

**The effect of transcranial DC stimulation (tDCS) on perception of effort  
in an isolated isometric elbow flexion task.**

Sofia I. Lampropoulou<sup>1</sup>, Alexander V. Nowicky<sup>2</sup>,

<sup>1</sup> Physiotherapy Department, Higher Technological Educational Institute of Patras,  
Aigio Campus, Psaron 6, Aigio, 25100, Greece

<sup>2</sup>School of Health Sciences and Social Care, Centre for Rehabilitation Research  
Brunel University, Uxbridge, UB8 3PH, United Kingdom  
Email: alexander.nowicky@brunel.ac.uk

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Corresponding Author: Dr. Sofia Lampropoulou

Physiotherapy Department, Higher Technological Educational Institute of Patras,  
Aigio Campus, Psaron 6, Aigio, 25100, Greece

Email: sofia.lampropoulou@yahoo.co.uk

## **Abstract**

Transcranial direct current stimulation (tDCS) applied to the Motor cortex (M1) produces long lasting effects on corticospinal excitability. Studies have demonstrated that anodal tDCS enhances force production and endurance time during fatiguing exercise. The increased excitability may also modulate the perception of effort associated with voluntary activation at a supraspinal level. Therefore we hypothesized that tDCS alone might alter perception of effort related to the motor command/efference copy of a repeated voluntary activation task under nonfatiguing conditions. We examined the possible after-effects of tDCS on subjective ratings of perception of effort using a numerical rating scale (0-10 NRS) in nonfatiguing bouts of a force matching task utilizing isometric elbow flexion. In a double blind, cross over study, 12 healthy volunteers received sham, anodal and cathodal tDCS in randomized order for 10 min (extracephalic montage, 1.5 mA, 62  $\mu\text{A}/\text{cm}^2$ ) through saline soaked sponges centred over left M1. We used transcranial magnetic stimulation (TMS) with surface electromyography (sEMG) to monitor motor evoked potentials (MEPs) and force-sEMG from right m. biceps and m. brachioradialis brachii. In a within subjects repeated measure ANOVA, no significant differences between type of stimulation in the post intervention period were found in: ratings of perception of effort, elbow flexion maximum voluntary force, or sEMG magnitude for the matching task. There were also no significant differences between type of stimulation in corticospinal excitability as monitored in TMS evoked MEPs. Application of tDCS over sensorimotor cortex did not

significantly alter perception of effort under conditions of a nonfatiguing repeated isometric elbow flexion task.

**Key Words:** tDCS; sensori-motor cortex; MEPs; TMS; ergogenic action; perception of effort; 0-10 NRS effort rating, elbow flexors

## **Introduction**

Transcranial direct current stimulation (tDCS) is a noninvasive method of brain stimulation producing polarity specific changes in neuronal activity (Bindman, Lippold & Redfearn, 1964; Priori, 2003). The applied electric field polarizes neuronal membrane potentials and hence changes the level of excitability in neuronal populations (Nitsche et al., 2008). Transcranial Magnetic Stimulation (TMS) studies have shown an increase in corticospinal excitability when anodal DC current was applied briefly over the primary motor cortex (M1), but a decrease with the reverse polarity (Nitsche & Paulus, 2000; Nitsche & Paulus, 2001). Stimulation after-effects on cortical excitability are dependent on intensity and duration of application and may last for 30 min. or more, and suggest that these may also activate synaptic plasticity mechanisms (Nitsche & Paulus, 2001; Nitsche et al., 2005). tDCS is now a well-established method for investigating cortical plasticity of motor and cognitive function in health and disease (Lang, Nitsche, Paulus, Rothwell & Lemon, 2004; Nitsche et al, 2008; Tanaka & Watanabe, 2009; Jacobson, Koslowsky & Lavidor, 2012). Neuroimaging studies have shown that modulatory actions of tDCS on cortical activity correlate with both localized and more widespread changes in brain activity underlying behaviour (Baudewig, Nitsche, Paulus & Frahm, 2001; Shafi, Westover, Fox & Pascual-Leone, 2012). Anodal tDCS centred over somatosensory (S1) cortex modulates somatosensory evoked potentials to median nerve stimulation (Dieckhofer et al, 2006; Matsunaga, Nitsche, Tsuji & Rothwell, 2004) and when centred over M1, increased pain perception thresholds of electrical stimulation (Boggio, Zaghi, Lopes & Fregni, 2008). These

studies suggest that acute anodal tDCS application over sensorimotor cortex elicits subjective perceptual changes.

Neuromuscular fatigue is associated with an exercise induced decrease in voluntary muscular force and is mediated by both central and peripheral factors which limit motor performance (Taylor, Butler & Gandevia, 2000; Gandevia, 2001; Taylor, Todd & Gandevia, 2006). TMS studies examining the effects of fatiguing exercise demonstrated that changes in corticospinal excitability were associated with reduced supraspinal drive, and hence confirm a contributory role of central factors in neuromuscular fatigue (Teo, Rodrigues, Mastaglia & Thickbroom, 2012; Taylor & Gandevia, 2008; Ross, Middleton, Shave, George & Nowicky, 2007). We have shown that in a (0-10) numerical rating scale of self-reported effort rating using an isometric elbow flexion task following fatiguing exercise, there was a significant increase in rating of effort at 30 min post exercise (Lampropoulou and Nowicky, 2012).

Anodal tDCS increased maximal voluntary force production in both lower and upper limb which outlasts the duration of the stimulation (Tanaka Hanakawa, Honda & Watanabe, 2009; Tanaka et al., 2011), and increased intramuscular coherence in sustained low force hand muscle activity, thereby suggesting that brief applications alter voluntary motor cortical activity (Power et al., 2006). Anodal tDCS applied over M1 also improved endurance time for a sustained isometric elbow flexion task which authors attributed this increased performance to factors such as reduced pain sensation or changes in motivation (Cogiamanian, Marceglia, Ardolino, Barbieri

& Priori, 2007). These studies suggest that tDCS may have novel ergogenic applications for motor performance.

Recently a study showed that perception of effort was correlated with the size of movement related cortical EEG potentials thus providing support for a link between this subjective perception and the central motor command for voluntary activation of muscles (deMorree, Klein and Marcora, 2012).

