# ANODAL TRANSCRANIAL DIRECT CURRENT STIMULATION DOES NOT IMPROVE PERFORMANCE IN A TIME TRIAL CYCLING ERGOMETER TEST

#### JON S. AAES AND DENNIS KNUDSEN

Master's thesis, sports science, Department of Health Science and Technology, Faculty of Medicine, Aalborg University, Aalborg, Denmark

# ABSTRACT

Anodal transcranial direct current stimulation (atDCS) has been shown to improve time to fatigue (TTF) in incremental- and constant load cycling tests, by increasing the cortical excitability, while also modulating heartrate (HR) and rate of (RPE) perceived exertion at submaximal intensities. The purpose of this study was to: Examine the effect of a-tDCS on performance during a 250 kJ time trial cycling test and examine the effect of a-tDCS on a 120 s. RPE-production test, with a subjective intensity at 13 on the RPE scale.

Twenty subjects underwent the 250 kJ time trial and the RPE-production test four times in a randomized order (familiarization, control, sham and a-tDCS). To assess physiological parameters, HR and Vo2 were measured, and RPE was obtained after every 25 kJ during the 250 kJ time trial. 11 subjects received transcranial magnetic stimulation (TMS) at sham and a-tDCS trials to examine Motor evoked potentials (MEP).

MEPs increased significantly after receiving 13 min of a-tDCS (tDCS\_Pre ( $452 \pm 374 \mu V$ ) and tDCS\_Post ( $676 \pm 642 \mu V$ ) (p = 0.038)). No significant difference was found in completion time of the 250 kJ time trial, the RPE-production test, in RPE or Vo2. One significant difference was found in HR at 200 kJ (p = 0.043) between the control ( $169 \pm 12$  bpm) and the sham ( $172 \pm 12$  bpm) condition (p = 0.023).

In conclusion, MEPs was significantly increased after a-tDCS. No differences in accumulated energy was observed in the RPE-production test in this study. a-tDCS appears to have no effect on completion time in a self-paced time trial test. Similarities in completion time, HR, Vo2, RPEproduction and RPE suggest that, 13min of a-tDCS was insufficient in modulating the central mechanisms involved in these factors.

#### **INTRODUCTION**

a-tDCS is a non-invasive brain stimulation technique which delivers a constant electrical stimulation to a targeted area of the brain of 1-2 mA (22). The stimulation is considered safe as more than 100 studies using tDCS on healthy participants or patients have found no side effects besides slight itching under the electrode and/or headache (22). tDCS is a well-known method, of modulating cortical excitability capable measured by motor evoked potentials (MEP) (6,14,18). The effect of tDCS is polarity specific and modulates the resting membrane potential of the targeted neurons, with anodal stimulation being excitatory and cathodal stimulation inhibitory (2). a-tDCS has been used as a rehabilitation tool to treat stroke patients (12,13) and chronic depression (7) with promising results.

There is an increasing interest in tDCS as a tool to enhance sports performance by trying to modulate the excitability in the motor cortex. The excitatory effect following a-tDCS may result in less excitatory input from the supplementary motor area (SMA) to M1, to produce the same muscle recruitment, which may lead to a lower rate of perceived exertion (RPE) (3,4,19). Studies finding an increased cortical excitability following a-tDCS suggest that the increase may lead to an increased descending drive while delaying supraspinal fatigue (9,23). Failure to maintain descending drive from the motor cortex corresponding to the requirement of the activity has been defined as central fatigue which together with peripheral fatigue is responsible for muscle fatigue (23). Promising results are observed when performing simple submaximal contractions until fatigue with an intensity of 20-35 %. Cogiamanian (9) assessed a 35 % MVC fatiguing isometric contraction of the left elbow flexor in 24 healthy subjects, where time to fatigue decreased significantly less after a-tDCS (-21.1 %) than after cathodal stimulation (-35.7 %) and the control condition (-39.3 %). This finding corresponds with Abdelmoula et al. (1) who found a similar less decreased endurance time after atDCS (-14.4 %) compared to sham (-23.3 %) during a 35 % MVC test of the right elbow flexor muscles. Oki et al. (2016) found an approximately 15 % increase in mean time to task failure on a 20 % MVC elbow flexor test, with a-tDCS compared to sham. Furthermore Angius et al. (4) found an improvement in a isometric 20 % MVC endurance test following a-tDCS (219  $\pm$  136 s) compared to sham  $(173 \pm 114 \text{ s})$  and control  $(187 \pm 121 \text{ s})$ .

