruited only patients with subcortical lesions. This possibly added high heterogeneity to our sample of patients, which may interfere with bilateral-tDCS. Indeed, Luft et al, (2004) showed that cortical activation of knee extension is similar between healthy participant and chronic sub-cortical stroke patients but differs in patients with chronic cortical stroke (Luft et al., 2005). However, we performed a statistical analysis by adding the lesion location (i.e., complete and deep location, visible in Table 2) as a categorical variable and it did not reveal any interaction of lesion location on the effects of bilateral-tDCS (data not presented). Despite our small sample size (which was calculated prior to the study), the non-significant results of our main variables are associated with small-to-medium partial eta-squared (0.02 for iMVC torque, 0.06 for voluntary activation, according to Cohen (1988) guidelines (Cohen, 1988). The probability of a type 2 error therefore is unlikely. Nevertheless, our results will need to be confirmed in a larger sample size, especially since we based our sample size calculation on the study of Tanaka et al. (2011) in which only 8 patients with chronic stroke were included. Finally, despite all our methodological precautions for installing patients on the isokinetic dynamometer, there is an inevitable difference in dynamometer and knee joint angles that may have affected the results of the present study (Arampatzis et al., 2004).

Conclusion

The results of the present study suggest that a single session of bilateral-tDCS does not significantly improve maximal voluntary strength of the knee extensors muscles by enhancing their efferent neural

drive in patients with chronic stroke as well as in healthy individuals. To date, only unilateral-tDCS has demonstrated its effectiveness to acutely compensate, at least in part, the maximal voluntary strength deficit in patients with chronic stroke (Sohn et al., 2013; Tanaka et al., 2011). For clinicians who wish to include tDCS sessions in the clinical management of patients with chronic stroke to improve their maximal muscle activation, we therefore advise to use unilateral-tDCS rather than bilateral-tDCS, pending further studies on bilateral-tDCS with larger sample and greater statistical power (which may confirm or invalidate our results).

