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1 Effect of transcranial direct current stimulation on exercise performance: a  
2 systematic review and meta-analysis

3

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22

## 1 ABSTRACT

2 **Background:** Transcranial direct current stimulation (tDCS) has been used to improve  
3 exercise performance, though the protocols used, and results found are mixed.

4 **Objective:** We aimed to analyze the effect of tDCS on improving exercise performance.

5 **Methods:** A systematic search was performed on the following databases, until December  
6 2017: PubMed/MEDLINE, Embase, Web of Science, SCOPUS, and SportDiscus. Full-text  
7 articles that used tDCS for exercise performance improvement in adults were included. We  
8 compared the effect of anodal (anode near nominal target) and cathodal (cathode near nominal  
9 target) tDCS to a sham/control condition on the outcome measure (performance in isometric,  
10 isokinetic or dynamic strength exercise and whole-body exercise).

11 **Results:** 22 studies (393 participants) were included in the qualitative synthesis and 11  
12 studies (236 participants) in the meta-analysis. The primary motor cortex (M1) was the main  
13 nominal tDCS target (n = 16; 72.5%). A significant effect favoring anodal tDCS (a-tDCS)  
14 applied before exercise over M1 was found on cycling time to exhaustion (mean difference =  
15 93.41 s; 95%CI = 27.39 s to 159.43 s) but this result was strongly influenced by one study  
16 (weight = 84%), no effect was found for cathodal tDCS (c-tDCS). No significant effect was  
17 found for a-tDCS applied on M1 before or during exercise on isometric muscle strength of the  
18 upper or lower limbs. Studies regarding a-tDCS over M1 on isokinetic muscle strength  
19 presented mixed results. Individual results of studies using a-tDCS applied over the prefrontal  
20 and motor cortices either before or during dynamic muscle strength testing showed positive  
21 results, but performing meta-analysis was not possible.

22 **Conclusion:** For the protocols tested, a-tDCS but not c-tDCS vs. sham over M1 improved  
23 exercise performance in cycling only. However, this result was driven by a single study,

1 which when removed was no longer significant. Further well-controlled studies with larger  
2 sample sizes and broader exploration of the tDCS montages and doses are warranted.

3

4 **Keywords:** Athletic Performance; Exercise Performance; Meta-analysis; Non-Invasive Brain  
5 Stimulation; Systematic Review; Transcranial Direct Current Stimulation.

6

7

8

## 9 **HIGHLIGHTS**

10

- 11 • In this systematic review and meta-analysis, we assessed the effect of tDCS for  
12 improving exercise performance in healthy adults.
- 13 • We did find a weak evidence for an exercise performance enhancement effect  
14 favoring anodal tDCS during whole-body dynamic cyclic exercise, but this result  
15 was strongly influenced by one study.
- 16 • However, there is no evidence that tDCS improves measures of isometric,  
17 isokinetic and dynamic strength.

18

19

## 1 INTRODUCTION

2

3 Exercise performance is influenced by several physical, physiological, and  
4 psychological factors [1–3]. Particularly in the sports context, there has always been a  
5 search for ergogenic aids to boost performance [4], with some athletes even using illegal  
6 drugs to this end [5]. In recent years, the focus has changed to the brain and how it  
7 could limit/improve performance. Many studies have shown that the brain plays a key  
8 role in the establishment of fatigue and, therefore, exercise performance [6–9]. In this  
9 regard, several centrally-acting performance modifiers have been shown to influence  
10 exercise performance [6,10].

11 Transcranial direct current stimulation (tDCS) is a technique that has received  
12 increasing attention due to its potential impact on brain activity in healthy subjects as  
13 well as patient populations. tDCS is a non-invasive, portable, easy to use, safe [11,12],  
14 well-tolerated [13], and economical technique, in which a weak electric direct current  
15 (up to 2 mA for tens of minutes) is applied to the scalp with the intention to modulate  
16 cortical excitability [14,15]. Classically, placement of the anode electrode near the  
17 nominal target (anodal tDCS, a-tDCS) is presumed to increase neuronal excitability and  
18 plasticity, while placement of cathode near the nominal target (cathodal tDCS, c-tDCS)  
19 is assumed to have opposite effects [14,15]. Whilst ongoing studies have shown this  
20 polarity-dependent approach to be over-simplistic due to a non-linear dose-response  
21 (e.g. anodal inhibiting or cathodal exciting) [16–18] and the inevitable presence and  
22 interaction of both the active and reference electrodes [19,20], we adopt the  
23 conventional anodal and cathodal terminology for the purpose of our literature review.

1 Generally, the effects of tDCS outlast the time of stimulation for up to 120 min after  
2 tDCS has ended [14,15,21].

3         Given the complexity involved in exercise performance, there are multiple brain  
4 regions that may be involved in exercise regulation/limitation and, therefore, the rationale  
5 for using tDCS for performance enhancement may vary accordingly. However, most  
6 studies on sporting and exercise performance fail to provide a clear or stated hypothesis  
7 for why positioning the electrodes in a specific location targeted to excite/inhibit a given  
8 brain region could lead to an improved exercise performance. Although this is not an  
9 extensive list, some of these regions include the primary motor cortex (M1), prefrontal  
10 cortex (PFC), insular cortex (IC), and supplementary motor area (SMA).

11         M1 is the region most related to exercise performance due to its role in driving the  
12 exercising muscles. It has been consistently demonstrated that central fatigue (e.g. due to  
13 neural factors) can impact on the physical performance of single-joint exercises involving  
14 low muscle mass (e.g. elbow flexion) as well as multiple-joint or whole-body exercises  
15 (e.g. cycling). Specifically, spinal and supra-spinal factors such as the reduction in  
16 excitability of the motoneuron pool and the inability or limited capacity of the M1 and  
17 other supraspinal areas to increase the neural drive to compensate for this decreased spinal  
18 excitability leads to the decrease in muscle capacity to produce strength/power and thus  
19 cause fatigue [9,22,23]. Therefore, one reason for using tDCS over M1 would be to  
20 increase excitability of this region which could result in a sustained neural drive for the  
21 motor neuron, delay in the decrease of the neural drive to the active muscle and, therefore,  
22 improved performance. In addition, other possible reason for applying tDCS over M1  
23 could be to modulate the pain perception. Although the exact mechanism is unclear, the  
24 reason for targeting M1 for pain modulation is due to its connections with the insula and

1 thalamus, as shown in studies with non-human animal models [24]. In fact, meta-  
2 analytical research has shown that anodal tDCS of M1 increases sensory and pain  
3 threshold in healthy individuals as well as pain level in patients with chronic pain [25].  
4 In this regard, it has been suggested that exercise-induced pain plays a key role in the  
5 regulation of exercise performance, in which individuals with the better capacity to  
6 tolerate or overcome pain would be more successful [26]. Thus, targeting M1 could also  
7 improve performance via the attenuation of exercise-induced pain.

8         The PFC is another region of interest considering its role in the cognitive control  
9 of behavior. It has been suggested that the PFC plays an important role in the processing  
10 of internal and external cues related to the exercise being performed [27]. PFC exerts a  
11 top-down influence that may result in alteration of pace to complete the task, prolong the  
12 motor output delaying exercise end or derecruitment of motor units causing exercise  
13 termination [27]. In this regard, the psychobiological model proposes that task  
14 disengagement (i.e. exercise termination) is an effort-based decision-making process  
15 which depends on the potential motivation (e.g. the maximum effort a person is willing  
16 to exert), perception of effort, knowledge of the endpoint of exercise and distance/time  
17 remaining, and previous experience/memory of perception of effort during exercise of  
18 varying intensity and duration [28]. A systematic review confirmed that interventions  
19 aiming to decrease the ability of the PFC to exert control over the body signals during  
20 exercise, such as mental fatigue (e.g. performing a cognitively demanding task for a  
21 prolonged time) may reduce endurance performance [29]. In fact, it has been consistently  
22 demonstrated that there is a decrease in PFC oxygenation before fatigue occurs [30,31].  
23 Therefore, applying tDCS over the PFC could strengthen the ability of this region to

1 disregard interoceptive cues (i.e. body signals), keeping the volitional drive to M1 and,  
2 thus, delaying task disengagement (i.e. exercise termination).

3 Another possible target for tDCS is the insular cortex (IC), which is involved in  
4 cardiac autonomic control. Non-human animal, experimental, and neuroimaging studies  
5 have demonstrated that the right IC is involved in sympathetic modulation while the left  
6 IC is involved in parasympathetic modulation [32–34]. The insula is a relatively deep  
7 brain structure and tDCS is thought to modulate, primarily, the excitability of cortical  
8 regions. However, considering the connections between the temporal cortex (TC) and IC,  
9 it has been shown by computational modeling and experimental studies that applying  
10 tDCS over the left TC probably modulates the activity of the IC resulting in an increased  
11 parasympathetic modulation at rest and during exercise [35,36]. At rest, the cardiac  
12 autonomic control is predominantly modulated by the parasympathetic branch and as  
13 exercise starts this modulation decreases progressively until its complete withdrawal. The  
14 point in which the parasympathetic withdrawal occurs can be measured using a marker  
15 termed heart rate variability threshold ( $HRV_{th}$ ) and it has been demonstrated to coincide  
16 with the ventilatory threshold (VT), an important marker of transition of the exercise  
17 intensity domain [37,38]. Thus, delaying the  $HRV_{th}$  would increase the time exercising  
18 with a lower cardiovascular load, which in turn could postpone fatigue resulting in an  
19 increased time to exhaustion (TTE) [35].