The aforementioned studies focused on single-joint exercises. These exercises give a more controlled exploration of physiological mechanisms associated with fatigue, while whole-body exercise are more representative for sporting competition (2). It is therefore important to examine whether these improvements in performance can be applied in different sports. Recently, several studies have been using incremental cycling tests with different durations and intensities to examine whether a-tDCS influences cycling performance. Okano et al. (19) performed a maximal incremental cycling test, starting at 15 W with increments of 25 W/min until the subjects were unable to sustain 80 rpm for longer than 5 seconds. They found an increased peak power (PP) and a significantly lower heart rate (HR) and RPE at submaximal intensities following a-tDCS. Angius et al. (3) performed a constant load cycling test and found a significantly longer time to fatigue (TTF) and significantly lower RPE at submaximal intensities, with no changes in HR following a-tDCS. Vitor-Costa et al. (25) performed a constant load cycling test, and found an increased TTF, but no changes in HR and RPE. Lattari et al. (15) performed a 100 % peak power cycling test, and also found a longer TTF with no changes in RPE following a-tDCS.

These results indicate that a-tDCS might not just give a longer TTF in single-joint exercises, but also in cycling performances of different nature and various intensities. Seeing as previous studies have tested on endurance time, which may not be representative of sporting performance, as enduring a specific intensity for a longer timeperiod, does not necessarily result in a faster completion time, it seems reasonable to examine the effect of a-tDCS on a time trial cycling test, at a fixed distance.

To our knowledge, only one study has investigated the effect of a-tDCS on a time trial cycling test with a fixed distance (20 km), finding no significant differences in completion time, HR or RPE following a-tDCS compared to sham (5). However, they placed the anode at the temporal cortex and not the motor cortex, which differs from other studies. Furthermore, the results from Angius et al. (3) and Okano et al. (19) indicate that a-tDCS might have an influence on RPE at submaximal intensities, which will result in a higher wattage produced after a-tDCS compared to no stimulation, with no changes in perceived effort, leading to a higher performance output at the same RPE.

The purpose of this study was therefore to: Examine the effect of a-tDCS on a time trial cycling test and examine the effect of a-tDCS on a 120 s. RPE-production test, with a subjective intensity at 13 on the RPE scale. Based on the increased performance in TTF during cycling tests found in previous studies (3,19,25), we hypothesized a faster completion time in the 250 kJ cycling test following a-tDCS, and an increased energy production in the RPE-production test.

# METHODS

# **Subjects**

Twenty recreationally trained subjects participated in this randomized controlled study. The subjects were on average 26 ( $\pm$  4) years old, 181.5 ( $\pm$  9.9) cm, and weighed 83.9 (± 17.9) kg. 11 subjects volunteered to receive TMS at the sham and atDCS trials. The subjects were excluded from the study, if they had any physical or neurological disorders, or if they failed the Transcranial Magnetic Stimulation Adult Safety Screen (TASS) for the TMS portion of the study (20). Prior to participation, subjects were given a verbal explanation of the test procedure and signed a written, informed consent. The study was conducted in accordance with the Helsinki Declaration and approved by the local Ethics Committee (VN20170081).

#### Procedure

Subjects attended the laboratory on four separate days, including a familiarization trial followed by three experimental trials. The three experimental trials; control, sham, and a-tDCS, were completed in a randomized counterbalanced order. Subjects were instructed to refrain from consuming alcohol, performing intense exercise 48 hours prior to a trial, and from consuming caffeine 6 hours prior to a trial. All trials were completed within 20 days and were separated by a minimum of 48 hours. Upon arrival of the first trial, subjects were familiarized with the laboratory equipment and the procedures of the following trials. A 3-minute warm-up of incremental intensity was performed on a bike ergometer (Excalibur sport, Lode, Groningen, Netherlands), followed by a 5-minute RPE production, where the subjects were instructed to cycle with an intensity corresponding a rating of 13 on the 6-20 RPE scale. Subjects then performed a time trial of 250 kJ, rating RPE at every completed 25 kJ. Throughout warm-up, RPE-production test and the 250 kJ time trial, Vo2 and HR were recorded using an automated on-line breath-by-breath system (Jaeger Vyntus CPX, Intramedic, Gentofte, Denmark). During the control trial, subjects underwent the same procedures as in the familiarization trial. At the atDCS and sham trial, 11 subjects received TMS prior to and after stimulation, and then underwent the RPE-production test and the 250 kJ time trial.