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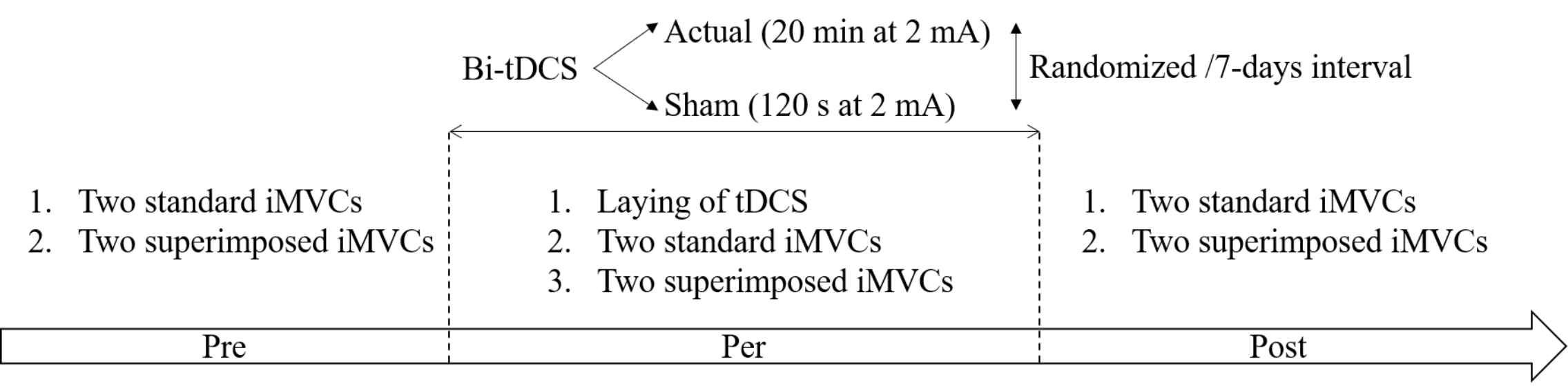
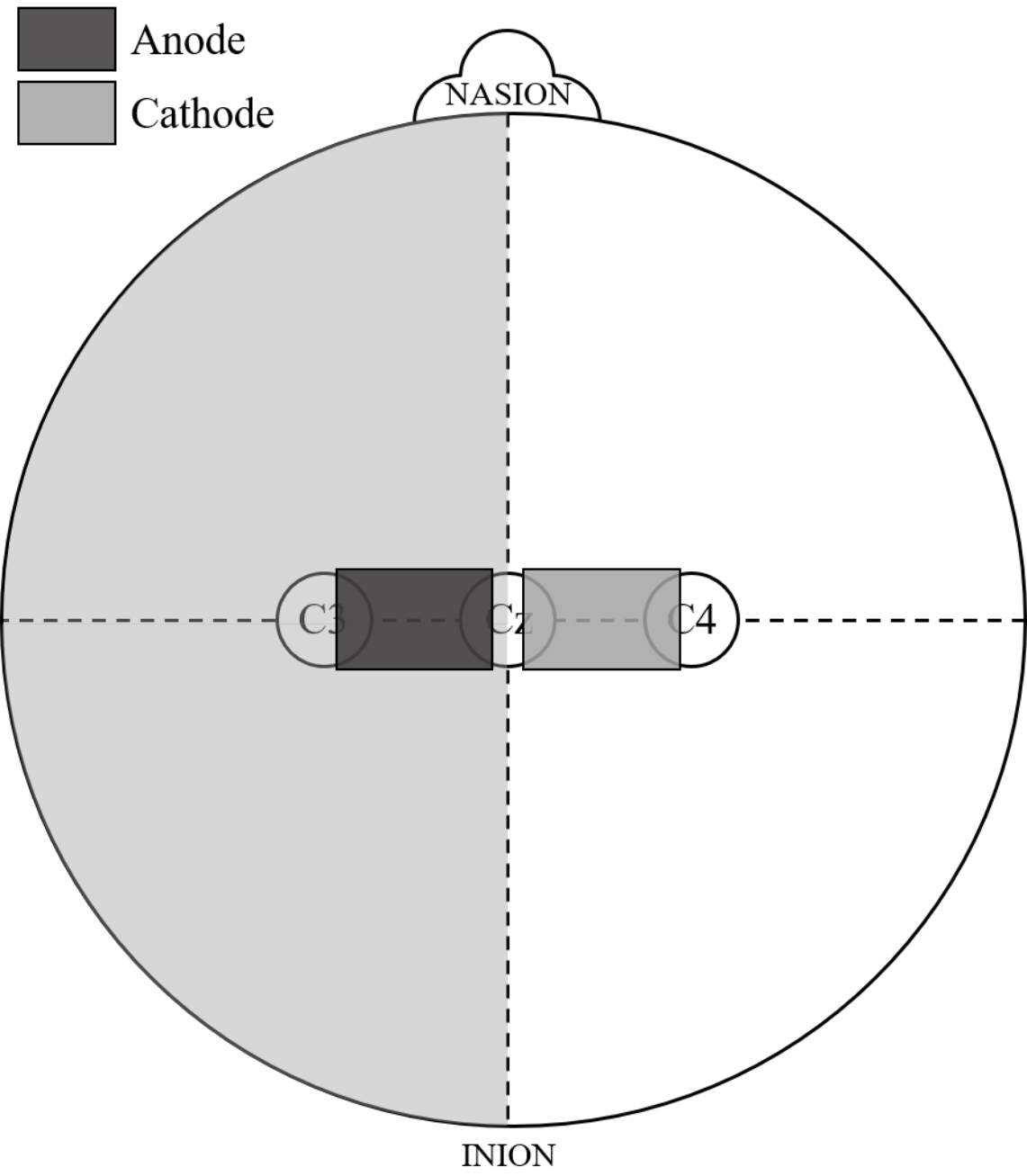
Figure captions

Fig 1 study design of the two visits and the Pre, Per and Post tDCS evaluations. iMVC: isometric maximum voluntary contraction; tDCS: transcranial direct current stimulation

Fig 2 schematic illustration of the bilateral-tDCS setup. The gray area represents the affected hemisphere for stroke patients and dominant or non-dominant hemisphere in healthy participants