Given the reported excitability effects of anodal tDCS on voluntary activity and enhancement of motor performance, in particular, we hypothesized that application of tDCS over sensorimotor area in the absence of fatiguing exercise may also modulate perception of effort in a polarity dependent manner. We therefore investigated the possible effects of tDCS using a self-reported rating of effort during a force matching –task (Lampropoulou & Nowicky, 2012) combined with TMS to monitor concomitant changes in corticospinal excitability of the elbow flexor muscles.

## **Methods**

### **Participants**

Twelve healthy volunteers (8 women and 4 men, 32±6 years, 11 right-handed), participated in the study using a double blind crossover design. Participants received each of the three stimulation treatments - anodal, cathodal or sham tDCS, in randomized order with each session separated by a week to minimize carryover

effects. Participants were advised to be refrain from strenuous activities for 24 hours prior to the experiments. The study had approval of University Ethics review board, and all participants gave written consent.

### **Measurement of Isometric Force and Surface Electromyography (sEMG)**

Force measurements were obtained from right elbow isometric flexion using a purpose-built static rig with a load cell (Model 615, S-Type Load Cell, Tedea-Huntleigh Electronics, UK) over wrist, while the forearm was supinated, the shoulder immobilized slightly flexed, and the elbow at 90° flexion.. The force signals were simultaneously recorded with surface EMG (sEMG) obtained from biceps brachii m. (BB), and the brachioradialis m. (BR) using pairs of silver/silver chloride (Ag/AgCl) disposable self-adhesive electrodes (KENDAL, SOFT-E, H59P, Henleys Medical, Welwyn Garden City, UK) using standard recording sites (Cram, Kasman & Holtz, 1998). The reference electrode was placed over the medial epicondyle of the humerus. The analogue force signal and the differentially recorded EMG signals were both amplified 300 or 1000 times, filtered [force signals: (high pass DC-offset, low pass 2 KHz), EMG signals: (20Hz high pass, 2KHz low pass), (Quad 1902, 4 channels, Cambridge Electronic Design (CED), Cambridge, UK)], and simultaneously sampled and digitized (4 KHz, micro 1401, CED). All digitized data (force and sEMG) were stored on a personal computer for subsequent analysis (Spike v6 and Signal v4 for Windows, CED).

### **Transcranial Magnetic Stimulation (TMS)**

Single-pulse TMS over the left motor cortex (at “hot spot” of Biceps and BR, 4 cm left and 0.5 cm posterior of vertex) was applied using biphasic magnetic stimulation (single pulse mode of Magstim Rapid, Magstim Company Ltd, Whitland, Wales, UK), through a 70mm figure of eight coil of maximum magnetic field strength of 2 Tesla (T). The resting motor threshold (RMT) was defined as the lowest stimulus intensity to elicit a reliable MEP in 50% of 10-12 consecutive stimuli with the muscle relaxed (Reid, Chiappa & Cros, 2002). Resting MEP responses were produced using a stimulus intensity 120% of the RMT for each participant, and were taken before an assessment of perceived effort throughout the time course of the session. Average MEP responses were determined from 15 consecutive evoked potentials to TMS (0.1Hz) and quantified by area method, from a 30ms fixed width window from the MEP onset using an automated analysis with visual inspection of background EMG to ensure a relaxed muscle state was maintained (Signal v4 for Windows, CED software). Mean MEPs were obtained in pre-stimulation period in two blocks one before and after force matching effort rating task, and then at 1, 20 and 40 min. post tDCS (Fig. 1).

<< Figure 1 about here >>

### **Use of 0-10 NRS for Force matching- Effort Rating**



Perception of effort was assessed during successive 15min-blocks of 3 trials (3-5 sec) of sustained isometric elbow flexion, at submaximal (30%, 50%, 70%) randomly applied levels of force and at 100% maximal voluntary contraction (MVC) with 30 second rest periods, according to previously published methods using a Numerical rating scale (0-10 NRS), (Lampropoulou & Nowicky, 2012). The two end points of the scale are 0, no effort at rest, and 10, maximum voluntary effort during production of the MVC of isometric elbow flexion determined at the outset of the session and at the outset of each new block. The MVC was determined for each participant with verbal encouragement so that fixed %MVC force levels could be automatically selected for all subsequent trials. In the post tDCS blocks we also added trials at 50% and 70% of the original MVC determined at the outset of the experiment. Participants were provided with visual feedback of force of each trial on a pc monitor and required to match the target force for 3-5 sec. guided by a horizontal line always set at the middle of the display window and then asked for a verbal rating of effort on the 0-10 NRS. The monitor provided no visual force scaling cues. Effort ratings were immediately recorded by keyboard entry by the experimenter and saved with force and EMG data for offline analysis. Effort scores were obtained in two blocks before and at 5, 25 and 45 min post tDCS.

### **Mood Rating Scale**

The Positive and Negative Affect Schedule (PANAS) was a secondary outcome measurement for assessing possible effects of tDCS on the general state of mood of the participants. The PANAS gauges changes in mood that might indirectly affect

perception of effort as psychological factors such as attention, mood, and motivation have been linked to fatigue and effects on exercise performance (Zwarts, Bleijenberg & van Engelen, 2008). Details on the PANAS for self reporting of mood have been detailed elsewhere (Crawford & Henry, 2004; Watson, Clark & Tellegen, 1988). Participants were asked to complete the PANAS at the beginning, immediately after tDCS and at end of each session (Fig. 1).

### **Transcranial Direct Current Stimulation (tDCS)**

1.5mA tDCS was applied for 10 minutes (current density,  $62 \mu\text{A}/\text{cm}^2$ ) using a battery operated device (DC-Stimulator: CX-6650, model TRCU-04A, Rolf Schneider Electronics, Germany) with either the anode or cathode centred over the left motor cortex hot spot identified for the elbow flexors by TMS, and the opposite electrode positioned on the left medial deltoid of the shoulder in an extracephalic montage. The conductive rubber electrodes were inserted into saline soaked sponge electrodes (wet dimensions of  $24.2 \text{ cm}^2$ ). This electrode montage was used previously for limiting the effects to one hemisphere (Nitsche et al., 2008; Cogiamanian et al., 2007), has been noted as safe in healthy volunteers without any significant cardio-respiratory and autonomic side effects and within recommended current limits (Poreisz, Boros, Antal & Paulus, 2007; Vandermeeren, Jamart & Osseman, 2010). For the verum stimulation, direct current was ramped on over 10 sec at onset and ramped off at 10 min, or for the sham-control stimulation 10 sec ramp at onset and then ramped off at 45 sec., as recommended for increasing

habituation to current and reducing detection (Gandiga et al, 2006). The duration of the sham stimulation used here is therefore unlikely to produce any long lasting effects.