# **Transcranial magnetic stimulation**

During TMS, surface electromyography electrodes (Neuroline 720; Ambu A/S; Denmark) were placed on the skin over rectus femoris (RF) on the right leg, which were located, shaved, abraded and in **SENIAM** cleaned accordance to recommendations. А Magstim stimulator (Magstim 200, Magstim Company, Dyfed, UK) was used to locate the hotspot of RF. Placed over Cz, the coil was moved in ~1 cm steps in anteriorposterior and lateral-medial directions, until the highest and most consistent MEP was elicited. The hotspot was marked on the subject's scalp with a felt pen. Resting motor threshold was found, defined as 5 out of 10 consecutive stimuli with a peak-to-peak amplitude of  $\geq 50 \ \mu V$  (21). Mean MEP amplitudes were calculated from the average of 20 peak-to-peak MEP responses elicited at 120 % of RMT stimulus intensity pre and post a-tDCS or sham (14).

#### **Transcranial direct current stimulation**

A-tDCS was delivered using a battery driven, constant current stimulator (Linear Stimulus Isolator A395. World Precision Instruments. Sarasota, Florida, USA), through two custom made electrodes, with the anode being  $9x4 \text{ cm} (36 \text{ cm}^2)$ and the cathode 7x5 cm (35 cm<sup>2</sup>). Before use, the electrodes were placed in a saline (150 mM NaCl) soaked sponge. Since both legs were used during the cycling test, both the right and left M1 (corresponding C3 and C4 on the 10-20 EEG system) were stimulated. The anode was centered over Cz using the EEG 20-10 system, resulting in 4.5 cm of each side of the motor cortex being stimulated (25), with the cathode placed at the right shoulder at the center of the deltoid muscle (4). During a-tDCS, subjects received an electric current amplitude of 2 mA for 13 minutes with a 10-second ramp up and ramp down. The sham stimulation consisted of a 10-second ramp up, directly followed by a 10-second ramp down, after which subjects received no stimulation for the remainder of the 13 minutes.

# **RPE-production test and 250 kJ time trial**

Oxygen consumption and heart rate were recorded during the RPE-production test, and the 250kJ time trial, using an online breath-by-breath system. Seating position on the bike ergometer was noted for each subject and used on every subsequent trial. The warm-up consisted of 3 minutes with incremental intensity, directly followed by the 5minute RPE-production test. During the RPEproduction test subjects were asked to stay at an intensity corresponding a rating of 13 on the 6-20 RPE scale (8). Following a 3-minute rest subjects then performed the 250 kJ time trial. During the time trial subjects were able to adjust the resistance of the bike ergometer and were able to see the completed amount of kJ of the test. At every completed 25 kJ, subjects were asked to rate their RPE. Verbal encouragement was given throughout the time trial.

#### **Data processing**

EMG signals were collected with a sampling frequency of 5 KHz, sensitivity of 500 mV/V and a bandwidth of 5-1000 Hz. Watt and accumulated energy was obtained from the cycling ergometer using the accompanying software Lode Ergometry Manager 9. Oxygen consumption and heart rate obtained through the accompanying was SentrySuite software of the Vyntus CPX system. Oxygen consumption was measured in breath-bybreath while heart rate was sampled at 2 second intervals. The TMS data was collected from Mr. Kick version 3 (Knud Larsen, Aalborg University).

# STATISTICAL ANALYSIS

All data were tested for sphericity using Mauchly's test. Furthermore, all data were tested for normality using the Shapiro-Wilk test, supported by visual inspection of histograms and QQ-plots, and calculation of skewness and kurtosis. A two-way RM ANOVA was used to compare differences among the within-subjects factors; condition (atDCS, sham) and time (pre, post). If any significant differences occurred, a Bonferoni post-hoc test was made. A one-way RM ANOVA was used to compare differences among accumulated energy in the RPE-production test, where only the last 120 s. were analysed, with conditions (control, sham and a-tDCS). To analyze, RPE, Vo2 and HR, a one-way ANOVA was made on each variable separately at every 25 kJ (from 0 - 250 kJ), with conditions; control, sham and a-tDCS. If any significant difference occurred, a Bonferoni post-hoc test was applied. The alpha level was set to  $\alpha = 0.05$ , and data is presented in mean ± SD. All data was analyzed using SPSS version 25.