Fig 3 illustration of the evolution of iMVC torque of knee extensors in: A) patients with chronic stroke; B) healthy subjects according to tDCS condition (effective or sham) and time (pre, per, post). iMVC: isometric maximum voluntary contraction; tDCS: transcranial direct current stimulation


Actual (20 min at 2 mA)
Bi-tDCS
Sham (120 s at 2 mA)
Randomized /7-days interval
1. Two standard iMVCs
2. Two superimposed iMVCs
1. Laying of tDCS
2. Two standard iMVCs
3. Two superimposed iMVCs
1. Two standard iMVCs
2. Two superimposed iMVCs
Pre
Per
Post


Anode
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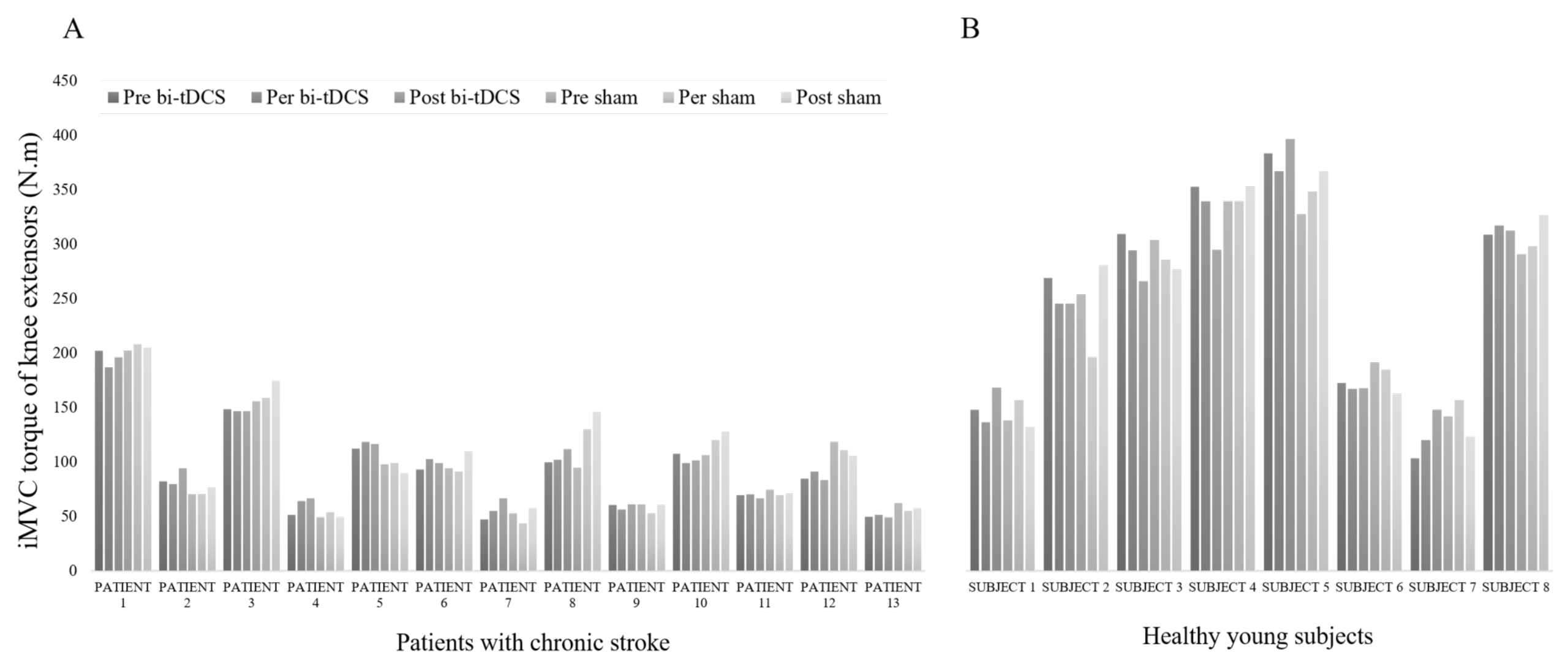
A
B
Pre bi-tDCS
Per bi-tDCS
Post bi-tDCS
Pre sham
Per sham
Post sham
iMVC torque of knee extensors (N.m)
450
400
350
300
250
200
150
100
50
0
PATIENT 1
PATIENT 2
PATIENT 3
PATIENT 4
PATIENT 5
PATIENT 6
PATIENT 7
PATIENT 8
PATIENT 9
PATIENT 10
PATIENT 11
PATIENT 12
PATIENT 13
Patients with chronic stroke
SUBJECT 1
SUBJECT 2
SUBJECT 3
SUBJECT 4
SUBJECT 5
SUBJECT 6
SUBJECT 7
SUBJECT 8
Healthy young subjects