### **Experimental procedure**

At the outset of each session, participants practiced visually guided stable isometric contractions to ensure reliability of the ratings of the perceived effort. The MVC was defined as the mean of 3 verbally encouraged maximum contractions undertaken as part of the force matching- effort rating task administered throughout the experiment. During the pre-stimulation period, two blocks of matching- effort rating trials formed the baseline assessment and for post-stimulation single blocks were obtained at 5, 20 and 45 minutes to monitor the duration of after-effects of tDCS. Additionally, motor cortex excitability and mood assessment were measured before and after the stimulation in the order and times indicated for each session shown in the experiment timeline (see Fig. 1). In all sessions both participants and the experimenter were blinded to the intervention type.

### **Data Analysis**

SEMG amplitude (mV) was quantified by root mean square (rms) method over 1 sec. during sustained peak force under visual inspection. All force and sEMG data were normalized to the MVC values at each time point for each participant and averaged

within each block. Average MEP responses following stimulation were normalized to pre-stimulation baseline MEP responses for each participant averaged over the two baseline assessments. The scores from the PANAS questionnaire were analyzed separately for the positive and negative affect questions for the mood assessment changes. The 0-10 NRS data for all intermediate force levels of three trials were averaged for each block before and after the stimulation. All dependent variables were tested for consistency at baseline across the three sessions.

We used within subjects repeated measures ANOVA ( 2 way - main factors: tDCS stimulation and time, additionally 3 way- force level) to assess changes in the MEP area, mood, perception of voluntary effort and the EMG activity of flexors due to tDCS. The Spearman's rho Correlation analysis ( $\rho$ ) was used for correlation between target level of force and produced voluntary force. The Intra Class Correlation (ICC) was used to assess the agreement between test and re-test effort ratings of each participants between the three sessions Means and Standard Deviations (SD) or 95% Confidence intervals (CI) are reported and Standard Error of Means (SEMs) are shown for figures. Significance level was set at  $p < 0.05$  and post hoc comparisons were by t-tests, with Bonferroni corrections. F ratio, p values and Partial  $\eta^2$  for effect size are reported. All statistical tests were performed using SPSS (version 15; SPSS for Windows, 2007 Chicago: SPSS Inc).

## Results

### Baseline Measures

12 healthy volunteers participated in the study, and data for subsequent measures were used, however, MEP data for all three sessions was not complete from 2 participants and were therefore excluded from this analysis. There were no significant baseline differences for the three sessions with respect to: MVC ( $F_{(2, 22)}=0.19$ ,  $p=0.83$ , Partial  $\eta^2=0.02$ ), the general mood of the participants for Positive Affect ( $F_{(2, 22)}=0.81$ ,  $p=0.50$ , Partial  $\eta^2=0.07$ ) or for Negative Affect ( $F_{(2, 22)}=0.34$ ,  $p=0.72$ , Partial  $\eta^2=0.03$ ) of the PANAS. Participants showed excellent correlation between target force and voluntary force production at baseline for the task across the three sessions (Spearman's  $\rho =0.98$ ,  $p<0.001$ ). Participants were also very consistent in ratings of effort perception across the three sessions at baseline (ICC = 0.96, 95% CI: 0.96 - 0.97).

The RMT (%MSO, maximum stimulator output) was not significantly different across the three sessions, before or 50 min. post tDCS in a two way ANOVA: (tDCS  $F_{(2,16)}=0.63$ ,  $p=0.55$ , Partial  $\eta^2=0.073$ ); (time  $F_{(1,8)}=1.62$ ,  $p=0.24$ , Partial  $\eta^2=0.17$ ); (tDCS x time  $F_{(2,16)}=2.16$ ,  $p=1.1$ , Partial  $\eta^2=0.12$ ). The mean RMT% at baseline across the three sessions was 66.0% MSO (95% CI: 61-71%MSO), and at the end of session of 67.3% MSO (95%CI: 63-71%MSO).

## Effect of tDCS

No participants reported any adverse effects of tDCS. There were no significant effects on the MVC following the repeated bouts of force matching- effort rating task for type of tDCS, ( $F_{(2,22)}=0.14$ ,  $p=0.83$ , Partial  $\eta^2=0.01$ ), time, ( $F_{(3,33)}=0.31$ ,  $p=0.87$ , Partial  $\eta^2=0.027$ ) or the interaction of tDCS x time, ( $F_{(6,66)}=0.50$ ,  $p=0.86$ , Partial  $\eta^2=0.04$ ). Figure 2 shows the group mean changes of %MVC following tDCS.

<< figure 2 about here >>

The force matching - effort ratings were analyzed using a 3 way repeated measures ANOVA for tDCS x time and 3 levels of force (30%,50%,70%) obtained at 5, 25 and 45 minutes post tDCS. The effect of tDCS was not significant ( $F_{(2,20)}=0.394$ ,  $p=0.68$ , Partial  $\eta^2=0.04$ ), nor the effect of time ( $F_{(2,20)}= 3.78$ ,  $p=0.086$ , Partial  $\eta^2=0.22$ ), but the effect of force was significant ( $F_{(2,20)}=355$ ,  $p<0.001$ , Partial  $\eta^2=0.97$ ). The interaction terms were not significant: tDCS x time ( $F_{(4,40)}=0.048$ ,  $p=0.99$ , Partial  $\eta^2=0.01$ ), tDCS x force ( $F_{(4,40)}=1.156$ ,  $p=0.345$ , Partial  $\eta^2=0.10$ ), force x time ( $F_{(4,40)}=1.096$ ,  $p=0.372$ , Partial  $\eta^2=0.1$ ) or tDCS x force x time ( $F_{(8,80)}=0.961$ ,  $p=0.472$ , Partial  $\eta^2=0.09$ ). Figure 3 shows the similar trend observed of a small increase in effort rating for the 50% MVC force level rating task, irrespective of type of tDCS. The factor, level of force, was significantly different between each other in post-hoc comparisons.