20 The supplementary motor area (SMA) has also been implicated in exercise  
21 performance. It was recently demonstrated that decreasing neuronal excitability of SMA  
22 using repetitive transcranial magnetic stimulation (rTMS), to apply theta-burst  
23 stimulation, resulted in a decreased in perceived exertion during exercise and willingness  
24 to reproduce the effort [39]. It is important to note that perceived exertion directly



1 influences exercise performance being determinant in the establishment of fatigue  
2 [6,7,28]. So far, however, no study tested whether tDCS applied to SMA could induce  
3 the same result as rTMS.

4         The interest in the potential role of tDCS for improving performance has  
5 increased in the past few years. Cogiamanian et al. [40] were the first to demonstrate  
6 that tDCS could postpone fatigue. They showed that tDCS significantly decreased the  
7 fatiguing effects of prior exercise in healthy individuals, with an apparent 50% longer  
8 TTE in an isometric contraction of the elbow flexors after a-tDCS over M1 compared to  
9 no stimulation. Later, Okano et al. [35] also showed that a-tDCS over the TC (targeting  
10 the left IC) improved cycling performance by 4% (i.e. maximal power output and TTE)  
11 in national-level road cyclists. These results were further supported, albeit with different  
12 electrode montages and measures of performance [41–43]. Although some studies  
13 showed positive performance enhancements using tDCS [35,40–42], others have failed  
14 to reproduce the positive findings [44–47]. The mixed findings could be due to  
15 variations in the protocols; for instance, in electrode placement, current intensity, and  
16 density, the type of exercise test used, participant's level of physical /activity fitness and  
17 sample size. Likewise, the timing of tDCS use is not consistent, as studies have used  
18 tDCS before and during testing as well as during training sessions.

19         These early studies with positive results [35-36] motivated commercial and  
20 consumer interest in tDCS for sports performance, including at elite levels [48]. Despite  
21 encouraging results of a few controlled experiments, there is apprehension that adoption  
22 of tDCS for performance enhancement in the naturalistic setting such as commercial  
23 gymnasiums has outpaced research [49,50]. In addition, several opinion articles and  
24 literature reviews have implicated tDCS as an effective technique for improving

1 performance [51–54], including the discussion regarding the fairness and ethics of its  
2 use in sport (e.g. as a “neurodoping” technique [51–53,55]), with some authors debating  
3 ethical modes of the use of tDCS in sports [49,54], and others suggesting anti-doping  
4 regulation agencies to include tDCS as an illegal strategy to enhance performance in  
5 sports [50,54]. Consequently, there has been a call for researchers to identify  
6 biomarkers of the use of tDCS in order to be able to test for its use in/out of competition  
7 (e.g. anti-doping testing) [54]. However, the practical debate around the fairness of  
8 tDCS in sports, as well as its practical use, presumes meaningful effectiveness of the  
9 technique, which has yet to fully reach a consensus in the research to date.

10         So far, however, it is not clear in the light of the current evidence whether tDCS  
11 improves exercise/sporting performance, in what sort of exercise it is effective, and in  
12 which electrode set-up. Hence, the purpose of this systematic review and meta-analysis  
13 was to analyze the effect of tDCS for improving performance in muscle strength  
14 (isometric, isokinetic and dynamic) exercise as well as during whole-body dynamic  
15 cyclic exercise (e.g. cycling) in healthy adults. Our findings will consolidate extant  
16 knowledge in the application of tDCS for sports and help to guide future investigations.

17

## 18 **METHODS**

### 19 **Protocol and registration**

20

21         A systematic review and meta-analysis was performed according to the  
22 recommendations of the Cochrane group [56], which involves the procedure of review,  
23 selection of eligible articles according to inclusion/exclusion criteria, quality assessment

1 of included studies, data extraction of outcomes and relevant variables, and quantitative  
2 synthesis (meta-analysis) of the results. This report follows PRISMA guidelines [57].  
3 Two reviewers independently selected articles and extracted the data according to an a  
4 priori elaborated data extraction checklist. Discrepancies we resolved by consensus and,  
5 if necessary, the inclusion of a third reviewer.

6 The protocol of the present review was registered into the International  
7 Prospective Register of Systematic Reviews – PROSPERO -  
8 (<https://www.crd.york.ac.uk/prospero/>) under the register number CRD42017076546  
9 and is publicly available  
10 ([https://www.crd.york.ac.uk/PROSPERO/display\\_record.php?RecordID=76546](https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=76546)).

11

## 12 **Literature review**

13

14 The review was performed in the following databases: PubMed/MEDLINE,  
15 Embase, Web of Science, SCOPUS, and SportDiscus. We searched for articles from the  
16 first data available in each database until 5 December 2017. The following keywords  
17 (MeSh) and Boolean terms were used: “exercise tolerance” OR "exercise" OR "fatigue"  
18 OR "physical exertion" OR "physical endurance" OR "athletic performance" AND  
19 "transcranial direct current stimulation" OR "tDCS" OR "HD-tDCS". In addition,  
20 further searches were performed in the reference list of the included articles and  
21 literature reviews on the subject in order to retrieve articles that were not covered by the  
22 database searches.

23

## 1 **Eligibility criteria**

2

3           We searched for full-text articles without language restrictions (only articles in  
4 English were found). Included articles had to: (a) enroll healthy adults; (b) perform  
5 transcranial direct current stimulation; (c) have a sham/control condition; (d) perform  
6 maximal physical testing (isometric, isokinetic or dynamic strength exercise and whole-  
7 body dynamic cyclic exercise); (e) provide data of at least one of the outcome measures  
8 (on the manuscript or upon request). The inter-reviewer agreement for the article  
9 selection was assessed using Kappa statistic (K) and the results show an “excellent”  
10 agreement between reviewers ( $k = 0.85$ ;  $p < 0.0001$ ).

11

## 12 **Quality assessment**

13

14           The assessment of study quality (risk of bias) was performed following the  
15 criteria proposed by Cochrane guidelines [56] that can negatively impact study: (a)  
16 assessments for sequence generation (randomization), (b) allocation sequence  
17 concealment, (c) blinding of participants and researchers, (d) incomplete outcome data,  
18 (e) selective outcome reporting and (f) ‘other issues’. Each of these items were deemed  
19 as “low risk of bias” (“+”), “high risk of bias” (“-”) or “unclear risk of bias” (“?”) in a  
20 table available in the Review Manager 5.3 software (Copenhagen: The Nordic Cochrane  
21 Centre), in which a description of what was reported to have happened in the study was  
22 included.

23

## 1 **Data extraction**

2

3 For each included article, we extracted data regarding sample size and  
4 characteristics (age, sex, level of physical activity, fitness or training, and type of  
5 exercise training), number and reasons for dropout, intervention characteristics  
6 (electrode location, current intensity density, and duration), side and adverse effects. For  
7 the outcome, we extracted the following data (absolute values): (a) TTE in whole-body  
8 dynamic exercise and isometric exercise for major muscle groups and (b) maximal  
9 isometric, isokinetic, and dynamic muscle strength.

10

## 11 **Quantitative analysis**

12

13 A separate meta-analysis was performed considering the type of exercise test  
14 used (isometric, isokinetic or dynamic strength exercise and whole-body dynamic cyclic  
15 exercise) as well as the brain region stimulated in each study.

16 To measure the intervention effect on continuous outcomes, we calculated the  
17 mean difference (MD) and 95% confidence interval (95%CI). The MD and 95%CI  
18 weighted by the inverse variance method was measured using a random-effects model.  
19 Heterogeneity was assessed using  $\text{Chi}^2$  ( $p < 0.1$  considered as significant) and  $I^2$   
20 ( $>75\%$ ), as well as the visual inspection of the forest plot. All analyses were performed  
21 using Review Manager 5.3 (Copenhagen: The Nordic Cochrane Centre). When it was  
22 not possible to perform a meta-analysis of the studies, MD and 95%CI was reported if  
23 sufficient data was provided in the article or upon request.