# RESULTS

Not all data were normally distributed, but all data met the recruitments for sphericity. Due to the robustness of the RM ANOVA, it was applied on all data (11).

#### Motor evoked potentials

No significant difference in MEPs was found in condition (p = 0.952) or interaction (p = 0.076), while a significant difference in time (p = 0.031) was found. The following Bonferroni post-hoc test showed a significant difference between tDCS\_Pre ( $452 \pm 374 \mu V$ ) and tDCS\_Post ( $676 \pm 642 \mu V$ ) (p = 0.038), and no significant difference between sham\_Pre ( $565 \pm 374 \mu V$ ) and sham\_Post ( $589 \pm 531 \mu V$ ) (p = 0.652) (Table 1, Figure 1).

### RPE production & 250kJ time trial

The one-way RM ANOVA showed no significant difference between conditions; control  $(18.9 \pm 3.9 \text{ kJ})$ , sham  $(19.8 \pm 4.5 \text{ kJ})$  and a-tDCS  $(19.2 \pm 4.5 \text{ kJ})$  (p = 0.096) in the RPE production test. No significant difference was found in the 250kJ time trial between conditions; control  $(1154.3 \pm 238.7 \text{ s})$ , sham  $(1133.9 \pm 248.9 \text{ s})$  and a-tDCS  $(1137.4 \pm 258.7 \text{ s})$  (p = 0.612) (Table 1, Figure 2)

	Condition	Mean ± SD	p value
	Sham_Pre	$565 \pm 374$	
	Sham_Post	$589 \pm 531$	p = 0.652
	a-tDCS_Pre	$452\pm374$	
MEP (µV)	a-tDCS_post	$676 \pm 642$	p = 0.038
	Control	$18.9 \pm 3.9$	
	Sham	$19.8 \pm 4.5$	
RPE production (kJ)	a-tDCS	$19.2 \pm 4.9$	<i>p</i> = 0.213
	Control	$1154.3\pm238.7$	
	Sham	$1133.9\pm248.9$	
250kJ timetrial (s)	a-tDCS	$1137.4 \pm 258.7$	p = 0.612

**Table 1**: Mean values and SD in MEP size, RPE production and 250 kJ time trial completion times. a-tDCS\_Post (676 ± 642  $\mu$ V) increased significantly from a-tDCS\_pre (452 ± 374  $\mu$ V) (p = 0.038).

# Rate of perceived exertion, Vo2 & heartrate

No significant differences were found in RPE and Vo2 during the 250 kJ time trial. One significant difference was found in HR at 200 kJ (p = 0.043) between the control (169 ± 12 bpm) and the sham (172 ± 12 bpm) condition (p = 0.023) (Table 2, Figure 3).

# **DISCUSSION**

The main findings of this study are that a-tDCS applied over M1 for 13 minutes increased MEPs by 49.5 % with sham showing no significant difference (p = 0.652). The increase in MEPs did not result in a faster completion time in the 250 kJ time trial (p = 0.612) or a greater accumulated energy in the RPE-production test (p = 0.096). Furthermore, the effect of a-tDCS did not influence RPE, HR or Vo2 development in the 250 kJ time trial.

#### Motor evoked potentials

The electrode size, current strength and stimulation time used in this study was the same as used in Vitor-Costa et al. (25), who found an increase in TTF in a cycling-based, constant- load cycling test following a-tDCS. Vitor-Costa et al. (25) did not measure MEPs in their study, but we are able to conclude that, in this study, the stimulation protocol did increase MEPs following a-tDCS (Figure 1, Table 1).

	RPE				Vo2 (mL/min)			HR (bpm)				
	Control	Sham	a-tDCS	р	Control	Sham	a-tDCS	р	Control	Sham	a-tDCS	р
25kJ	14.1	13.8	14.05	0.107	2392	2473	2461	0.376	137	139	138	0.499
50kJ	14.55	14.4	14.5	0.815	2875	2974	2990	0.289	152	156	154	0.175
75kJ	15.05	15.1	15.15	0.900	2893	2967	2980	0.502	157	161	159	0.205
100kJ	15.5	15.4	15.45	0.727	2778	2859	2879	0.395	160	164	162	0.186
125kJ	15.8	15.8	15.85	0.909	2718	2780	2804	0.444	163	166	165	0.178
150kJ	16.15	16.2	16.1	0.845	2614	2655	2697	0.395	164	167	168	0.087
175kJ	16.75	16.65	16.6	0.544	2566	2561	2589	0.905	167	170	169	0.129
200kJ	17.5	17.35	17.55	0.561	2511	2503	2519	0.965	169	172	171	0.043
225kJ	18.4	18.4	18.35	0.619	2511	2453	2439	0.441	173	175	175	0.104
250kJ	19.75	19.65	19.75	0.827	2367	2293	2342	0.533	179	181	180	0.105