<< figure 3 about here>>

Changes in  $EMG_{biceps}$  for the three intermediate levels of force during the task were similarly analyzed in a 3 way repeated measures ANOVA of normalized EMG data at post 5, 25 and 45 minutes post tDCS. The effect of type of tDCS was not significant ( $F_{(2,20)}=0.82$ ,  $p=0.45$ , Partial  $\eta^2=0.08$ ), the effect of time was not significant ( $F_{(3,30)}=2.47$ ,  $p=0.081$ , Partial  $\eta^2=0.20$ ), but the effect of force was significant ( $F_{(2,20)}=418.4$ ,  $p<0.001$ , Partial  $\eta^2=0.9$ ). The two way interaction terms were not significant: tDCs x time ( $F_{(6,60)}=1.95$ ,  $p=0.087$ , Partial  $\eta^2=0.16$ ) and tDCS x force ( $F_{(4,40)}=0.713$ ,  $p=.6$ , Partial  $\eta^2=0.07$ ) and time x force ( $F_{(6,60)}=1.12$ ,  $p=0.36$ , Partial  $\eta^2=0.10$ ). The three way interaction term, tDCS x force x time, was also not significant ( $F_{(12,120)}=0.879$ ,  $p=0.57$ , Partial  $\eta^2=0.08$ ). Figure 4 shows the time course of the biceps EMG for the 50% effort level.

<< figure 4 about here>>

In order to evaluate possible fatigue related shifts in force matching –effort rating we also used 50% and 70% levels of the  $MVC_{pre}$  obtained from the outset of the experiment, in addition to those force levels adjusted at each time point for each post tDCS monitoring time period. The unadjusted effort rating was analyzed in a

two way repeated measures ANOVA for the 50% MVC level only. The effect of type of tDCS was not significant ( $F_{(2,20)}=0.39$ ,  $p=0.68$ , Partial  $\eta^2=0.04$ ), the effect of time was not significant ( $F_{(1.3,13.1)}=2.48$ ,  $p=0.109$ , Partial  $\eta^2=0.20$ ) and the two way interaction of tDCs x time was also not significant ( $F_{(4,40)}=0.185$ ,  $p=0.945$ , Partial  $\eta^2=0.02$ ).

Finally, in order to examine possible effects of tDCS in M1 excitability, the mean MEPs over time were also analyzed. There was no significant effect of type of tDCS on normalized  $MEP_{biceps}$  ratios ( $F_{(2,18)}=0.981$ ,  $p=0.39$ , Partial  $\eta^2=0.1$ ), time ( $F_{(2,18)}=0.1$ ,  $p=0.91$ , Partial  $\eta^2=0.011$ ), or interaction of tDCS x time ( $F_{(4,36)}=0.65$ ,  $p=0.63$ , Partial  $\eta^2=0.067$ ). Figure 5 shows the group mean changes in  $MEP_{biceps}$  over the duration of the experiment. Similarly, for the  $MEP_{brachioradialis}$ , there was no significant effect of type of tDCS, ( $F_{(2,18)}=0.68$ ,  $p=0.52$ , Partial  $\eta^2=0.07$ ), no significant effect of time ( $F_{(1.22,10.9)}=4.55$ ,  $p=0.061$ , Partial  $\eta^2=0.34$ ), and no significant effect of tDCS x time ( $F_{(2.314,20.82)}=0.14$ ,  $p=0.96$ , Partial  $\eta^2=0.012$ ).

<< figure 5 about here >>

## Discussion

This double blind, cross over study examined the possible effects of 10 min of tDCS applied over M1 using an extracephalic montage on the perception of effort



assessed through repeated bouts of a force matching task in the absence of fatigue. We found no significant difference between the anodal, cathodal or sham tDCS over time on isometric flexion maximal voluntary force. The small maximal force changes observed were not different to sham stimulation and show that changes of this magnitude (<10%) represent some variability with repeated bouts of nonfatiguing assessment of maximal force here (Lampropoulou & Nowicky, 2012). This finding corroborates that such a task used for assessment of effort over time (1 hour) was not overtly fatiguing, and subjects were able to accurately and reliably rate effort during the force task. A previous study using a cephalic montage over M1 lower limb location, however 10 min of anodal current resulted in a significant 20% increase in lower limb maximal force 30 min. post stimulation, but used a higher (2mA) current (Tanaka et al., 2009). The Cogiamanian et al. (2007) study using an extracephalic orientation found that anodal but not cathodal tDCS increased endurance time in a sustained, submaximal isometric elbow flexion task. However they did not find a significant effect of tDCS on MVC following the fatiguing exercise task. Because of these effects on endurance time we also adopted an extracephalic electrode montage with a similar intensity (1.5mA) and duration (10min) but with a 44% higher current density (62 rather than 43  $\mu\text{A}/\text{cm}^2$ ) achieved with a smaller (24.4 $\text{cm}^2$  rather than 35  $\text{cm}^2$ ) electrode area, since a study noted this montage was found to be less effective than a cephalic one (Moliadze et al., 2010). However the observed effect on endurance time following anodal tDCS over M1 in the fatiguing protocol was attributed speculatively to modulatory effects on motor/premotor excitability and changes in muscle synergy, reduced pain or improved motivation.

No significant polarity specific effects of tDCS on perception of effort rating in repeated bouts of the force matching task during the 45 min. were observed. We also did not find a significant effect of tDCS on underlying SEMG<sub>biceps</sub> sustained during the task. This latter finding strongly indicates that no observable time dependent change in voluntary drive and hence unlikely to have altered motor command/efference copy generated for each forces level of the matching task used in this experiment. However an absence of tDCS changes in effort and force could imply inefficiency of the cortical stimulation of this montage given that here we also did not observe significant changes in TMS evoked MEP responses from elbow flexors. One other possibility is that the site of stimulation over the cortex centred over M1 hot spot for biceps, may not have been optimal for modulating sensory-perceptual changes. However use of a relatively large electrode size (4x6cm) here, despite being positioned over this M1 location identified using TMS, also overlays adjacent somatosensory cortical areas. deMoree et al (2013) found that effort ratings and EMG increased with weight and was correlated with the increase in movement related cortical potential recorded in EEG over Cz (vertex).