## 1 RESULTS

### 2 Overview

3

4 A total of 1588 unique records were screened, and 27 full texts were assessed for  
5 eligibility. The most common reason for exclusion at the screening phase was studies  
6 involving exercise related performance with patients (e.g. multiple sclerosis, stroke,  
7 Parkinson's disease, Alzheimer's disease), as well as elderly and adolescents. Twenty-  
8 two studies were included enrolling 393 participants in the qualitative synthesis and 11  
9 studies enrolling 236 participants in the quantitative synthesis (meta-analysis). The low  
10 number of studies included in the meta-analysis were, primarily, due to variations of  
11 stimulated area (i.e. PFC, M1, TC) and outcomes (e.g. isometric, isokinetic, dynamic  
12 muscle strength or TTE, sprint, time trial, peak power output in cycling), which did not  
13 allow quantitative synthesis. Only one study was included from the references of the  
14 included articles, which represents that our search strategy was sensitive to cover the  
15 literature regarding tDCS and exercise performance. This systematic review covered the  
16 period from 1966 to December 2017. Figure 1 summarizes the flow of the study.

17

18 **\*\*\*INSERT FIGURE 1 AROUND HERE\*\*\***

1

## 2 **Study characteristics**

3

4 A comprehensive summary of the characteristics of the included studies  
5 examining the effects of tDCS on improving exercise performance can be found in  
6 Table 1. All included studies were randomized, 20 (90.9%) were crossover and 2 (9.1%)  
7 were parallel. Nineteen studies (86.4%) had a sham condition/group as a comparator,  
8 two (9.1%) had both sham and control (no stimulation), and one study (4.5%) had only  
9 a control group as a comparator. Seventeen studies (77.3%) performed only a-tDCS,  
10 while five (22.7%) studies applied both a-tDCS and c-tDCS. The current intensity  
11 applied was 1.5 or 2 mA, with a current density of (mean  $\pm$  SD)  $0.104 \pm 0.110$  mA/cm<sup>2</sup>  
12 (from 0.043 to 0.44 mA/cm<sup>2</sup>), and duration of  $15.1 \pm 4.8$  min (ranging from 10 to 20  
13 min).

14 Studies assessed both men and women, with mean  $\pm$  SD sample size per study  
15 was  $14.4 \pm 5.7$  (from 6 to 24 participants) with a median of 12, aged from 17 to 42 years  
16 and different levels of physical activity/fitness (ranging from low active individuals to  
17 athletes). Regarding tDCS timing, 16 studies (72.7%) applied tDCS before exercise,  
18 three studies (13.6%) applied tDCS during exercise, one study (4.5%) applied tDCS  
19 both before and during exercise, one study (4.5%) applied tDCS over repeated sessions,  
20 and one (4.5%) during exercise training [58]. The effect of tDCS for improving exercise  
21 performance was assessed for muscle strength in 15 studies (68.2%), from which 10  
22 (45.5%) used isometric, three (13.6%) used isokinetic, and two (9.1%) used dynamic  
23 strength exercise. Seven studies (31.8%) assessed the effect of tDCS on improving  
24 whole-body cycling exercise performance. The most stimulated area was M1 (n = 16;

1 72.5%), but there were also studies stimulating dorsolateral PFC (n= 2; 9.1%), left TC  
2 (n = 3; 13.6%), and both M1 and lateral PFC (n = 1; 4.5%). Figure 2 presents electrode  
3 montage for the tDCS protocols used in the included studies.

4

5

**\*\*\*INSERT TABLE 1 AROUND HERE\*\*\***

6

7

**\*\*\*INSERT FIGURE 2 AROUND HERE\*\*\***

8

### 9 **tDCS for improving performance in whole-body cycling exercise**

10

11 We found an increased TTE with constant load cycling exercise after a-tDCS (Figure  
12 3A). Although a significant effect in favor of a-tDCS was found without a significant  
13 heterogeneity ( $\text{Chi}^2 = 0.45$ ,  $P = 0.80$  and  $I^2 = 0\%$ ) the study of Vitor-Costa et al. [42]  
14 presented a disproportionate weight in the analysis (84.8%). After excluding that study from  
15 the analysis, the result was non-significant [MD = 114.96 s, 95%CI = -23.07 s to 312.99 s; Z  
16 = 1.69;  $P = 0.09$ ] (Figure 3B). Similarly, there was no effect of c-tDCS on the time to  
17 exhaustion in constant load cycling exercise (Figure 3C). Although no significant  
18 heterogeneity was found ( $\text{Chi}^2 = 0.03$ ,  $P = 0.87$  and  $I^2 = 0\%$ ) the study of Vitor-Costa et al.  
19 [42] also had a disproportionate weight (94.9%).

20

21 **\*\*\*INSERT FIGURE 3 AROUND HERE\*\*\***

22



1           Four other studies that used tDCS to improve whole-body cycling exercise were  
2 found. However, they could not be quantitatively synthesized due to differences in brain  
3 areas and/or type of exercise testing performed. Okano et al. [35] and Barwood et al.  
4 [44] applied a-tDCS (2 mA for 20 min) over the left TC (T3) before exercise, but while  
5 the former used maximal incremental exercise, the latter used a 20-km time trial and a  
6 TTE test at 75% of peak power. Okano et al. [35] reported a significant increase the MD  
7 did not confirmed this significant improvement in peak power (MD = 12.20 W; 95% CI  
8 = -10.03 W to 34.43 W) and TTE (MD = 27.70 s; 95% CI = -24.66 s to 80.06 s).  
9 Barwood et al. [44] found no difference in either time trial completion time (MD = 0.00  
10 s; 95% CI = -83.46 s to 83.46 s) or TTE (MD = -77.00 s; 95% CI = -418.31 s to 264.31  
11 s).

12           On the other hand, Latarri et al. [59] applied a-tDCS over the dorsolateral PFC  
13 before exercise in physically active women and reported a significantly longer TTE at  
14 100% of peak power but the MD did not confirm these positive result (MD = 62.40 s;  
15 95% CI = -9.47 s to 134.27 s). Sasada et al. [60] applied a-tDCS and c-tDCS over M1  
16 before a maximal 30 s sprint on a cycle ergometer in a sample of athletes from various  
17 modalities and found a significantly higher mean power output after a-tDCS compared  
18 to c-tDCS, but this was not different from the sham condition.

19

## 20 **tDCS for improving muscle strength in isometric exercise**

21

22           There was no effect of a-tDCS applied before exercise compared to sham on  
23 isometric muscle strength of either the upper limbs or the lower limbs (Figure 4).

1 Particularly for the upper limbs a significant heterogeneity was found ( $\text{Chi}^2 = 11.51$ ,  $P =$   
2  $0.009$  and  $I^2 = 74\%$ ; Figure 3A). Likewise, no significant effect of a-tDCS applied during  
3 exercise compared to sham on isometric muscle strength was found (Figure 4C).

4 Two studies were not included in the quantitative synthesis due to the assessment of  
5 different muscles or the use of repeated tDCS sessions. Hazime et al. [61] applied a-tDCS  
6 over the M1 of handball athletes and found an unchanged maximal isometric voluntary  
7 contraction (MIVC) of the external and internal rotators of the shoulder during tDCS (MD =  
8  $0.10$  N/Kg; 95%CI =  $-0.05$  N/Kg to  $0.25$  N/Kg and MD =  $0.10$  N/Kg; 95%CI =  $0.00$  N/Kg to  
9  $0.20$  N/Kg, respectively), but it increased 30 min (MD =  $0.20$  N/Kg; 95%CI =  $0.05$  N/Kg to  
10  $0.35$  N/Kg, for both) and 60 min (MD =  $0.20$  N/Kg; 95%CI =  $0.05$  N/Kg to  $0.35$  N/Kg, for  
11 both) after stimulation. Frazer et al. [62] assessed the effect of a-tDCS applied over M1 on  
12 four consecutive days and reported a significant improvement in the MIVC of the wrist  
13 flexors by 8% compared to 3% by sham.

14

15 **\*\*\*INSERT FIGURE 4 AROUND HERE\*\*\***

16

#### 17 **tDCS for improving muscle strength in isokinetic exercise**

18

19 Only three studies that analyzed the effect of tDCS on isokinetic muscle strength  
20 were found [58,63,64]. However, they could not be quantitatively synthesized due to the  
21 different brain areas stimulated. Two of these studies used similar tDCS parameters (2 mA  
22 for 20 min,  $0.057$  mA/cm<sup>2</sup>), isokinetic assessment (2-3 sets of 5 and 10 repetitions of knee  
23 extensors at  $60^\circ \cdot s^{-1}$ ), and sample (physically active men). Montenegro et al. [63] applied a-  
24 tDCS over M1, while Sales et al. [64] applied a-tDCS over TC. The former reported no

1 significant effect of tDCS on torque, total work or work fatigue, while the latter found a  
2 significant effect on the total work at both  $60^{\circ} \cdot s^{-1}$  (MD = 117.47 J; 95%CI = 0.05 J to 234.89  
3 J) and  $180^{\circ} \cdot s^{-1}$  (MD = 77.40 J; 95%CI = 0.32 J to 154.48 J) movement speeds. Maeda et al.  
4 [58] applied a-tDCS over non-dominant M1 during the execution of isokinetic eccentric knee  
5 extension and flexion training over seven sessions and found no difference between a-tDCS  
6 and sham in knee extension (MD = -3.70 Nm; 95%CI = -66.74 Nm to 59.34 Nm) and knee  
7 flexion (MD = 7.50 Nm; 95%CI = -18.23 Nm to 33.23 Nm).