**Table 2:** Mean values in RPE, Vo2 and HR for each condition (control, sham and a-tDCS) at each 25 kJ (25 - 250kJ), from the 250 kJ time trial. One significant difference occurred in HR at 200 kJ. The following Bonferroni post-hoc test showed significant difference between the control (169  $\pm$  12 bpm) and the sham ( $172 \pm 12$  bpm) condition (p = 0.023).



**Figure 1**: Changes in motor evoked potentials (MEP) pre and post following a-tDCS and sham stimulation. The dotted lines present the development in MEP's for each subject, while the thick black line presents the mean development. There was no significant difference from pre sham (565  $\pm$  451  $\mu$ V) to post sham (589  $\pm$  531  $\mu$ V), while MEPs increased significantly from pre a-tDCS (452  $\pm$  374  $\mu$ V) to post a-tDCS (676  $\pm$  642  $\mu$ V) (p = 0.038).

However, we are unable to conclude on the hypothesis, that the size and placement of the anode should increase MEPs in both legs, as measurements were only taken on rectus femoris on the subjects' right leg, which is a limitation of this study. It is however, reasonable to assume, that MEPs of the left rectus femoris also increased following a-tDCS, due to the anode covering both right and left M1. Vitor-costa et al. (25) and Cogiamanian et al. (9) both measured EMG activity following a-tDCS but did not find any alterations in EMG activity. These results indicate that increased MEPs does not increase EMG activity during submaximal intensities, but more likely decreases muscle fatigue (9). Failure to generate output from motor cortex corresponding to the requirement of the activity has been defined as central fatigue which together with peripheral fatigue is responsible for muscle fatigue (23). Previous studies suggests that changes in excitability of the motor cortex have influence on the development of central fatigue, which may lead to increased endurance during time to fatigue tests (23) together with a lower RPE rating (3,19). The decreased central fatigue following a-tDCS is suggested to be due to a modulation of premotor areas, meaning that a lesser input from these areas is required to give the same MEP size, which will lead to a decreased central fatigue (9). The excitability is mainly facilitated by N-methyl-daspartate (NMDA) receptors.

NMDA receptors have an influence on excitatory synaptic transmission and induction of synaptic plasticity, and has shown to be unaffected following a-tDCS (10,16). Gamma-aminobutyric acid (GABA), which is known to act inhibitory on transmembrane potentials, has shown to have a reduced activity after a-tDCS (10). The unchanged NMDA receptor sensitivity together with the decreased GABA activity is suggested to be an explanation for the increased MEPs following a-tDCS (10,16). It is believed that a-tDCS caused these effects in the present study, which can explain the increased MEPs following a-tDCS, which is in agreement with other studies (6,9,14,17).

#### **RPE-production test**

In the present study, it was expected that a-tDCS would modulate the performance output during the RPE-production test, as suggested by Barwood et al. (5). Previous studies has shown that a-tDCS has an effect on lowering RPE at submaximal intensities, leading to increased performance compared to sham or control (3,19). However, no significant differences in produced kJ were found between the three conditions during the RPE-production test (Figure 2, Table 2). To our knowledge no previous study, has used this method to assess the effect of a-tDCS on submaximal performance.



**Figure 2**: Mean accumulated kJ produced in the control, sham and atDCS condition during the 120 seconds RPE production test. There was no significant difference between conditions; control (18.9  $\pm$  3.9 kJ), sham (19.8  $\pm$  4.5 kJ) and a-tDCS (19.2  $\pm$  4.9 kJ) (p = 0.096).

However, Vitor-Costa et al. (25) have shown an increase in TTF during a cycling test, pedalling at a load of 80 % of a previously completed incremental test, following a-tDCS (491  $\pm$  100 s) compared to cathodal-tDCS (443  $\pm$  11 s) and sham  $(407 \pm 69 \text{ s})$  (p = 0.020). Furthermore, Angius et al. (3) found TTF to be significantly longer in a cycling test at 70 % of subjects' W<sub>peak</sub> after a-tDCS  $(13.25 \pm 4.34 \text{ min.})$  compared to cathodal-tDCS  $(11.10 \pm 4.28 \text{ min.})$  and sham  $(10.76 \pm 3.03 \text{ min.})$ while simultaneously rating RPE significantly lower compared to cathodal-tDCS (p = 0.023) and sham (p = 0.008). These results indicate that atDCS has an effect on TTF at submaximal intensities, but no such effect is present during the RPE-production test. According to in Barwood et al. (5) a-tDCS has the potential to modulate central mechanisms regarding perception of physiological strain, but this was not observed in the present study.