In our previous study a 10 min submaximal fatiguing exercise protocol, caused an overall mean increase of 1.6 in the effort rating accompanied by a significant increase in both sEMG<sub>Biceps</sub> and sEMG<sub>brachioradialis</sub> for 45 min post exercise period (Lampropoulou & Nowicky, 2012). Therefore use of non-fatiguing conditions likely explains why we did not observe a significant effect of tDCS on 0-10 NRS effort ratings here as they are unlikely to arise from changing excitability in sensorimotor

cortex. Both central and peripheral neuromuscular factors contribute to changes in voluntary drive and hence effort in fatiguing exercise. Changes in afferent activity from peripheral alterations in proprioceptive and cutaneous signals may be a necessary linkage for perception of effort changes and as such to central actions (Feldman, 2009). Previous reports tDCS effects on somatosensory perception did inform our study. Thermal detection thresholds were increased following cathodal but not anodal stimulation applied over the somatosensory cortex (S1) in healthy participants (Grundmann et al., 2011). Furthermore, application of anodal tDCS for 20 min. over S1 improved spatial tactile acuity which lasted for 40 min. following stimulation (Ragert, Vandermeeren, Camus & Cohen, 2008). While these effects result from application over the somatosensory cortex, previous work has also shown that 5 min. of anodal tDCS applied over M1 increased both perceptual and pain thresholds to electrical stimulation of the digits (Boggio et al., 2008). Thus evidence suggests that stimulation effects are capable of altering perceptual processes.

Concurrent changes in M1 excitability induced by tDCS in elbow flexor MEP responses to TMS, were not significantly with type of stimulation. An explanation for this lack of an observed change in corticospinal excitability comes from TMS studies which showed the magnitude and polarity of the excitability changes induced by M1 tDCS were state dependent. The magnitude of the effects of anodal tDCS on hand muscle corticospinal excitability were more pronounced in a quiet relaxed state, but attenuated when participants were engaged in either cognitive or motor tasks (i.e., brief submaximal sustained hand contractions), (Antal, Begemeier,

Nitsche & Paulus, 2008; Thirugnanasambandam et al., 2011 ). Similarly a recent study found brief bouts of nonfatiguing exercise in hand muscles depressed corticospinal excitability and is linked to reduced motor performance (Crupi et al. 2013). We observed a similar magnitude of an increase in MEP responses following both cathodal and anodal stimulation compared to control, but again this elevation was not significantly greater than compared with sham tDCS stimulation (see figure 4). These findings suggest that in our study changes in excitability following tDCS may have been attenuated with execution of the force matching task where effects of voluntary muscle activity alone has persistent after effects.

Our study utilized a within subjects design and a double blind administration of tDCS as recommended for studies of noninvasive brain stimulation on behaviour (Brunoni et al., 2011). We found with the sham stimulation there were small consistent change in our measures over time, suggesting that for studies utilizing TMS in behavioural motor tasks, it may be important to utilize a true matched sham control. Given the advantages of using a within subject design to reduce the effects of individual variability (i.e., increased power), we did not observe a polarity specific effect on ratings of perception of effort during nonfatiguing exercise.

In conclusion, for a brief application over the sensorimotor cortex, our study did not detect any significant polarity specific tDCS changes of subjective, self-reported force matching- effort rating isometric elbow flexion task. Further investigation could examine the application parameters of tDCS and over other relevant cortical areas as well as during fatiguing exercise conditions for possible effects on

perception of effort changes which are associated with voluntary control of sustained muscle activity.

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**Conflict of interest:**

Authors declare no conflict of interest.

## References

- Antal, A., Begemeier, S., Nitsche, M. A., & Paulus, W. (2008). Prior state of cortical activity influences subsequent practicing of a visuomotor coordination task. *Neuropsychologia, 46*(13), 3157-3161.
- Antal, A., Terney, D., Poreisz, C., & Paulus, W. (2007). Towards unravelling task-related modulations of neuroplastic changes induced in the human motor cortex. *The European Journal of Neuroscience, 26*(9), 2687-2691.
- Baudewig, J., Nitsche, M. A., Paulus, W., & Frahm, J. (2001). Regional modulation of BOLD MRI responses to human sensorimotor activation by transcranial direct current stimulation. *Magnetic Resonance in Medicine : Official Journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine, 45*(2), 196-201.
- Bindman, L. J., Lippold, O. C., & Redfearn, J. W. (1964). The action of brief polarizing currents on the cerebral cortex of the rat (1) during current flow and (2) in the production of long-lasting after-effects. *The Journal of Physiology, 172*, 369-382.
- Boggio, P. S., Zaghi, S., Lopes, M., & Fregni, F. (2008). Modulatory effects of anodal transcranial direct current stimulation on perception and pain thresholds in healthy volunteers. *European Journal of Neurology : The Official Journal of the European Federation of Neurological Societies, 15*(10), 1124-1130.
- Brunoni, A. R., Nitsche, M. A., Bolognini, N., Bikson, M., Wagner, T., Merabet, L., et al. (2011). Clinical research with transcranial direct current stimulation (tDCS): Challenges and future directions. *Brain Stimulation, 175*-195.

- Cogiமானian, F., Marceglia, S., Ardolino, G., Barbieri, S., & Priori, A. (2007). Improved isometric force endurance after transcranial direct current stimulation over the human motor cortical areas. *The European Journal of Neuroscience*, 26(1), 242-249.
- Cram, J. R., Kasman, G. S., & Holtz, J. (1998). *Introduction to surface electromyography* (1st ed.). USA: Aspen.
- Crawford, J. R., & Henry, J. D. (2004). The positive and negative affect schedule (PANAS): Construct validity, measurement properties and normative data in a large non-clinical sample. *The British Journal of Clinical Psychology / the British Psychological Society*, 43(Pt 3), 245-265.
- Crupi, D., Cruciata, G., et al. (2013) Protracted exercise without overt neuromuscular fatigue influences cortical excitability. *Journal of Motor Behavior*, 45(2), 127-138.
- deMorree, H.M., Klein, C. and Marcora, S.M. (2012) Perception of effort reflects central motor command during movement execution. *Psychophysiology* 49, 1242-1253.
- Dieckhofer, A., Waberski, T. D., Nitsche, M., Paulus, W., Buchner, H., & Gobbele, R. (2006). Transcranial direct current stimulation applied over the somatosensory cortex - differential effect on low and high frequency SEPs. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, 117(10), 2221-2227.
- Feldman, A.G. (2009). New insights into action-perception coupling. *Experimental brain research. Experimentelle Hirnforschung. Expérimentation cérébrale* 194 (1), 39-58.