8

### 9 **tDCS for improving muscle strength in dynamic exercise**

10

11 Only two studies that assessed the effect of tDCS on dynamic muscle strength were  
12 found. Lattari et al. [65] applied a-tDCS and c-tDCS (2 mA, 0.057 mA/cm<sup>2</sup>, for 20 min)  
13 before performing a second 10-repetition maximum test (i.e. workload needed to allow the  
14 execution of up to 10 repetitions) of elbow flexors in trained men and found a significant  
15 higher number of repetitions after a-tDCS compared to sham tDCS (MD = 4.28; 95%CI =  
16 2.56 to 6.00). Interestingly, c-tDCS decreased the number of repetitions compared to sham  
17 tDCS (MD = -2.52; 95%CI = -3.75 to -1.28). Hendy and Kidgel [66] applied a-tDCS alone  
18 and a-tDCS/sham over M1 of the non-dominant hand while performing resistance exercise  
19 with the dominant hand. The authors reported that a single a-tDCS session, when associated  
20 with resistance exercise, could improve the maximum voluntary dynamic strength of the  
21 wrist extensors of the untrained limb more than sham + resistance exercise and a-tDCS  
22 alone, but the 95%CI of the MD did not confirm the positive effect (MD = 0.46 kg; 95%CI =  
23 -2.00 kg to 2.92 kg and MD = 0.56 kg; 95%CI = -2.01 kg to 3.13 kg, respectively) [66].

1

## 2 **Risk of bias**

3

4           The risk of bias regarding tDCS for improving exercise performance was deemed low  
5 for the majority of the studies. However, approximately 25% of the studies presented a high  
6 risk of bias regarding the blinding of the outcome assessment. The risk-of-bias graphs and  
7 summary are presented in Figure 5.

8

9 **\*\*\*INSERT FIGURE 5 AROUND HERE\*\*\***

10

## 11 **DISCUSSION**

12

13           This systematic review with meta-analysis included 22 studies with 393  
14 participants examining the effects of tDCS on exercise performance. For the protocols  
15 tested, we found weak evidence of a significant effect favoring a-tDCS applied before  
16 testing over the M1 on TTE in cycling, but this result was strongly influenced by a  
17 single study, with no significant effect for c-tDCS for the same outcome. In addition, for  
18 the protocols tested, no significant effect was found for a-tDCS applied either before or  
19 during exercise on isometric muscle strength of the upper or lower limbs. Although it  
20 was not possible to synthesize the evidence quantitatively, the studies present mixed  
21 results related to the application of a-tDCS on isokinetic muscle strength. The only two  
22 studies using a-tDCS applied over PFC and M1 either before or during dynamic muscle

1 strength testing also showed mixed results, although a quantitative synthesis was not  
2 possible due to different areas of stimulation.

3         The quantitative synthesis showed a significant effect of a-tDCS over the M1  
4 improving TTE in cycling by approximately 93 seconds, suggesting that a-tDCS could,  
5 in fact, enhance performance and be used for this purpose before training sessions  
6 and/or competition. However, caution should be taken when interpreting this result,  
7 given that a single study [42] had a disproportionate weight in the analysis (84.5%), and  
8 when removed from the analysis this result became non-significant (Figure 3B).  
9 Considering that in a meta-analysis each study is weighted by the inverse of its variance  
10 plus the variance between-studies (if using random-effects model), the greater weight  
11 can be explained by the lower variance presented by the study [42].

12         The improvement in cycling performance is of particular interest as in top-level  
13 competitions an improvement even by seemingly trivial percentage (i.e. 1%) might have  
14 an impact on the sporting outcome such as changing positions in the podium in intense  
15 Olympic events [67]. Nevertheless, it should be noted that only three studies (13.6%)  
16 assessed actual athletes [35,60,61], the other studies included samples with different  
17 levels of physical activity and fitness (ranging from low active to active individuals),  
18 which may have influenced the variation in the results. Furthermore, even though most  
19 studies were conducted with small sample sizes and individual data were almost always  
20 unavailable, it is worth noting that the cost-effectiveness of tDCS may seem favorable,  
21 particularly when considering that no detrimental effect in exercise performance has  
22 been reported on the assessed tasks. However, it is possible that a negative impact on  
23 other tasks could occur as it has been shown, for instance, that tDCS may present  
24 improvements in some cognitive functions at the expense of other cognitive abilities

1 [68,69]. Furthermore, the use of tDCS outside the lab by the wider community may  
2 produce uncertain results due to inadequate electrode positioning, contact, impedance,  
3 and current flow. It should be noted that only two studies (9.1%) used tDCS for  
4 performance improvement over repeated sessions, with four [62] or seven sessions [58],  
5 and the safety for daily use of tDCS such as before/during training sessions is still to be  
6 evaluated. Therefore, the widespread application of tDCS outside the lab, such as with  
7 commercial devices, should be treated with significant caution until clear scientific  
8 evidence supports its safety and efficacy.

9         The meta-analysis of studies involving isometric muscle strength exercise  
10 showed no significant differences between a-tDCS and sham for the upper and lower  
11 limbs, for a-tDCS applied both before and during exercise (Figure 4). In addition, for  
12 fatiguing isometric contraction of elbow flexors, a significant heterogeneity in the  
13 results of the included studies was detected. Importantly, the studies that used isometric  
14 muscle strength as the outcome used surprisingly low percentages of MIVC ranging  
15 from 20% to 35%. The transferability of performance from this type of task to both  
16 exercise practice and sports performance is very limited. Future studies should consider  
17 using higher intensities that are more representative of the sporting context, for  
18 example, in combat sports that involves isometric actions such as Judo or Brazilian Jiu-  
19 Jitsu. So far, the available evidence does not support using a-tDCS to improve isometric  
20 muscle strength performance.

21         Regarding isokinetic muscle strength performance, the available studies  
22 stimulated different brain regions and found opposing results. Sales et al. [64] found  
23 improved isokinetic muscle strength of the knee extensors after a-tDCS applied to the  
24 left TC, while Montenegro et al. [63] found no difference after a-tDCS applied to M1.

1 In addition, Maeda et al. [58] applied a-tDCS over M1 during isokinetic training and  
2 found no effect of eccentric knee extension and flexion. Interestingly, the only two  
3 studies involving dynamic strength exercise showed contrasting results, where a single  
4 session of a-tDCS before exercise improved the number of maximum repetitions in  
5 elbow flexion exercise [65] and a single-session of strength training associated with a-  
6 tDCS did not change the maximal strength of the contralateral wrist extensors more than  
7 strength training or a-tDCS alone [66]. However, the effect size of these improvements  
8 ranged from very small to very large, which suggest heterogeneity in the findings.  
9 Therefore, the current evidence does not support the efficacy of tDCS for improving  
10 performance in isometric, isokinetic of dynamic muscle strength.

11 Interestingly, although commercial companies are selling tDCS devices for  
12 exercise performance enhancement to the wider community (for an overview see  
13 Edwards et al. [49]), in this systematic review, no published peer-reviewed study testing  
14 the effects and validity of these commercial devices on exercise performance were  
15 found. It is worth noting that only laboratory studies in a controlled environment used  
16 tDCS for performance enhancement and, therefore, the widespread use of tDCS outside  
17 this environment (e.g. commercial, home-based, do-it-yourself) must be taken with  
18 caution. This issue has raised concerns in the research community, particularly  
19 considering the safety of uncontrolled, prolonged, and repeated use of tDCS [49,70,71].

20 It should be noted that methodological aspects of tDCS may have an impact on  
21 the stimulation effects, and this must be considered in future studies using tDCS for  
22 performance enhancement. In recent years, the adoption of computational forward  
23 models of brain current flow has increased [72] as it provides more insight into brain  
24 current flow patterns and, in some cases, can even challenge simplified electrode-

1 placement based on the “classical” polarity-dependent assumption [20,73]. Of the 22  
2 studies included, only three (13.6%) used computational modeling to predict the  
3 electrical field generated by tDCS in the target area. Generally, the application of tDCS  
4 using large electrode pads (termed as “conventional” tDCS) leads to diffuse brain  
5 current flow, therefore, presenting low focality, with peak intensity often not located at  
6 the nominal target, as is usually suggested [21,74,75]. To overcome this limitation,  
7 “High-Definition” tDCS (HD-tDCS) uses arrays of smaller electrodes arranged in  
8 various configurations including the 4x1-ring HD-tDCS montage [74,76–79]. The 4x1  
9 HD-tDCS has shown improved focality compared to conventional tDCS with a gyri  
10 precise stimulation [21,74,78] having a potentially greater magnitude and duration of its  
11 aftereffects [21]. So far, only two studies (9.1%) have tested the effect of HD-tDCS for  
12 performance enhancement, but they found no significant change on the TTE an  
13 isometric contraction of the elbow flexors and knee extensors [80,81]. Moreover,  
14 studies on tDCS for sporting performance are mostly underpowered with a median of 12  
15 (from 6 to 24 participants), which present a reduced chance of detecting a true effect  
16 and increasing the possibility of a false negative. Only five (22.7%) of the included  
17 studies performed a priori sample size estimation or a posteriori achieved power  
18 analysis. Underpowered studies are not specific to this field and have been criticized  
19 broadly in the brain sciences [82].