Table 1: Patients' characteristics. A complete stroke location means an involvement of cortical and subcortical lesions, a deep location means only a subcortical lesion.

Patients	*Sex*	*Age (year)*	*Weight (kg)*	*Size (cm)*	*Time since onset (year)*	*Side of paresia*	*Stroke type*	*Stroke location*
1	Man	55	106	176	10	Right	Ischemia	Complete
2	Man	55	84	172	1	Left	Ischemia	Deep
3	Man	52	50	160	10	Left	Ischemia	Deep
4	Man	63	70	170	8	Right	Ischemia	Deep
5	Woman	71	58	152	11	Left	Ischemia	Deep
6	Woman	40	55	160	7	Right	Hemorrhage	Deep
7	Man	66	66	178	6	Right	Ischemia	Complete
8	Man	74	80	174	10	Right	Hemorrhage	Complete
9	Man	45	86	186	18	Left	Hemorrhage	Complete
10	Man	39	72	170	12	Left	Hemorrhage	Complete
11	Man	51	57	170	16	Left	Hemorrhage	Deep
12	Man	68	102	175	2	Left	Ischemia	Deep
13	Man	66	105	193	2	Right	Ischemia	Deep
Mean (SD)		57.3 (11.6)	76.2 (19.4)	172 (10.8)	8.7 (5.1)			
Summary	11 Men 2 Women					7 Left 6 Right	8 Ischemia 6 Hemorrhage	5 Complete 8 Deep

Table 2: Effect of real and sham bilateral-tDCS on electrophysiological and mechanical properties of knee extensors in stroke patients. MVC: maximum voluntary contraction; VA: voluntary activation; TW_{pot}: potentiated twitch; Contraction Time; HRT: half relaxation time; $RF_{EMG-RMS/M}$ is the rationalized root mean square (RMS) by the M-wave of the rectus femoris (RF); $VL_{EMG-RMS/M}$ is the rationalized RMS by the M-wave of the vastus lateralis (VL); $RF_{M\text{-}wave\ amp}$ is the amplitude of the M-wave of the RF; $VL_{M\text{-}wave\ amp}$ is the amplitude of the M-wave of the VL; $RF_{M\text{-}wave\ duration}$ is the duration of the M-wave of the RF; $VL_{M\text{-}wave\ duration}$ is the duration of the M-wave of the VL.

	Real bilateral-tDCS			Sham bilateral-tDCS		
	Pre	*Per*	*Post*	*Pre*	*Per*	*Post*
MVC (N.m)	82.9 (29.3)	84.0 (28.8)	87.8 (27.3)	87.3 (30.7)	87.4 (34.9)	92.9 (38.2)
VA (%)	66.0 (26.1)	81.5 (13.5)	74.7 (21.8)	71.9 (20.0)	68.3 (21.2)	75.2 (17.5)
TW_{pot} (N.m)	26.5 (12.5)	27.3 (13.4)	25.3 (13.7)	22.9 (11.9)	27.8 (12.9)	26.9 (13.2)
Contraction Time (s)	0.078 (0.022)	0.082 (0.025)	0.081 (0.025)	0.085 (0.024)	0.078 (0.030)	0.082 (0.025)
HRT (s)	0.096 (0.041)	0.108 (0.053)	0.114 (0.069)	0.097 (0.046)	0.106 (0.049)	0.098 (0.046)
$RF_{EMG-RMS/M}$	0.039 (0.02)	0.042 (0.01)	0.040 (0.01)	0.062 (0.02)	0.052 (0.02)	0.051 (0.02)
$VL_{EMG-RMS/M}$	0.043 (0.02)	0.041 (0.01)	0.040 (0.01)	0.048 (0.02)	0.041 (0.02)	0.043 (0.01)
$RF_{M\text{-}wave\ amp}$ (mV)	1.00 (0.53)	1.03 (0.57)	0.99 (0.59)	0.78 (0.52)	0.84 (0.55)	0.98 (0.44)
$VL_{M\text{-}wave\ amp}$ (mV)	1.60 (0.88)	1.80 (1.10)	1.62 (0.96)	1.63 (0.98)	1.72 (1.16)	1.75 (0.93)
$RF_{M\text{-}wave\ duration}$ (s)	0.015 (0.006)	0.015 (0.006)	0.016 (0.006)	0.011 (0.007)	0.013 (0.070)	0.011 (0.006)
$VL_{M\text{-}wave\ duration}$(s)	0.009 (0.005)	0.009 (0.005)	0.010 (0.006)	0.010 (0.007)	0.011 (0.006)	0.009 (0.005)