In contrast, Okano et al. (19) found significant lower RPE ratings at 50 - 175 W in their incremental cycling test. The mean watt produced in the RPE-production test was  $144.36 \pm 34.49$  W, which is within the limit of effort shown in Okano et al. (19). The lack of difference in RPE between conditions can therefore be due to other factors such as electrode placement. Okano et al. (19) placed the anode over the T3 area, and the cathode over the Fp2 area. They suggest that the electrode placement may have modulated the brain regions involved in the cortical cardiovascular regulation and decision making, such as the prefrontal cortex (24), to tolerate high levels of effort. The nature of the RPE-production test does not facilitate high levels of effort, and it is not known if the montage used in the present study would elicit the same effect. It is notable that Barwood et al. (5) used the same montage as in Okano et al. (19), but did not find any differences in RPE during their 55 % maximal power output cycling test or in their 20 km time trial. Okano et al. (19) found significant lower RPE scores in intensities below ~50 %, suggesting that the intensity used in Barwood et al. (5) is too intense to detect differences in RPE. A similar RPE-production test, or a test with different fixed intensities below 50 % of maximal power output, could therefore be examined in future studies.

#### 250 kJ time trial

The 250 kJ time trial was performed to simulate a more sports specific test, and is different from other cycling tests, used in other studies to investigate the effect of a-tDCS (3,15,19,25). Vitor-Costa et al. (25) found an increased TTF following a-tDCS in their constant load cycling test, most likely due to decreased central fatigue. In the present study, we did not find a faster completion time, why a-tDCS might not influence high intensity self-paced activities. Both Angius et al. (3) and Okano et al. (19) used an incremental cycling test starting at a 15 W and 100 W respectively, and both found a longer TTF. These tests are not self-paced, in contrast to the 250 kJ time trial, where subjects could adjust the resistance at free will. The Vo2 curve (Figure 3) indicates a peak in Vo2 from 25 kJ to 50 kJ, followed by a linear decrease throughout the test. During testing, a tendency was seen that subjects chose to decrease the resistance around this point and then increase the resistance again around the last 25 kJ. Pacing strategy is therefore to be considered as an important factor of the 250 kJ time trial. Barwood et al. (5) performed a 20 km time trial to investigate the effects of atDCS.



Figure 3: Development of mean RPE, Vo2 and HR during the 250 kJ time trial. There was one significant difference in HR marked with \*, while no significant differences were found in RPE and Vo2 between conditions (Table 2).

They found no difference in power output and no difference in pacing strategy. In the present study, pacing strategy was not assessed, but it is believed, that there was no difference, seeing as no differences in completion time were observed. Based on previous studies, it seems that a-tDCS influences incremental- and constant load tests, but in self-paced time trials, a-tDCS's effect on decreased muscle fatigue does not have an influence on completion time. During the incremental tests performed in Angius et al. (3) and Okano et al. (19) the subjects rated a lower RPE the first half of the test. As the subjects rated lower during the test, it can be assumed, that a-tDCS may improve exercise tolerance by decreasing discomfort, thereby lowering RPE leading to a longer TTF(19). The significant lower RPE ratings in Okano et al. (19) is present until the subjects reaches 175 W, while rating a RPE of ~13-14. In the 250 kJ time trial the subjects rated a mean RPE at the first 25 kJ to ~14 in all conditions (Table 2). The intensity throughout the 250 kJ time trial may therefore have been consistently too high to benefit from the effect of a-tDCS on central fatigue.

As the 250 kJ time trail was not a TTF test, it is not known if the subjects could have performed longer at their maximal effort at the end of the test.

No difference in RPE was found between the control, sham or a-tDCS conditions (Figure 3, Table 2), which may describe the lack of improvement in completion time. Angius et al. (3) and Okano et al. (19) found lower RPE's at onset of testing, with no differences at more demanding intensities. Furthermore, Lattari et al. (15) performed a 100 % peak power test to exhaustion and found no difference in RPE. The effect of a-tDCS on RPE seems to be present in lower intensities, but not when the intensity of an exercise reach a certain level. The 250 kJ time trial may have been above this level at onset, leading to no changes in RPE, as discussed previously.