20       Regarding tDCS mechanisms, the positive charge imposed by a-tDCS is  
21 hypothesized to cause sub-threshold depolarization and c-tDCS hyperpolarization due to  
22 its negative charge. This assumption generated the “classical” polarity-dependent effect  
23 of tDCS (i.e. a-tDCS excite and c-tDCS inhibit), inferring that the effect of tDCS would  
24 be mediated by changes in neuronal excitability. Studies with non-human animals have  
25 shown that tDCS-induced changes in neuronal excitability may result from



1 phosphorylation of  $\alpha$ -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid (AMPA)  
2 receptors and its translocation from the cytosol to the synapse [83]. In humans, the most  
3 common way to assess tDCS-induced changes in neuronal excitability (i.e. corticospinal  
4 excitability) is by using transcranial magnetic stimulation (TMS) to elicit motor-evoked  
5 potential (MEP). Increased MEP amplitude for the same TMS pulse intensity compared  
6 to baseline represent increased excitability and vice-versa. Previous studies using MEP  
7 have reinforced the “classical” polarity-dependent effect of tDCS and suggested that a-  
8 tDCS increases neuronal excitability and c-tDCS causes the opposite effect [14,15].  
9 However, recent studies have shown large inter-individual variability in response to  
10 tDCS [84–86]. For instance, Wiethoff et al. [86] showed that 50% of the participants  
11 had minor or no change in MEP amplitude after 2 mA of either a-tDCS or c-tDCS over  
12 M1. The sub-group who responded to the stimulation, 36% presented the “classical”  
13 polarity-dependent response in cortical excitability (i.e. anode-excite and cathodal-  
14 inhibit), while 21% of participants displayed the inverted “classical” response to tDCS  
15 (i.e. anode-inhibit and cathode-excite), 38% and 5% showed an excitatory and  
16 inhibitory response for both polarities, respectively. The results of these studies have  
17 questioned the “classical” polarity-dependent effect of tDCS as previously stated  
18 [14,15].

19 In the context of exercise, researchers have used tDCS with their hypothesis  
20 based on the “classical” polarity-dependent assumption. However, only one study has  
21 actually found significant performance decrease after c-tDCS with dynamic strength  
22 exercise [65] with the rest of studies showing no change in performance [40,42,43]. In  
23 addition, this meta-analysis showed that c-tDCS had no detrimental effect on cycling  
24 performance, rather showing a non-significant trend toward increasing performance  
25 (MD = 35.20 s; 95% CI = -5.02, 75.43 s;  $p = 0.09$ ; Figure 4C). This result is in-line with

1 a previous experimental investigation by Batsikadze et al. [18] who showed that 2 mA  
2 of c-tDCS for 20 min over M1 increased cortical excitability, instead of decreasing it.  
3 The measurement of MEP, however, is restricted to the motor cortex and measures of  
4 change in excitability by tDCS in other areas are difficult. Recent studies have used  
5 magnetic resonance spectroscopy [87] or electroencephalography [88,89] to assess the  
6 changes in cortico-cortical excitability of non-motor areas. However, only a handful of  
7 studies in the sporting field have directly measured changes in neuronal excitability as  
8 expressed by MEP amplitude [40,41,43,62,66,90]. Therefore, future research needs to  
9 identify that the hypothesized change to the brain area has actually occurred. Ideally, the  
10 effect of the proposed tDCS montages should be tested in terms of change in  
11 excitability before testing its effect on exercise performance. Interestingly, although  
12 studies have confirmed that changes in MEP are associated with performance  
13 improvement [40], others have shown that change in performance may occur without  
14 alterations in MEP [41,62,90]. Thus, multimodal measures of corticospinal, cortico-  
15 cortical, cortico-thalamic and cortico-sub-cortical excitability, depending on the area of  
16 stimulation, are highly recommended to help to clarify whether there is an effect of  
17 tDCS and through which mechanisms it could impact on performance. Monitoring  
18 tDCS neuromodulatory effects can be measured using electroencephalography (EEG) in  
19 conjunction with near-infrared spectroscopy (NIRS) [91]. Simultaneous use of one or  
20 two neuroimaging modalities can reveal bi-directional or uni-directional information  
21 flow patterns between the SMC, PMC and DLPFC brain regions, the three core regions  
22 of the cortical sensorimotor network for movement control. Recently, by combining  
23 fNIRS, EEG and fMRI neuroimaging methods, the effective connectivity of the same  
24 cortico-cortical sensorimotor networks (SMC, PMC, and DLPFC) during different

1 finger movement tasks has been assessed [92]. The dynamics of the significant  
2 connections for the cortical sensorimotor network during tDCS is not well known.

3 A review by Li, Uehara, Hanakawa [85] summarized several factors associated  
4 with the inter-individual variability in response to tDCS, which includes anatomical  
5 variations [93], organization of local circuits, basal level of function, psychological  
6 state, level of neurotransmitters and receptor sensibility, baseline neurophysiological  
7 state, and genetic aspects [94]. Regarding the anatomical variations, there is evidence  
8 that individuals who displayed improvement in behavioral outcomes (i.e. working  
9 memory) presented greater current density at the nominal target of tDCS (i.e.  
10 dorsolateral PFC) as compared to those with no behavioral change [84]. This implies  
11 that tDCS montages should be individualized, aiming at increasing the likelihood of  
12 eliciting performance change [93]. No study, however, has tested the influence of  
13 anatomical variations on the effect of tDCS on motor performance. In addition, studies  
14 have shown that the baseline level of motor function influences the after-effects of  
15 tDCS. So that, individuals with lower baseline level of function show (greater)  
16 improvements after tDCS while those with higher levels of function display lower  
17 improvements or no change in performance [95,96]. However, those studies were  
18 performed with fine motor skills (i.e. playing an instrument), and the effect of tDCS on  
19 individuals with different performance levels in gross motor skills such as running,  
20 cycling, lifting or resisting weights is still to be tested. More widely, the inter-individual  
21 factors that determine responsiveness to tDCS, particularly in exercise, are not fully  
22 understood [86].

23 Regarding tDCS montages, most studies target the M1 (72.5%), with less  
24 attention being directed to other areas such as the dorsolateral PFC (9.1%), left TC

1 (13.6%), and lateral prefrontal cortex (4.5%). As already presented in the introduction,  
2 various brain areas are involved in exercise performance. Briefly, the rationale for  
3 stimulating M1 is aimed at increasing its excitability in order to extend the neural drive  
4 to the active muscles and delay central fatigue or changing exercise-induced pain  
5 processing via the connection between M1, thalamus and insular cortex (IC), thus  
6 increasing performance by decreasing pain sensation. PFC stimulation is aimed at  
7 improving the top-down control over M1 output due to an improved processing of the  
8 physiological and psychological states. TC stimulation, which is performed targeting  
9 the left insular cortex, is aimed at increasing parasympathetic control to postpone its  
10 withdrawal during exercise, which could result in delayed fatigue. Finally, inhibition of  
11 the SMA may reduce perceived exertion, a factor that contributes to task cessation and  
12 reductions in exercise intensity [6,7,28], which has been demonstrated with non-  
13 invasive brain stimulation during a handgrip exercise [39]. However, the  
14 aforementioned study was performed using theta-burst using rTMS, and this result has  
15 not been replicated with tDCS. These examples do not cover all areas related to exercise  
16 performance, and indeed multiple possibilities of different tDCS montages exist. In fact,  
17 it is estimated that when taking into account electrode location, size, number, density,  
18 polarities, and duration, there are between four million to eight trillion possibilities of  
19 tDCS montages (V.P. Clarck; Personal communication at the NIMH-sponsored tES  
20 workshop held on September 29th and 30<sup>th</sup>, 2016). Even if the anodal electrode is  
21 placed at the same anatomical location, variations in the position of the return electrode  
22 may induce changes in the current path, current density concentration and, thus, impact  
23 on the possible effect of tDCS [20]. For instance, a computational modeling study  
24 suggested that the non-cephalic montage (i.e. when the return electrode is not positioned  
25 on the head) showed the highest current density for two different montages under both

1 M1 and dorsolateral PFC, with a current density of 6-9 times greater compared to the  
2 HD-tDCS configuration and 2.5-4.4 times greater compared to the bi-cephalic  
3 configuration (i.e. when both active and return electrode are positioned on the head)  
4 [97].