Table 3: Effect of real and sham bilateral-tDCS on electrophysiological and mechanical properties of knee extensors in healthy participants. MVC: maximum voluntary contraction; VA: voluntary activation; TW_{pot}: potentiated twitch; Contraction Time; HRT: half relaxation time; $RF_{EMG\text{-}RMS/M}$ is the rationalized root mean square (RMS) by the M-wave of the rectus femoris (RF); $VL_{EMG\text{-}RMS/M}$ is the rationalized RMS by the M-wave of the vastus lateralis (VL); $RF_{M\text{-}wave\ amp}$ is the amplitude of the M-wave of the RF; $VL_{M\text{-}wave\ amp}$ is the amplitude of the M-wave of the VL; $RF_{M\text{-}wave\ duration}$ is the duration of the M-wave of the RF; $VL_{M\text{-}wave\ duration}$ is the duration of the M-wave of the VL.

	Real bilateral-tDCS			Sham bilateral-tDCS		
	Pre	*Per*	*Post*	*Pre*	*Per*	*Post*
MVC (N.m)	248.5 (99.8)	242.2 (93.8)	246.4 (97.0)	242.2 (79.2)	239.6 (78.7)	243.7 (83.5)
VA (%)	80.9 (9.20)	83.9 (11.8)	83.1 (10.9)	86.6 (17.0)	86.9 (12.4)	88.1 (12.0)
TW_{pot} (N.m)	55.9 (16.6)	54.2 (15.7)	53.2 (16.4)	46.5 (26.0)	46.7 (23.4)	40.1 (18.9)
Contraction Time (s)	0.039 (0.008)	0.038 (0.006)	0.035 (0.004)	0.038 (0.007)	0.036 (0.006)	0.037 (0.007)
HRT (s)	0.057 (0.009)	0.059 (0.007)	0.057 (0.005)	0.048 (0.013)	0.050 (0.005)	0.046 (0.011)
$RF_{EMG\text{-}RMS/M}$	0.124 (0.07)	0.126 (0.07)	0.099 (0.06)	0.087 (0.04)	0.097 (0.04)	0.087 (0.03)
$VL_{EMG\text{-}RMS/M}$	0.091 (0.05)	0.090 (0.05)	0.083 (0.05)	0.088 (0.06)	0.074 (0.03)	0.106 (0.06)
$RF_{M\text{-}wave\ amp}$ (mV)	0.98 (0.54)	0.82 (0.43)	1.00 (0.47)	1.32 (0.30)	1.33 (0.36)	1.12 (0.46)
$VL_{M\text{-}wave\ amp}$ (mV)	1.36 (0.87)	1.35 (0.84)	1.30 (0.82)	1.80 (0.96)	1.94 (1.15)	1.58 (0.96)
$RF_{M\text{-}wave\ duration}$ (s)	0.008 (0.002)	0.010 (0.005)	0.008 (0.002)	0.009 (0.003)	0.009 (0.004)	0.010 (0.004)
$VL_{M\text{-}wave\ duration}$(s)	0.007 (0.004)	0.007 (0.002)	0.006 (0.002)	0.008 (0.005)	0.007 (0.004)	0.006 (0.004)