- Gandevia, S. C. (2001). Spinal and supraspinal factors in human muscle fatigue. *Physiological Reviews*, *81*(4), 1725-1789.
- Gandiga, P. C., Hummel, F. C., & Cohen, L. G. (2006). Transcranial DC stimulation (tDCS): A tool for double-blind sham-controlled clinical studies in brain stimulation. *Clinical Neurophysiology*, *117*(4), 845-850.
- Grundmann, L., Rolke, R., Nitsche, M. A., Pavlakovic, G., Happe, S., Treede, R. D., et al. (2011). Effects of transcranial direct current stimulation of the primary sensory cortex on somatosensory perception. *Brain Stimulation*, *4*(4), 253-260.
- Hummel, F. C., Voller, B., Celnik, P., Floel, A., Giraux, P., Gerloff, C., et al. (2006). Effects of brain polarization on reaction times and pinch force in chronic stroke. *BMC Neuroscience*, *7*, 73.
- Jacobson, L., Koslowsky, M., & Lavidor, M. (2012). tDCS polarity effects in motor and cognitive domains: A meta-analytical review. *Experimental Brain Research. Experimentelle Hirnforschung. Experimentation Cerebrale*, *216*(1), 1-10.
- Lampropoulou, S., & Nowicky, A. V. (2012). Evaluation of the numeric rating scale for perception of effort during isometric elbow flexion exercise. *European Journal of Applied Physiology*, *112*(3), 1167-1175.
- Lang, N., Nitsche, M. A., Paulus, W., Rothwell, J. C., & Lemon, R. N. (2004). Effects of transcranial direct current stimulation over the human motor cortex on corticospinal and transcallosal excitability. *Experimental Brain Research. Experimentelle Hirnforschung. Experimentation Cerebrale*, *156*(4), 439-443.
- Matsunaga, K., Nitsche, M. A., Tsuji, S., & Rothwell, J. C. (2004). Effect of transcranial DC sensorimotor cortex stimulation on somatosensory evoked potentials in



humans. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, 115(2), 456-460.

Moliadze, V., Antal, A., & Paulus, W. (2010). Electrode-distance dependent after-effects of transcranial direct and random noise stimulation with extracephalic reference electrodes. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, 121(12), 2165-2171.

Nitsche, M. A., Cohen, L. G., Wassermann, E. M., Priori, A., Lang, N., Antal, A., et al. (2008). Transcranial direct current stimulation: State of the art 2008. *Brain Stimulation*, 1(3), 206-223.

Nitsche, M. A., Fricke K, Henschke U, Schlitterlau A, Liebetanz D, Lang, N., Henning S., Tergau F, Paulus, W. (2003). Pharmacological modulation of cortical excitability shifts induced by transcranial direct current stimulation in humans. *The Journal of Physiology*, 553, 293-301.

Nitsche, M. A., & Paulus, W. (2000). Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *The Journal of Physiology*, 527 Pt 3, 633-639.

Nitsche, M. A., & Paulus, W. (2001). Sustained excitability elevations induced by transcranial DC motor cortex stimulation in humans. *Neurology*, 57(10), 1899-1901.

Nitsche, M. A., Seeber, A., Frommann, K., Klein, C. C., Rochford, C., Nitsche, M. S., et al. (2005). Modulating parameters of excitability during and after transcranial direct current stimulation of the human motor cortex. *The Journal of Physiology*, 568(Pt 1), 291-303.

- Poreisz, C., Boros, K., Antal, A., & Paulus, W. (2007). Safety aspects of transcranial direct current stimulation concerning healthy subjects and patients. *Brain Research Bulletin*, 72(4-6), 208-214.
- Power, H. A., Norton, J. A., Porter, C. L., Doyle, Z., Hui, I., & Chan, K. M. (2006). Transcranial direct current stimulation of the primary motor cortex affects cortical drive to human musculature as assessed by intermuscular coherence. *The Journal of Physiology*, 577(Pt 3), 795-803.
- Priori, A. (2003). Brain polarization in humans: A reappraisal of an old tool for prolonged non-invasive modulation of brain excitability. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, 114(4), 589-595.
- Ragert, P., Vandermeeren, Y., Camus, M., & Cohen, L. G. (2008). Improvement of spatial tactile acuity by transcranial direct current stimulation. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology*, 119(4), 805-811.
- Reid, A. E., Chiappa, K.H. & Cros, D. (2002). In Pascual-Leone A., Davey N. J., Rothwell J. C. & Wassermann, E.M. and Puri, B.K.(Eds.), *Motor threshold, facilitation and the silent period in cortical magnetic stimulation in (pp97-111)*. (1st ed.). New York: Handbook of Transcranial Magnetic Stimulation.
- Ross, E. Z., Middleton, N., Shave, R., George, K., & Nowicky, A. (2007). Corticomotor excitability contributes to neuromuscular fatigue following marathon running in man. *Experimental Physiology*, 92(2), 417-426.
- Shafi, M. M., Westover, M. B., Fox, M. D., & Pascual-Leone, A. (2012). Exploration and modulation of brain network interactions with noninvasive brain

stimulation in combination with neuroimaging. *The European Journal of Neuroscience*, 35(6), 805-825.

Tanaka, S., Hanakawa, T., Honda, M., & Watanabe, K. (2009). Enhancement of pinch force in the lower leg by anodal transcranial direct current stimulation. *Experimental Brain Research. Experimentelle Hirnforschung. Experimentation Cerebrale*, 196(3), 459-465.

Tanaka, S., Takeda, K., Otaka, Y., Kita, K., Osu, R., Honda, M., et al. (2011). Single session of transcranial direct current stimulation transiently increases knee extensor force in patients with hemiparetic stroke. *Neurorehabilitation and Neural Repair*, 25(6), 565-569.

Tanaka, S., & Watanabe, K. (2009). Transcranial direct current stimulation--a new tool for human cognitive neuroscience. *Brain and Nerve = Shinkei Kenkyu no Shinpo*, 61(1), 53-64.