5         So far, however, only one study in the exercise/sporting field has compared the  
6 bi-cephalic (anodal over left M1 and cathodal over dorsolateral PFC) to the non-cephalic  
7 (anodal over left M1 and cathodal over the shoulder) types of tDCS configuration and  
8 showed that the latter resulted in increased TTE of an isometric contraction of the knee  
9 extensor, while former resulted in no significant change [90]. In addition, the literature is  
10 scarce regarding the comparison of stimulation of different brain areas for the same  
11 outcome. Only a single study performed by Radel et al. [80] compared the effect of tDCS  
12 using HD-tDCS applied over the PFC and M1 on the TTE of an isometric contraction of  
13 the elbow flexors and found no changes in physical performance or perceived exertion.  
14 Therefore, there is still an open field for researchers to compare the efficacy and  
15 efficiency of different electrode montages, current intensity, and forms of application  
16 (e.g. comparison of bi-cephalic and non-cephalic montages to HD-tDCS). Unfortunately,  
17 the results of the present study do not allow us to suggest a specific montage, given that  
18 a meta-analysis was possible only for studies that applied tDCS over M1. In addition,  
19 individual results of the studies present mixed findings for stimulation of the TC  
20 (targeting the insular cortex) and the PFC, which also prevent us from recommending one  
21 of them.

22         The current study presents some limitations concerning individual studies and,  
23 thus, in the meta-analysis itself: (a) a considerably large variation in current intensity  
24 with a coefficient of variation of 105.8%; (b) different placement of the return electrode

1 (e.g. ipsilateral or contralateral shoulder, contralateral forehead or occipital  
2 protuberance); (c) different areas of stimulations (all of these can lead to variations in  
3 the amount of electrical current applied to the nominal target area and, therefore, impact  
4 on the outcomes); (d) lack of measures of reliability of the outcome variable; and (e)  
5 low sample size with mixed physical activity and fitness levels. On the one hand,  
6 existing studies exhibit protocol heterogeneity, while on the other hand, the theoretically  
7 optimal dose of tDCS remains largely unexplored (e.g. current above 2 mA [98]; weeks  
8 of session repetition as might be used in practical training) such that existing dose  
9 protocols should be considered as pilots rather than an optimized protocol.

10

## 11 **CONCLUSION**

12

13 The results of this systematic review and meta-analysis showed that for the  
14 protocols tested, anodal but not cathodal tDCS vs. sham over the motor cortex resulted  
15 in a longer TTE in cycling. However, this result was strongly driven by a single study  
16 and when removed the results were no longer significant. For the protocols tested, no  
17 significant improvement was found comparing a-tDCS vs. sham on isometric muscle  
18 strength of the upper and lower limbs. It was not possible to perform a quantitative  
19 synthesis of isokinetic and dynamic muscle strength performance, as studies are  
20 heterogeneous. In order to test the putative effects of tDCS on sporting performance,  
21 future studies should try to individualize tDCS protocols, such as using computational  
22 modeling with individual MRI data for defining the most efficient electrode placement  
23 (including the reference electrode) for achieving a given target. In addition, optimizing  
24 the timing of the application of tDCS (e.g. before training, during training, before

1 competing), for both acute and repeated days of stimulation, would help assess its  
2 efficacy and safety in relation to use in sport and exercise [99]. An assessment of a  
3 wider range of tDCS intensities, particularly those that go beyond the usual 2 mA,  
4 would also be helpful to identify whether there is a dose-response relationship [98].  
5 Finally, a comparison of different tDCS montages for a given outcome, especially using  
6 newer techniques such as the HD-tDCS, should be explored [21].

7

### 8 **Conflict of interests**

9 CUNY has patents with M Bikson as an inventor. M Bikson is an advisor for and has  
10 equity in Soterix Medical Inc. AR Brunoni has received grants from São Paulo  
11 Research State Foundation and honorarium from Neuroacademy group and Delta  
12 Medical. DGS Machado, SM Andrade, G Unal, A Moreira, LR Altimari, S Perrey, AR  
13 Mauger, and AH Okano declare they have no conflict of interest with regard to the  
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15

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22

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## FIGURE LEGENDS

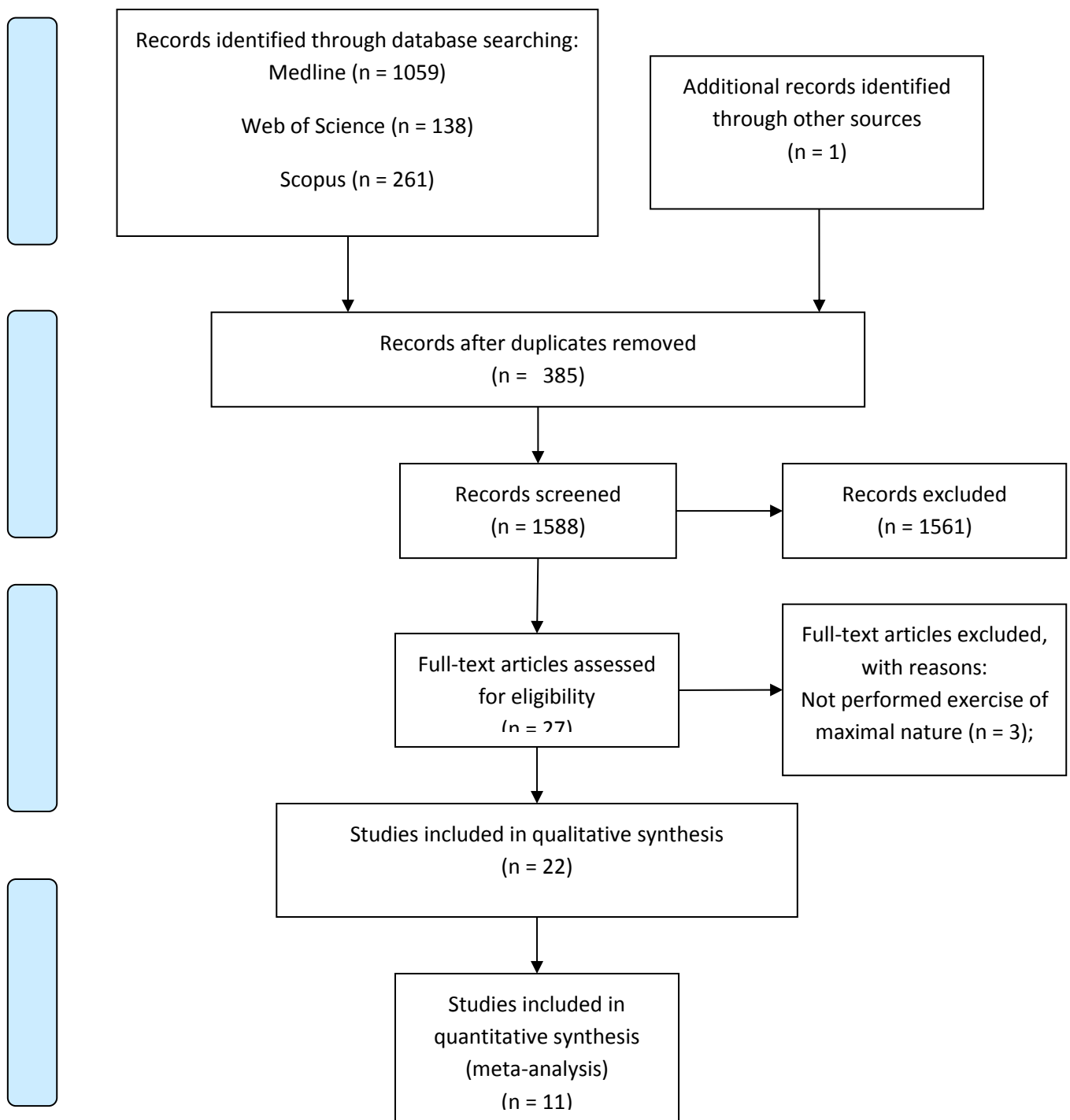
**Figure 1** Study flow diagram.

**Figure 2** Electrode placement, polarity, and size of the studies using transcranial direct current stimulation for performance enhancement in isometric (superior), isokinetic (middle left) and dynamic strength exercise (middle right), and cycling exercise (inferior). In all figures: anode = red; cathode = blue. Rationale for tDCS montages: **primary motor cortex** (M1) stimulation is aimed at increasing M1 excitability to extend its neural drive to the active muscles and delay central fatigue or changing the exercise-induced pain processing via the connection between M1, thalamus and insular cortex (IC) increasing performance by decreased pain sensation; **prefrontal cortex** (PFC) stimulation is aimed at improving the top-down control over motor output due to an improved processing of the physiological and psychological states; **temporal cortex** stimulation is performed targeting the left IC aimed at increasing parasympathetic control to postpone its withdrawal during exercise, which could result postpone fatigue.