During the 250 kJ time trial only one significant difference was found for HR at 200 kJ between control and sham (p = 0.043). This is in line with previous research which have found no changes in HR after a-tDCS during TTF tests (3,5,25).

Furthermore, Barwood et al. (5) found no changes in HR after a 20-km time trial (p = 0.755) nor during rest, a 25-minute fixed intensity test (55 % PMax) or during a TTF test (75 % PMax) (p = 0.212). Only Okano et al. (19) have found significantly lower HR after a-tDCS (p < 0.05) during a maximal incremental cycling test, however only at submaximal intensities. They speculate that a-tDCS may have increased the parasympathetic modulation or reduced the sympathetic modulation, resulting in a decreased HR. To this, Barwood et al. (5) adds, that the parasympathetic pathways predominantly regulate HR at rest and at low intensity exercise. Furthermore, Barwood et al. (5) state, that during their 20-km time-trial, the duration of their exercise task can have encouraged the adoption of a higher exercise intensity, leading to a predominantly sympathetic HR response, which may not be affected by a-tDCS. Seeing as the present study utilized a test with half the distance completed of Barwood et al. (5) it is reasonable to assume, that exercise intensity will have been higher, thereby leading to a predominantly sympathetic HR response. As such, the present study supports the findings of both Barwood et al. (5) and Okano et al. (19) in regards to changes in HR during exercise at high intensity.

In conclusion, a significant increase in MEPs was found after a-tDCS; pre  $(452 \pm 374 \ \mu\text{V})$  to post  $(676 \pm 642 \ \mu\text{V})$  (p = 0.038). No effect of a-tDCS on low exercise intensities was observed in the RPE-production test in this study. Furthermore, a-tDCS has no effect on completion time in a self-paced time trial test. Similarities in completion time, HR, Vo2, RPE-production and RPE suggest that, 13min of a-tDCS was insufficient in modulating the central mechanisms involved in these factors.

# REFERENCES

 Abdelmoula, A, Baudry, S, and Duchateau, J. Anodal transcranial direct current stimulation enhances time to task failure of a submaximal contraction of elbow flexors without changing corticospinal excitability. *Neuroscience* 322: 94–103, 2016.

- 2. Angius, L, Hopker, J, and Mauger, AR. The ergogenic effects of transcranial direct current stimulation on exercise performance. *Front Physiol* 8, 2017.
- Angius, L, Mauger, AR, Hopker, J, Pascual-Leone, A, Santarnecchi, E, and Marcora, SM. Bilateral extracephalic transcranial direct current stimulation improves endurance performance in healthy individuals. *Brain Stimul* 11: 108– 117, 2018.Available from: https://doi.org/10.1016/j.brs.2017.09.017
- Angius, L, Pageaux, B, Hopker, J, Marcora, SM, and Mauger, AR. Transcranial direct current stimulation improves isometric time to exhaustion of the knee extensors. *Neuroscience* 339: 363–375, 2016.Available from: http://linkinghub.elsevier.com/retrieve/pii/ S0306452216305589
- Barwood, MJ, Butterworth, J, Goodall, S, House, JR, Laws, R, Nowicky, A, et al. The Effects of Direct Current Stimulation on Exercise Performance, Pacing and Perception in Temperate and Hot Environments. *Brain Stimul* 9: 842–849, 2016.Available from: http://dx.doi.org/10.1016/j.brs.2016.07.006
- Bastani, A and Jaberzadeh, S. Withinsession repeated a-tDCS: The effects of repetition rate and inter-stimulus interval on corticospinal excitability and motor performance. *Clin Neurophysiol* 125: 1809–1818, 2014.
- 7. Boggio, PS, Rigonatti, SP, Ribeiro, RB, Myczkowski, ML, Nitsche, MA, Pascual-Leone, A, et al. A randomized, doubleblind clinical trial on the efficacy of cortical direct current stimulation for the treatment of major depression. *Int J Neuropsychopharmacol* 11: 249–254, 2008.Available from: https://academic.oup.com/ijnp/articlelookup/doi/10.1017/S1461145707007833