Taylor, J. L., Butler, J. E., & Gandevia, S. C. (2000). Changes in muscle afferents, motoneurons and motor drive during muscle fatigue. *European Journal of Applied Physiology*, 83(2-3), 106-115.

Taylor, J. L., & Gandevia, S. C. (2008). A comparison of central aspects of fatigue in submaximal and maximal voluntary contractions. *Journal of Applied Physiology (Bethesda, Md.: 1985)*, 104(2), 542-550.

Taylor, J. L., Todd, G., & Gandevia, S. C. (2006). Evidence for a supraspinal contribution to human muscle fatigue. *Clinical and Experimental Pharmacology & Physiology*, 33(4), 400-405.

- Tergau, F., Geese, R., Bauer, A., Baur, S., Paulus, W., & Reimers, C. D. (2000). Motor cortex fatigue in sports measured by transcranial magnetic double stimulation. *Medicine and Science in Sports and Exercise, 32*(11), 1942-1948.
- Thirugnanasambandam, N., Sparing, R., Dafotakis, M., Meister, I. G., Paulus, W., Nitsche, M. A., et al. (2011). Isometric contraction interferes with transcranial direct current stimulation (tDCS) induced plasticity: Evidence of state-dependent neuromodulation in human motor cortex. *Restorative Neurology and Neuroscience, 29*(5), 311-320.
- Vandermeeren, Y., Jamart, J., & Osseman, M. (2010). Effect of tDCS with an extracephalic reference electrode on cardio-respiratory and autonomic functions. *BMC Neuroscience, 11*, 38.
- Watson, D., Clark, L. A., & Tellegen, A. (1988). Development and validation of brief measures of positive and negative affect: The PANAS scales. *Journal of Personality and Social Psychology, 54*(6), 1063-1070.
- Zwarts, M. J., Bleijenberg, G., & van Engelen, B. G. (2008). Clinical neurophysiology of fatigue. *Clinical Neurophysiology : Official Journal of the International Federation of Clinical Neurophysiology, 119*(1), 2-10.

## **Legends**

Figure 1.

Flow chart of the experimental procedure. The horizontal blue line represents the real time line of the experiment. At the sunset of every session participants were familiarized with the force rig, the effort scale and the isometric contractions. Additionally they were prepared in regards the hot spot and the Resting Motor Threshold (RMT) of elbow flexors for the Transcranial Magnetic Stimulation. The EMG recording electrodes were placed over muscles of interest and participants were strapped to the force rig. The PANAS questionnaire was also answered as part of the mood assessment at the beginning of the session. The mood assessment was also repeated immediately after the tDCS intervention and at the end of the session. Two blocks of MEPs and effort measurements were taken before (baseline 1 and baseline 2) and three after (post 1, post 2, post3) the intervention. The vertical small arrows represent the measurements taken at every time point during the experiment. The grey box corresponds to the tDCS intervention. Three sessions were repeated and a different type of tDCS polarity was used (anodal, cathodal and sham) at every session until three types have been completed.

Figure 2.

Effects of tDCS on Group Mean Normalized MVC during time course of experiment were analyzed by using within subjects - repeated measures ANOVA. No significant differences were observed for type of stimulation (see text). MVC responses were normalized to first baseline time point. Administration of blocks of perception of effort rating for intermediate force levels are at five times throughout the experiment (small bars). Application of tDCS for 10 min (1.5mA) is shown by hatched bar between -10 and 0 min of experimental time course. Group Means and Standard Error of Mean (n=12) are shown at each time points. Legend shows type of tDCS (sham, anodal, cathodal) with symbol – line combinations.

Figure 3.

Effects of tDCS on Effort rating of 50% MVC force level during time course of experiment were analyzed by using within subjects - repeated measures ANOVA. No significant differences were observed for type of stimulation (see text).

Administration of blocks of perception of effort rating for intermediate force levels are at five times throughout the experiment and the group mean effort ratings are shown at indicative time points before and after tDCS. Application of tDCS for 10 min (1.5mA) shown by block between -10 and 0 min. Group Means and Standard Error of Mean are shown (n=12) are shown at each time points. Legend shows type of tDCS (sham, anodal, cathodal) with symbol – line combinations.

Figure 4.

Effects of tDCS on biceps sEMG for 50% MVC, normalized to MVC of the perception of effort rating task during the time course of experiment were analyzed by using within subjects - repeated measures ANOVA. No significant differences were observed for type of stimulation (see text). Administration of blocks of perception of effort rating for intermediate force levels are at five times throughout the experiment and the corresponding mean biceps sEMG for 50%MVC are shown at indicative time points before and after tDCS. Application of tDCS for 10 min (1.5mA) shown by block between -10 and 0 min. Group Means and Standard Error of Mean (n=12) are shown at each time points. Legend shows type of tDCS (sham, anodal, cathodal) with symbol – line combinations.



Figure 5.

Effects of tDCS on Group Mean Normalized Biceps MEP responses during time course of experiment were analyzed by using within subjects - repeated measures ANOVA. No significant differences were observed for type of stimulation (see text). MEP responses were normalized to second baseline time point and expressed as a ratio here. Administration of blocks of perception of effort rating for intermediate force levels are at five times throughout the experiment (small bars). Application of tDCS for 10 min (1.5mA) shown by hatched bar between -10 and 0 min of experimental time course. Group Means and Standard Error of Mean are shown (n=10) are shown at each time points. Legend shows type of tDCS (sham, anodal, cathodal) with symbol – line combinations.