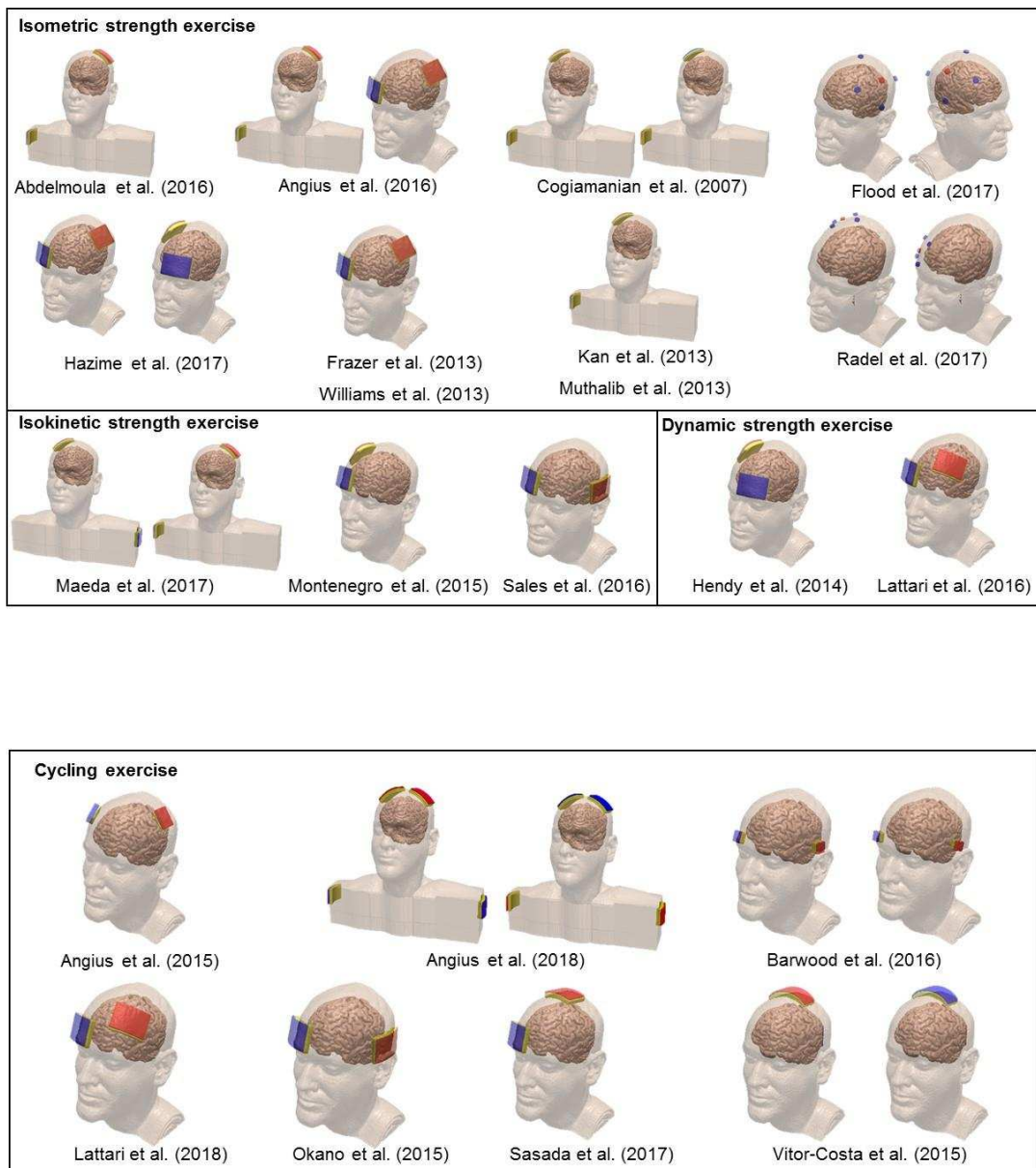
**Figure 3** Forest plot showing mean difference from the comparison between anodal vs. sham (A) and cathodal vs. sham (C) transcranial direct current stimulation applied before exercise in terms of time to exhaustion in whole-body cycling exercise. Note: given that the result of the anodal vs. sham analysis shown in panel A was driven by one single study (Vitor-Costa et al., 2015), it was removed from the analysis and the results were not significant (panel B).

**Figure 4** Forest plot showing mean difference from the comparison between anodal vs. sham transcranial direct current stimulation applied before (A and B) and during (C) exercise in terms of time to exhaustion in isometric strength exercise of the upper (A and C) and lower (B) limbs.

**Figure 5** Risk of bias graph (A): review authors' judgments about each risk of bias item presented as percentages across all included studies; and risk of bias summary (B): review authors' judgments about each risk of bias item for each included study.



**Fig. 1** Study flow diagram.



**Fig 2.**

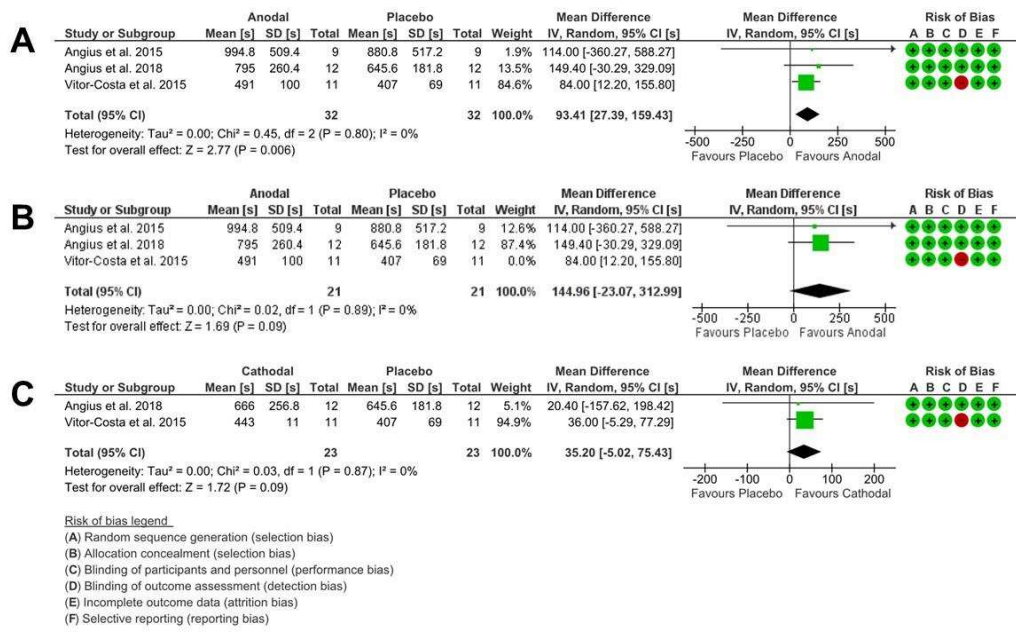


Fig 3.