- Borg, GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 14: 377–381, 1982.Available from: http://www.ncbi.nlm.nih.gov/pubmed/715 4893
- Cogiamanian, F, Marceglia, S, Ardolino, G, Barbieri, S, and Priori, A. Improved isometric force endurance after transcranial direct current stimulation over the human motor cortical areas. *Eur J Neurosci* 26: 242–249, 2007.
- 10. Das, S, Holland, P, Frens, MA, and Donchin, O. Impact of Transcranial Direct Current Stimulation (tDCS) on Neuronal Functions. *Front Neurosci* 10, 2016.Available from: http://journal.frontiersin.org/article/10.338 9/fnins.2016.00550/full
- Feir-Walsh, BJ and Toothaker, LE. An Empirical Comparison of the Anova F-Test, Normal Scores Test and Kruskal-Wallis Test Under Violation of Assumptions. *Educ Psychol Meas* 34: 789–799, 1974.
- Hummel, F, Celnik, P, Giraux, P, Floel, A, Wu, WH, Gerloff, C, et al. Effects of noninvasive cortical stimulation on skilled motor function in chronic stroke. *Brain* 128: 490–499, 2005.
- Hummel, FC, Voller, B, Celnik, P, Floel, A, Giraux, P, Gerloff, C, et al. Effects of brain polarization on reaction times and pinch force in chronic stroke. *BMC Neurosci* 7: 73, 2006.
- Jeffery, DT, Norton, JA, Roy, FD, and Gorassini, MA. Effects of transcranial direct current stimulation on the excitability of the leg motor cortex. *Exp Brain Res* 182: 281–287, 2007.
- 15. Lattari, E, de Oliveira, BS, Oliveira, BRR, de Mello Pedreiro, RC, Machado, S, and Neto, GAM. Effects of transcranial direct current stimulation on time limit and ratings of perceived exertion in physically active women. *Neurosci Lett* 662: 12–16, 2018.Available from:

https://doi.org/10.1016/j.neulet.2017.10.00 7

- Liebetanz, D. Pharmacological approach to the mechanisms of transcranial DCstimulation-induced after-effects of human motor cortex excitability. *Brain* 125: 2238–2247, 2002.Available from: https://academic.oup.com/brain/articlelookup/doi/10.1093/brain/awf238
- Nitsche, MA and Paulus, W. Excitability changes induced in the human motor cortex by weak transcranial direct current stimulation. *J Physiol* 527: 633–639, 2000.
- Nitsche, MA and Paulus, W. Sustained excitability elevations induced by transcranial DC motor cortex stimulation in humans. *Neurology* 57: 1899–1901, 2001.
- Okano, AH, Fontes, EB, Montenegro, RA, Farinatti, P de TV, Cyrino, ES, Li, LM, et al. Brain stimulation modulates the autonomic nervous system, rating of perceived exertion and performance during maximal exercise. *Br J Sports Med* 49: 1213–1218, 2015.Available from: http://bjsm.bmj.com/lookup/doi/10.1136/bj sports-2012-091658
- 20. Rossi, S, Hallett, M, Rossini, PM, and Pascual-Leone, A. Safety, ethical considerations, and application guidelines for the use of transcranial magnetic stimulation in clinical practice and research. *Clin Neurophysiol* 120: 323–330, 2012.
- Rösler, KM and Magistris, MR. The size of motor-evoked potentials: Influencing parameters and quantification. In: The Oxford handbook of transcranial stimulation. Wassermann, E and Epstein, C, eds. . Oxford University Press, 2012.
- Stagg, CJ and Nitsche, MA. Physiological basis of transcranial direct current stimulation. *Neuroscientist* 17: 37–53, 2011.Available from: https://doi.org/10.1177/107385841038661

23. Taylor, JL, Butler, JE, Allen, GM, and Gandevia, SC. Changes in motor cortical excitability during human muscle fatigue. J *Physiol* 490: 519–528, 1996.Available from: http://eutils.ncbi.nlm.nih.gov/entrez/eutils/

elink.fcgi?dbfrom=pubmed&id=8821 148&retmode=ref&cmd=prlinks

- 24. Verberne, AJM and Owens, NC. Cortical modulation of the cardiovascular system. *Prog Neurobiol* 54: 149–168, 1998.
- 25. Vitor-Costa, M, Okuno, NM, Bortolotti, H, Bertollo, M, Boggio, PS, Fregni, F, et al. Improving cycling performance: Transcranial direct current stimulation increases time to exhaustion in cycling. *PLoS One* 10: 1–15, 2015.Available from: http://dx.doi.org/10.1371/journal.pone.014 4916