## Figures

Figure 1

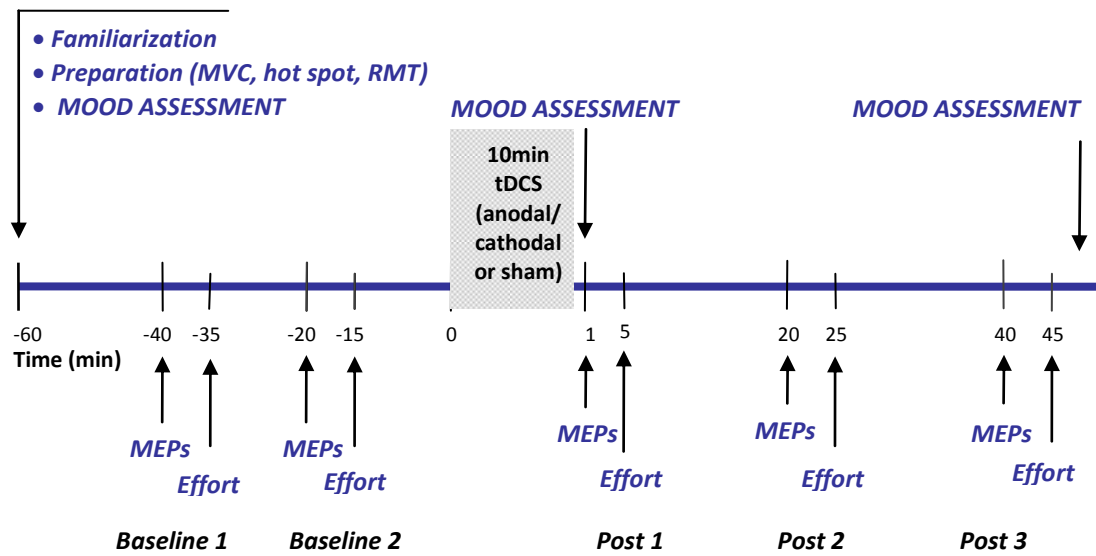


Figure 2

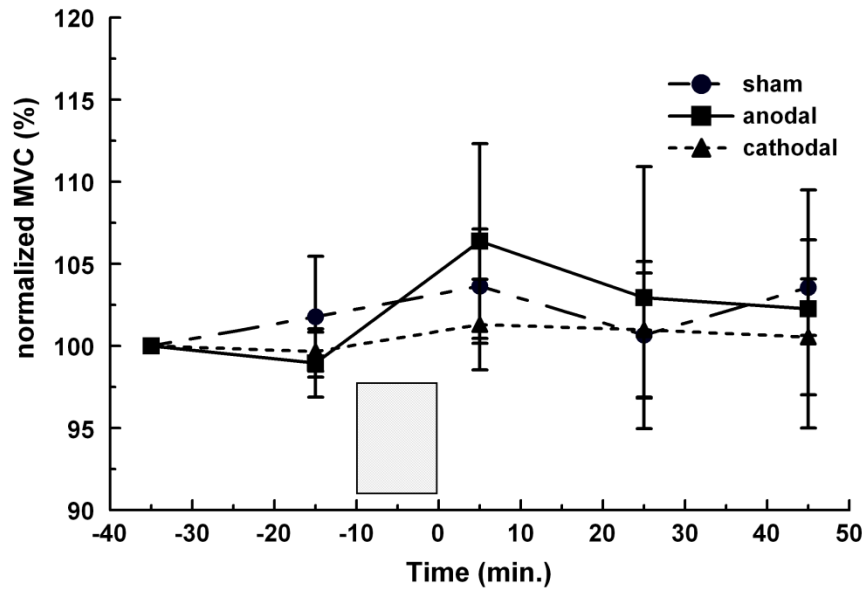


Figure 3.

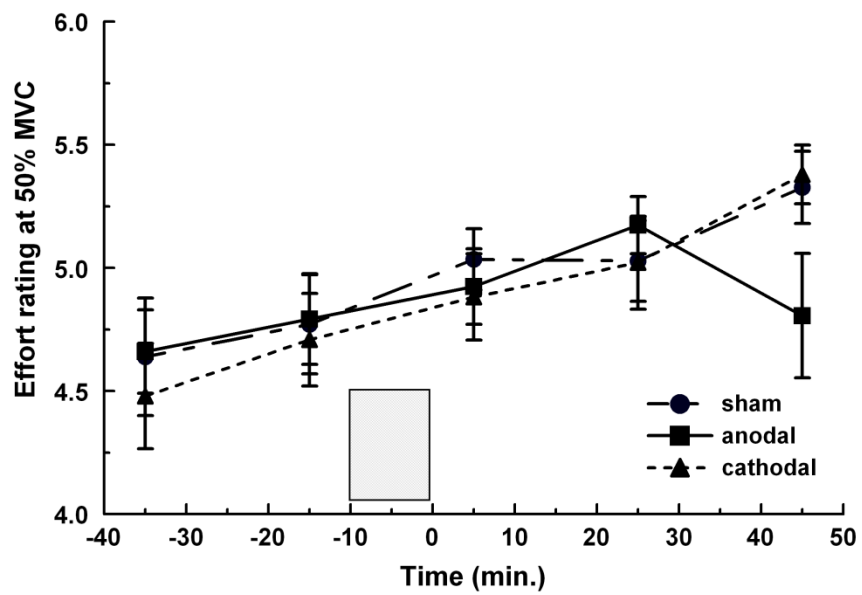


Figure 4.

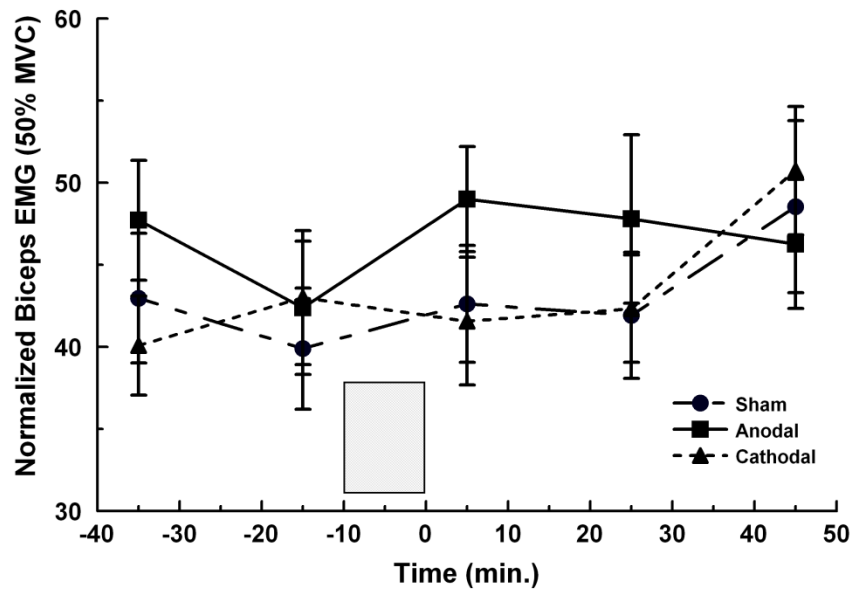


Figure 5.