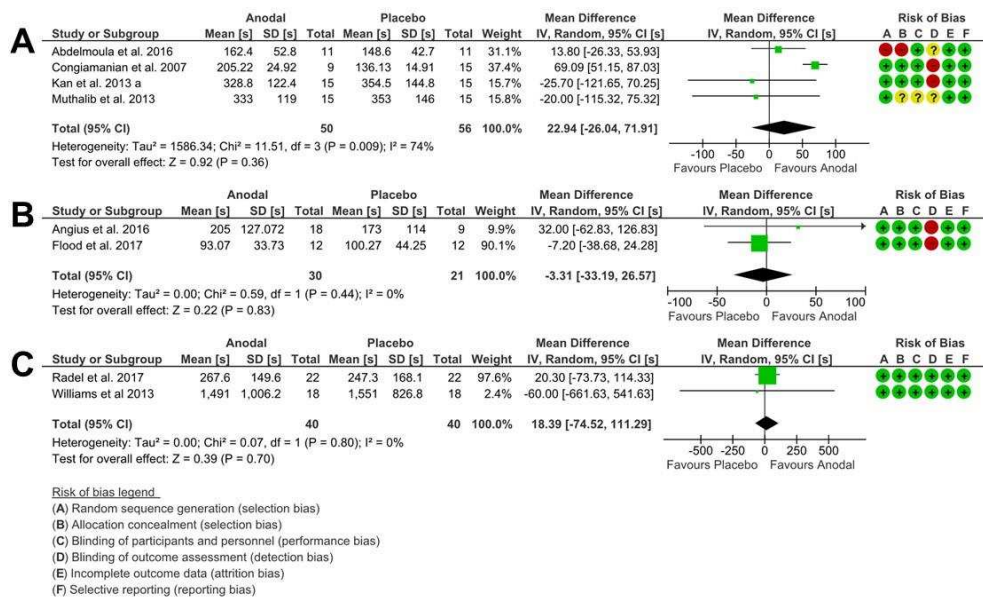
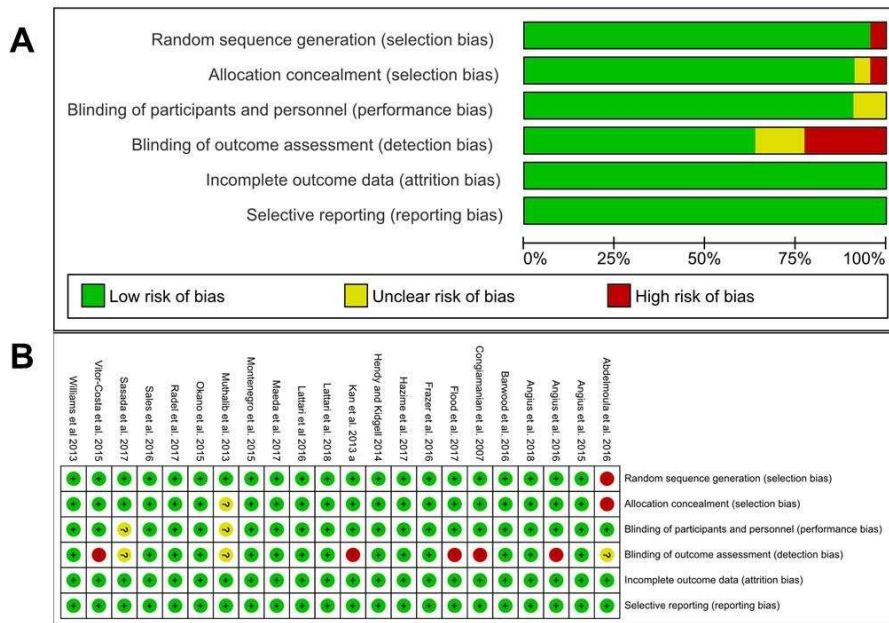


Fig 4.



**Fig 5.**



1 **Table 1** Characteristics of the included studies.

Study information					Sample		tDCS set-up			
Authors	Design	Exp	Exercise type	Exercise Protocol	n (M/W)	Training status	Anode or cathode Return electrode	Intensity (mA)	Density (mA/cm <sup>2</sup> )	Duration (Min)
Abdelmoula et al. [41]	Cross	1	Isometric strength	35% of MIVC of elbow flexion	11 (8M/3W)	N/D	Left M1 Right shoulder	1.5	0.043	10
Cogiamanian et al. [40]	Parallel	1	Isometric strength	35% of MIVC of elbow flexion	24 (10M/14W)	N/D	A Right M1 Right shoulder	1.5	0.043	10
	Parallel	2	Isometric strength	35% of MIVC of elbow flexion	24 (10M/14W)	N/D	C Right M1 Right shoulder	1.5	0.043	10
Kan et al. [45]	Cross	1	Isometric strength	30% of MIVC of elbow flexion	15 (M)	N/D	Right M1/ Right shoulder	2.0	0.083	10
Muthalib et al. [46]	Cross	1	Isometric strength	30% of MIVC of elbow flexion	15 (M)	N/D	Right M1/ Right shoulder	2.0	0.083	10
Radel et al. [80] <sup>a</sup>	Cross	1	Isometric strength	35% of MIVC of elbow flexion	22 (13M/9W)	N/D	A C2 and C 4 cm around (HD-tDCS 4x1)	2.0	N/D	N/D
	Cross	2	Isometric strength	35% of MIVC of elbow flexion	22 (13M/9W)	N/D	HD-tDCS (A) AF4 and (C) 4 cm around	2.0	N/D	N/D
Williams et al. [100] <sup>a</sup>	Cross	1	Isometric strength	20% of MIVC of elbow flexion	18 (9M/9W)	9 active / 9 low active	Right M1 Fp2	1.5	0.043	≤20

2 **Note:** <sup>a</sup> = tDCS applied during exercise; A/C = anode/cathode electrode; Cross = crossover design; Exp = experiment; HD-tDCS = high-definition transcranial direct  
3 current stimulation; M/W = men/women; M1 = primary motor cortex; MIVC = maximal isometric voluntary contraction; N/D = not described; tDCS = transcranial  
4 direct current stimulation

**Table 1** Characteristics of the included studies (*continuation...*)

Study information					Sample		tDCS set-up			
Authors	Design	Exp	Exercise type	Exercise Protocol	n (M/W)	Training status	Anode/Cathode Return electrode	Intensity (mA)	Density (mA/cm <sup>2</sup> )	Duration (Min)
Angius et al. [90]	Cross	1	Isometric strength	20% MIVC of knee extension	9 M	Recreationally active	A Left M1/Fp2	2.0	0.17	10
	Cross	2	Isometric strength	20% MIVC of knee extension	9 M	Recreationally active	A Left M1 Shoulder	2.0	0.17	10
Flood et al. [81]	Cross	1	Isometric strength	30% MIVC of knee extension	12 (M)	Recreationally active	C3/C4 and 5 cm around (HD-tDCS 4x1)	2.0	0.057	20
Hazime et al. [61]	Cross	1	MIVC	Shoulder internal/external rotators	8 (W)	Handball athletes	C3/C4 Fp2/Fp1	2.0	0.057	20
Frazer et al. [62] <sup>b</sup>	Cross	1	MIVC	Wrist flexors	14 (6M/8W)	N/D	Left C3 Fp2	2.0	0.08	20
Maeda et al. [58] <sup>a</sup>	Parallel	1	Isokinetic strength	5 reps of eccentric knee extension/flexion	24 (12M/12W)	N/D	M1 Shoulder	2.0	0.08	10
Montenegro et al. [63]	Cross	1	Isokinetic strength	10 reps of knee extension/flexion	14 (M)	Trained in RT (≥6 months)	Left M1 Fp2	2.0	0.057	20
Sales et al. [64]	Cross	1	Isokinetic strength	5 reps of knee extension	19 (M)	Physically active	T3 Fp2	2.0	0.057	20
Hendy et al. [66] <sup>a</sup>	Cross	1	Dynamic strength	1RM wrist extension	10 (5M/5W)	N/D	Right M1 Fp1	2.0	0.08	20
Lattari et al. [65]	Cross	1	Dynamic strength	10RM elbow flexion	10 (M)	Trained in RT (≥6 months)	F3 Fp2	2.0	0.057	20

**Note:** <sup>a</sup> = tDCS applied during exercise; <sup>b</sup> = multiple tDCS sessions; A/C = anode/cathode electrode; Cross = crossover design; Exp = experiment; HD-tDCS = high-definition transcranial direct current stimulation; M/W = men/women; M1 = primary motor cortex; MIVC = maximal isometric voluntary contraction; N/D = not described; RM = repetition maximum; RT = resistance training; tDCS = transcranial direct current stimulation.

**Table 1** Characteristics of the included studies (*continuation...*)

Study information					Sample		tDCS set-up			
Authors	Design	Exp	Exercise type	Exercise Protocol	n (M/W)	Training status	Anode/Cathode Return electrode	Intensity (mA)	Density (mA/cm <sup>2</sup> )	Duration (Min)
Angius et al. [43]	Cross	1	Cycling	TTE at 70% PP	12 (8M/4W)	Recreationally active	A both M1/shoulders	2.0	0.057	10
	Cross	2	Cycling	TTE at 70% PP	12 (8M/4W)	Recreationally active	C both M1/shoulders	2.0	0.057	10
Angius et al. [47]	Cross	1	Cycling	TTE at 70% PP	9 (M)	Recreationally active	Right M1/F4	2.0	0.17	10
Barwood et al. [44]	Cross	1	Cycling	20km time trial	6 (M)	Physically active	T3/Fp2	1.5	0.43	20
	Cross	2	Cycling	TTE at 75% PP	8 (M)	Physically active	T3/Fp2	2.0	0.44	20
Lattari et al. [59]	Cross	1	Cycling	TTE at 100% PP	11 (W)	Moderately active	F3/Fp2	2.0	0.057	20
Okano et al. [35]	Cross	1	Cycling	Incremental maximum	10 (M)	Athletes (cyclists)	T3/Fp2	2.0	0.057	20
Sasada et al. [60]	Cross	1	Cycling	Wingate test	23 (17M/6W)	Athletes (various)	Cz/Fp2	2.0	0.057	15
Vitor-Costa et al. [42]	Cross	1	Cycling	TTE at 80% PP	11 (M)	Physically active	A both M1/ Inion	2.0	0.056	13
	Cross	2	Cycling	TTE at 80% PP	11 (M)	Physically active	C both M1/ Inion	2.0	0.056	13

**Note:** A/C = anode/cathode electrode; Cross = crossover design; Exp = experiment; M/W = men/women; M1 = primary motor cortex; PP = peak power; tDCS = transcranial direct current stimulation; TTE = time to exhaustion.

